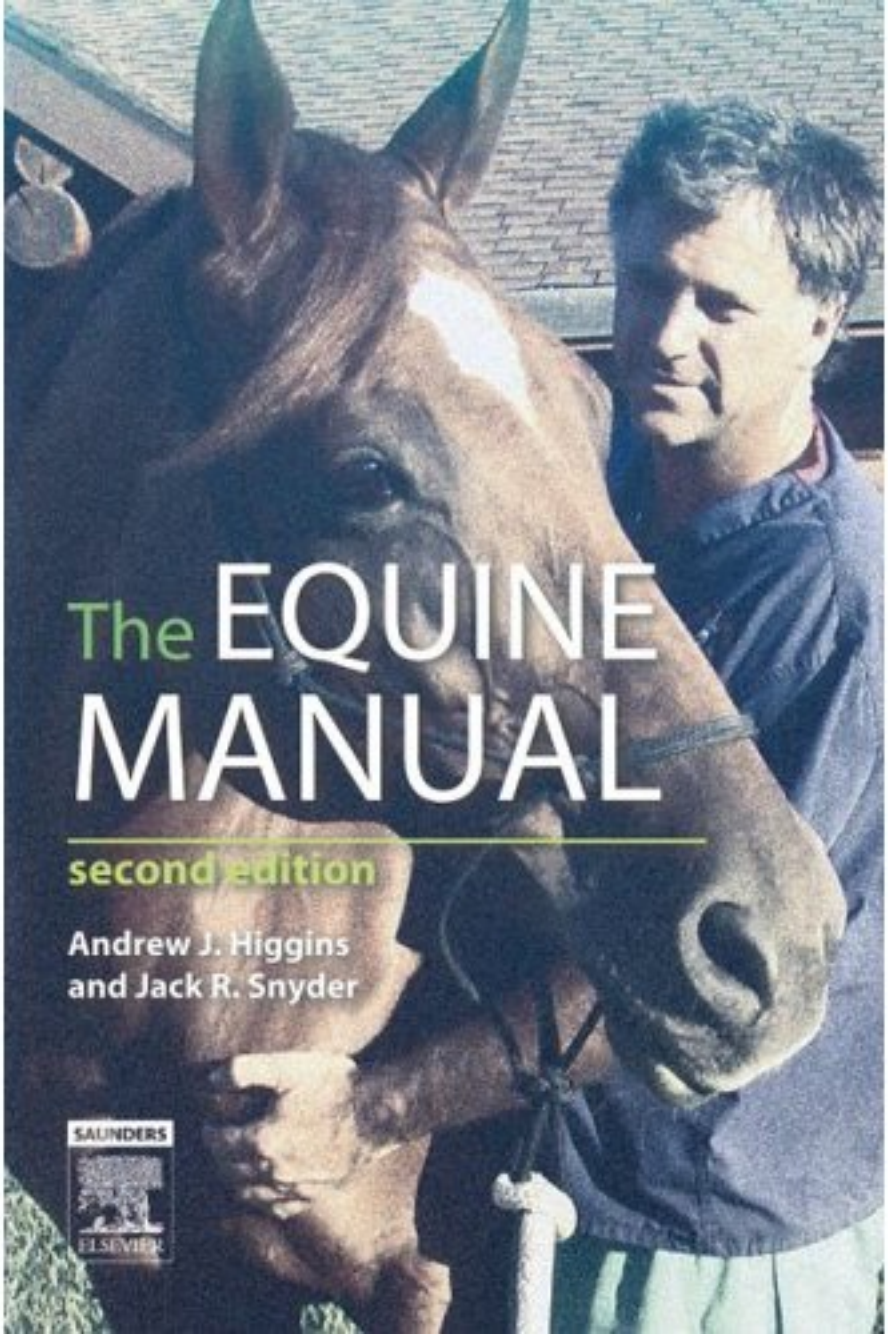
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second edition
Andrew J. Higgins
and Jack R. Snyder
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Note

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Introduction

It is a formidable undertaking to produce a book that aims to serve as a ready reference for equine practitioners while at the same time providing sufficient detail for it to be comprehensive without becoming a turgid reference book. The first edition of *The Equine Manual* appeared in 1995 and proved to be popular with clinicians, students and others who spend much of their lives working with horses. The publishers of that edition, W.B. Saunders Company, are now part of Elsevier, who decided that the time had come for an updated and revised second edition. This is it.

We have increased the size of the book to accommodate additional chapters that we felt were missing from the first edition. This time there are chapters devoted to anesthesia, pre-purchase examination, and intensive care medicine. There are sections on wound care, skin grafts and euthanasia; on new techniques ranging from contact lenses to blood and plasma therapy, and DNA technology. There is even a glossary of immunologic terms for those who may feel a little compromised in that area. All chapters have been updated and modified, and many completely revised. The Consultant Editors are world authorities in their fields and have attracted some impressive teams of co-authors with a wealth of applied clinical experience.

The editors took the view that indexing and cross-referencing were critical in a book of this nature. We have tried therefore to provide key words, which are shown in bold type, and a comprehensive, detailed index. A systems approach has been adopted in the 23 chapters, and an indication of contents is listed at the start of each. We have deliberately omitted all but a very few literature references as we feel there are other sources of information readily available for the research worker or the clinician who needs greater detail. A list of abbreviations can be found at the back of the book.

We want to acknowledge the amazing commitment and dedication of our Consultant Editors. They have worked with determination and perseverance, and the flow across continents of emails with attachments relating to this book has been impressive. Each deadline was met and the editors can only express their admiration and gratitude to all authors for achieving what often seemed like impossible targets. The participation of so many authors means, of course, that there will be some variation in style and emphasis, and some duplication, but we have endeavored to reduce distractions to a minimum.

Our focus has been to provide an easy reference for the veterinarian at the farm gate, for the clinician preparing for rounds or wishing to check back on the day, for the veterinary or equine studies undergraduate who needs ready access to relevant and topical information, and for technicians, farriers, nutritionalists, behavioralists, dentists, nurses and other specialized paraprofessionals who want knowledge and facts about the diagnosis, treatment, prevention and control of diseases and disorders in equines. In fact, it is a book for anyone wanting to know more about the health of the horse.

Reference is made in the book to specific agents, drugs and vaccines which could be used in the treatment or prevention of a particular condition. Mention of any agent in this manual does not, of course, imply endorsement of the product, and no guarantee can be given regarding any recommendations made by any contributor. As always, the clinical judgment of the attending veterinarian remains paramount.

We welcome your comments, criticisms and suggestions for changes in the hope that these will help us to improve future editions.

Newmarket and Davis, 2006 *Andrew Higgins and Jack Snyder*

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Chapter 1

Infectious diseases

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Chapter contents

INTRODUCTION

During the last decade the increase in the international movement of horses and trade in semen has contributed significantly to the spread of equine

infectious diseases. While trade is the main reason for international travel, extensive temporary movement of horses takes place for competition and breeding purposes. Influenza, equine herpesvirus, strangles, equine arteritis virus, contagious equine metritis, piroplasmosis and Venezuelan encephalitis virus are among the infectious agents that have been spread as a result of international movement. In certain instances, mandatory testing prior to importation has been abolished in order to facilitate trade, and in others horses and semen have been incorrectly certified as disease free.

Veterinarians should inform their clients of the risks and advise them to test imported horses before mixing them with their own stock. It is not known how **West Nile virus (WNV)** (*q.v.*) was introduced into the United States in 1999 but this virus has now become endemic in the Western hemisphere. In 2002 over 14 000 equine cases were reported with a fatality rate of around 30%. The problem was considered of sufficient magnitude to warrant the production of a vaccine, and mass vaccination of horses in the USA has been undertaken.

Vaccination is one of the most cost effective methods of controlling many infectious diseases. Novel technologies offer opportunities for improving existing vaccines particularly where there are genuine reasons for concern about safety and/or efficacy. Recombinant vaccines are particularly attractive to manufacturers when handling viruses that are human pathogens such as the alphaviruses **eastern encephalitis virus (EEV), western encephalitis virus (WEV)** and **Venezuelan encephalitis virus (VEV)** (*q.v.*) and the flaviviruses **Japanese encephalitis virus (JEV)** and **WNV** (*q.v.*).

Recombinants allow vaccine production under low biocontainment conditions as there is no requirement for large-scale production of a dangerous pathogen. Canarypox virus vector vaccines have recently been licensed for WNV and equine influenza. Such recombinants express the inserted foreign gene(s) in the absence of productive viral replication. A live temperature sensitive **intranasal vaccine** against **equine influenza** is now available in North America and like the live recombinant canarypox virus vaccine it provides partial clinical protection in the absence of high levels of serum antibody. This suggests that both vaccines are inducing protective cellular immune responses (*q.v.*) or priming the immune system so that an effective anamnestic response is rapidly induced on exposure to natural challenge.

Traditionally it has been possible to predict the level of protection that the influenza vaccination has induced by measuring the horse's levels of antibody against the hemagglutinin. These new vaccines present a challenge to virologists who now need to determine other correlates of protection and develop reproducible methods of quantifying them. Clinicians need not only to inform and advise their clients about alternatives to classical vaccines but also to evaluate them carefully in the field. Second generation vaccines are often more expensive than conventional products. Some products fail to fulfill expectations and their performance in the field does not always reflect the results of experimental challenge studies.

New developments that have the potential significantly to improve the control of certain diseases include a live temperature sensitive **equine herpesvirus 1** (*q.v.*) **vaccine**, which protects against respiratory infection and viremia, and a gene-deleted live vaccine for **equine arteritis virus** (*q.v.*), which allows serologic discrimination between vaccinated and infected horses. The advent

of reverse genetics should facilitate the development of **live attenuated equine influenza vaccines** that can be easily updated as new strains of virus emerge.

The correct treatment and management of a disease depends on an accurate, specific diagnosis. Conditions that are clinically indistinguishable nevertheless frequently necessitate different therapy and management procedures. The latter are particularly important in the case of viral disease. Although there are **no antiviral drugs** available at present for administration to horses it is important to identify which virus is involved in a disease outbreak. In the case of a training yard experiencing an outbreak of viral respiratory disease, where the aim is to minimize the sequelae and loss of training days, far more stringent management procedures are required if the causal agent is equine herpesvirus 1 than if it is equine rhinitis virus.

The ongoing incorporation of the **polymerase chain reaction (PCR)** as a routine test in diagnostic laboratories is of major benefit to clinicians in the prompt treatment and management of disease. PCR is a method of amplifying the amount of nucleic acid in a sample. Over a million copies of a specific target DNA sequence can be synthesized in a few hours. Thus viruses and bacteria that can take days or even weeks to propagate in the laboratory can be detected using PCR within 24 h. PCR is an invaluable diagnostic tool. However, it detects the target DNA independently of whether the infectious agent is active, latent or dead and the significance of positive results occasionally needs careful consideration. Furthermore, this sensitive technique carries with it a risk of **false positive** results due to contamination at the time of collection or in a laboratory. It is important that clinicians adopt the correct procedures when collecting samples and submit their material to a reputable laboratory in order to ensure the reliability of the results.

The use of antimicrobials and anthelmintics has increased significantly in veterinary practice. These products need to be used in a responsible manner to ensure their continuing effectiveness. **Multi drug resistance** among *Salmonella* and *Pseudomonas* spp. (*q.v.*) isolated from horses has been documented. Methicillin resistant *Staphylococcus aureus* (MRSA) is a major threat to human patients in hospitals and has been isolated from both horses and personnel in equine hospitals. Many national veterinary associations have now drawn up codes of practice for the judicious use of antimicrobials. It is important that clinicians comply with these codes.

The emergence of **anthelmintic resistance** (*q.v.*) is seriously jeopardizing parasite control in many parts of the world. Clinicians need to inform their clients that increasing anthelmintic treatment can lead to the development of resistance and to educate them in management procedures that reduce selection pressure. They also need to monitor resistance and report treatment failure to the product manufacturers and to their national collating centers. Failure to highlight resistance will result in complacency and a failure to invest in the development of new products.

In recent times there has been a huge increase not just in the international movement of horses but also of veterinarians who travel all over the world to work in practices and hospitals and to manage stud farms and racing establishments. Thus, veterinarians need to be familiar with the clinical signs and methods of diagnosis of diseases that occur in different parts of the world, for

example African horse sickness, Japanese encephalitis, glanders, rabies, vesicular stomatitis, babesiosis, trypanosomosis, anthrax and Potomac horse fever (*q.v.*). Veterinarians also need to know which diseases are **notifiable** in the country in which they are practicing and to be familiar with voluntary "Codes of Practice" such as exist for the control of several bacterial and viral diseases in the United Kingdom, Ireland, Italy, Germany and France (*q.v.*).

The recent emergence of **WNV** (*q.v.*) as a significant pathogen of horses and humans in the Western hemisphere illustrates the need for ongoing cooperation between the veterinary profession, the medical profession and colleagues in Public Health. Australia's exotic disease preparedness was put to the test with the emergence of **Hendra virus** (*q.v.*) in 1994, a disease previously unknown anywhere in the world. Veterinarians, doctors and scientists worked together to control the outbreak, allay public fears, develop rapid diagnostic tests and determine the method of virus spread. We are all at risk from the introduction of exotic diseases and from the emergence of new pathogens. Technological advancements increase our capability each year but the control of infectious disease continues to be a major challenge.

VIRAL DISEASES

EQUINE HERPESVIRUSES

Equine herpesviruses are endemic in horse populations worldwide. Equine herpesvirus abortions result in significant financial loss to horse breeders each year and herpesvirus respiratory disease is a major cause of loss of performance in racehorses and in competition horses.

Etiology

Herpesviruses are enveloped DNA viruses. There are five equine herpesviruses. **Equine herpesvirus 1 (EHV-1)** is associated with respiratory disease, abortion and a neurologic syndrome. **Equine herpesvirus 3 (EHV-3)** causes coital exanthema and **equine herpesvirus 4 (EHV-4)**, formerly known as EHV-1 subtype 2, is a respiratory pathogen that has occasionally been associated with abortion. Neither equine herpesvirus 2 (EHV-2) nor equine herpesvirus 5 (EHV-5) has been conclusively implicated in a disease syndrome.

EHV-1 and EHV-4 are more closely related to each other than either is to EHV-2 or EHV-3. They can be differentiated by DNA restriction endonuclease analysis and PCR using type specific primers, or immunofluorescence using specific monoclonal antibodies.

The nucleotide sequence of the entire EHV-4 genome has been determined, as have the sequences of the genomes of two different isolates of EHV-1, one associated with abortion and the second with neurologic disease. It is hoped that the availability of these sequence data will facilitate the identification of virulence markers.

Epidemiology

Serologic studies indicate that infection with EHV-1 and EHV-4 is **universally common** and that most horses are exposed to these viruses early in life.

EHV-4 is more commonly associated with respiratory disease than EHV-1. It is also associated with sporadic abortion but very rarely with neurologic disease.

EHV-4 respiratory disease is endemic in horse populations worldwide. Although the immune response elicited by respiratory EHV-4 infection is not very durable, repeated exposure does lead to a gradual build-up of immunity. Clinical disease is most prevalent in **young stock**.

The rate of virus spread varies with the age of the horses, the type of husbandry and the training regimen. The spread of the disease in a group of **yearlings** in a barn can be rapid (within a week) with a morbidity rate of up to 100%. In older horses, virus spread is slower. It is not unusual for EHV-4 to circulate in a training yard for several months with a few different horses becoming infected each week. Infection in **older horses** is often subclinical but can result in a loss of performance.

EHV-1 is more virulent than EHV-4, and respiratory disease caused by EHV-1 is usually more severe. EHV-1 spreads more rapidly, the morbidity rate is higher and infection can result in neurologic disorders.

Both **sporadic and multiple abortions** due to EHV-1 infection occur each stud season in countries where horse breeding is an important industry. It is widely accepted that abortion is usually **preceded by a respiratory infection** that is often subclinical or so mild that it is not readily observed by handlers. Mares in **mixed yards** are most at risk as horses or ponies can be exposed to the virus at race meetings, shows, hunts or sales and serve as a source of infection for brood mares.

The average incubation period is 3 wk but it has been shown to vary between 9 days and 4 mo. However, it is not feasible to place an upper limit on the incubation period as EHV-1, like all herpesviruses, has the ability to establish a **latent infection** and to reactivate at any stage during the host's lifetime. Abattoir surveys suggest that the majority of adult horses are latently infected. **Stress factors** such as transport over long distances or illness may induce a reactivation of latent virus and precipitate abortion.

Although abortion due to EHV-1 infection usually occurs during the last third of pregnancy, it has been recorded as early as 4 mo and a foal may be carried to term and **born alive but infected**.

Fetuses aborted as a result of EHV-1 infection are **heavily contaminated** with virus and serve as a source of infection to other horses that come in contact with them. Thus, **multiple abortions** often follow the abortion of a fetus in a field where several pregnant mares are grazing. Up to 100% of mares exposed to virus on a stud farm may abort but the morbidity rate is usually lower.

EHV-1 abortion appears to stimulate a durable protective immune response and it is unusual for a mare to abort more than once following exposure to EHV-1.

Abortions due to EHV-4 infection are uncommon and usually sporadic in nature.

EHV-1 neurologic disease is uncommon but since it was first recognized in 1966 it has been recorded in all parts of the world where large numbers of horses are maintained. A few cases occur annually in many countries. The disease has occurred in association with respiratory disease and/or abortion in

competition yards, in training yards and on stud farms. Outbreaks have been recorded on stud farms with no concurrent cases of EHV-1 abortion.

Horses of all ages and both sexes can be affected but **recently foaled mares** seem to be most susceptible. Morbidity may be as high as 100% in some groups of horses. The disease can be **fatal** and severely affected cases necessitate euthanasia. **Direct contact** seems to be necessary for transmission of virus. Affected horses may remain viremic for extended periods and in some outbreaks new cases arise over several months.

EHV-4 has only rarely been isolated from cases of neurologic disease and its role in the etiology of the disease needs to be elucidated.

Outbreaks of **coital exanthema** caused by infection with **EHV-3** are frequently observed during the breeding season. Transmission is primarily by the **venereal** route. Clinically, stallions are less severely affected than mares but many show a **reactivation of latent virus** each season and infect the mares they cover. Lesions are sometimes observed on the mammary glands of mares and the muzzles of foals.

EHV-2 is endemic worldwide and is commonly isolated from **healthy** horses. Sick foals shed large quantities of EHV-2 and the virus has been associated with **keratoconjunctivitis** (*q.v.*).

Clinical signs

Respiratory disease

Respiratory disease caused by EHV-1 and EHV-4 is characterized by a transient elevation of temperature to 38.9–40.0°C, inappetance, nasal discharge, pharyngitis, depression and sometimes limb edema. Affected horses usually give a few coughs but coughing is not a major feature of uncomplicated EHV respiratory disease. There may be slight enlargement of the mandibular and retropharyngeal lymph nodes. Horses frequently suffer from **secondary bacterial infections**, which prolong the recovery time.

Abortion

Abortion usually occurs without any premonitory signs and **the placenta is not retained**. The mare's subsequent **fertility is unimpaired**.

Foals that are infected in utero but survive to full term are usually abnormal from birth and show signs of acute respiratory distress. Their mucous membranes are often jaundiced. They usually die before 2 wk of age.

Neurologic syndrome

Neurologic signs usually occur 7–10 days after an episode of respiratory disease. At the time when the nervous signs are evident, the horse usually shows no signs of respiratory disease and its body temperature and appetite are normal. Nervous signs vary from **mild ataxia** followed by complete recovery to **fatal paralysis**. Early signs may include stiffness, posterior incoordination and urinary incontinence. Uveitis, hypopyon, subcutaneous edema of the hindlimbs, colic, diarrhea, and scrotal edema and prolapse of the penis (*q.v.*) are sometimes encountered. These may be followed by sternal and then lateral recumbency, dyspnea, convulsions and death. Sudden death with no prior clinical signs has been recorded.

Pulmonary vasculotropic form

Several cases of **generalized peracute EHV-1 disease** have been reported in young adult horses. Neurologic signs are absent and the main clinical sign is respiratory distress. There is a high mortality rate and affected horses may be found dead.

Coital exanthema

Coital exanthema is manifested by **vesicles** that become pustular and ulcerate. Scabs develop which persist for 2–3 wk and may leave white scars. Mares develop **lesions on the vulva**, on the vaginal mucosa and on the perineal skin around the anus. In severe cases the lesions may extend to the hindquarters and hindlimbs. The mare may experience extreme **irritation on urinating**.

Stallions tend to be less susceptible than mares but lesions may occur on the prepuce and penis resulting in an **unwillingness to cover**. The lesions usually heal within 2 wk.

Pathogenesis

Abortion

Our current understanding of the mechanism by which a virus is transported to the fetus is that EHV-1 **infected peripheral blood mononuclear cells**, predominantly monocytes and T lymphocytes, carry virus to sites of replication such as the endothelium of endometrial blood vessels. Studies using PCR indicate that the virus establishes a **latent infection** in leukocytes but the factors involved in **reactivation** of virus and the activation of endothelial cells to facilitate the adhesion of their surface receptors to infected leukocytes need to be elucidated.

It appears that fetal infection is not a prerequisite for EHV-1 induced abortion and a severe infection of the endometrium can result in **extensive thrombosis** and ischemic infarction (*q.v.*) which in turn lead to premature placental separation and abortion of a **virologically negative fetus**. However, this appears to be relatively uncommon and in most cases the virus is transferred across the uteroplacental barrier, the fetal viscera are infected and a fetus with characteristic necrotic lesions and significant virus load is expelled. It has been suggested that it is the **endotheliotropism** of the virus strain that determines the degree of thrombosis and thus the outcome of virus challenge. However, not all abortigenic isolates are endotheliotropic and it is likely that the outcome of infection is also influenced by host factors.

Neurologic disease

Outbreaks of EHV-1 paralysis are much more uncommon than outbreaks of respiratory disease or abortion and the factors which predispose to their occurrence have not been identified. The occurrence of large abortion storms without concurrent neurologic signs militates against the size of the virus challenge being the predominant factor.

EHV-1 differs from several other herpesviruses in that it does not appear to be primarily neurotropic. The severity of the clinical signs can be correlated to the degeneration of neural tissue but this degeneration is due to **hypoxia** initiated by **vasculitis**. Damage to vessel walls leads to a flow of plasma proteins into perivascular sites impeding the exchange of blood and tissue metabolites

in adjacent areas. In the central nervous system (CNS) this results in **malacia** (*q.v.*). It has been suggested that the condition may be the result of an immunologic process and that inflammatory changes in the CNS may be a reaction to virus antigen and antibody complexes.

Post mortem findings

Abortion

The most consistent lesions in aborted fetuses and foals that die soon after birth are severe pulmonary edema, petechiation of the mucous membranes, excessive fluid in the pleural and peritoneal cavities, jaundice, splenomegaly and areas of focal necrosis in the liver.

Microscopically, the lesions are bronchiolitis, pneumonitis and necrosis of the spleen and liver. **Acidophilic intranuclear inclusion bodies** are found in the affected tissues and the presence of EHV antigen may be detected by immunohistochemical methods such as immunofluorescence and immunoperoxidase.

Fetuses aborted prior to the sixth month of gestation are often severely autolyzed. In such cases the classic lesions of EHV-1 abortion may not be present but the intranuclear inclusion bodies will be observed on histologic examination.

Neurologic disease

Gross pathologic findings in horses with the neurologic syndrome are often minimal. There is usually congestion of the mucous membranes and petechial, ecchymotic and hemorrhagic changes are often widespread. Hemorrhage around the spinal nerve roots is a common finding. Foci of malacia in the brain and spinal cord may be visible macroscopically. Intussusception (*q.v.*) has been observed in foals.

The predominant histopathologic changes are **vasculitis** and **degeneration of nervous tissue**. A non-suppurative inflammation of the blood vessels is accompanied by thrombosis and hemorrhage and exudation of plasma into the perivascular tissues. The arteries and arterioles of the CNS are principally affected but vasculitis is sometimes evident elsewhere in the body, for example in the endometrium of pregnant mares, uvea and lungs. Veins are affected less frequently but sometimes more severely.

Axons in the brain and spinal cord are often swollen and dystrophic. Foci of malacia in both gray and white matter, gliosis and neuronal degeneration are the most consistent findings in the CNS.

Pulmonary vasculotropic form

This form of EHV-1 disease is characterized by vasculitis, hemorrhage and edema in the lungs.

Diagnosis

Respiratory disease

Upper respiratory tract infection caused by EHV must be differentiated from equine rhinovirus, equine influenza virus, equine arteritis virus, bacterial infections and allergic rhinitis (*q.v.*).

Serologic diagnosis can be made on the basis of a significant rise (4-fold or greater) in antibody titer, which requires the collection of blood samples during the **acute stage** of the disease and 10–14 days later. The majority of diagnostic laboratories routinely use the complement fixation test (CFT) for the measurement of EHV antibodies. CF antibodies against EHV-1 and EHV-4 tend to reach a peak 10–14 days post infection and usually decline to their original level within 3 mo. Serum neutralizing (SN) antibody titers persist for longer than CF antibodies and are a less reliable indicator of recent exposure.

Because of close antigenic relatedness, infections with EHV-1 and EHV-4 are difficult to differentiate on the basis of serology. A **type specific enzyme-linked immunosorbent assay (ELISA)** has been used extensively in epidemiologic surveys but it is not quantitative and has not replaced more conventional techniques in the majority of diagnostic laboratories.

Equine herpesviruses are isolated in tissue culture. EHV-1 will grow on a variety of commercially available cell lines such as rabbit kidney cells (RK13) but EHV-4 is more fastidious and with a few exceptions tends to grow only on cells of equine origin. Virus isolates can be typed by immunofluorescence with specific monoclonal antibodies or by PCR. PCR can also be used for **rapid virus detection** in diagnostic samples and in some laboratories has been shown to be more sensitive than virus isolation. Some caution must be exercised in the interpretation of positive PCR results for blood samples as **leukocytes are a site of latency** for EHV-1 and EHV-4. The isolation of EHV-1 or EHV-4 from a **nasal swab** depends on the amount of virus the horse is shedding at the time of sampling. Although virus isolation is sometimes achieved within 24 h, it can take 2 wk or more. PCR can yield a result in less than a day.

Abortion

Diagnosis of EHV abortion is routinely based on **post mortem examination** of the fetus and on virus isolation. Samples of liver, lung, spleen, adrenal, thymus and kidney from **every** aborted fetus should be submitted to a **virus isolation laboratory** for routine screening for EHV. This also applies to the remainder of any fetus that has been partially eaten by predators as the virus can survive for several weeks in a moist environment.

A fetus aborted as a result of EHV infection is usually heavily contaminated with virus. Thus, EHV-1 can often be isolated from positive cases and typed within 48 h. EHV-4 tends to grow more slowly than EHV-1 in tissue culture. Most laboratories passage fetal tissue for at least 1 wk in tissue culture before they declare them negative. PCR is type specific and can be used to detect virus within 24 h of receipt of tissue samples.

The recent finding that naturally infected mares can abort **virologically negative fetuses** poses a problem for both pathologists and virologists and indicates the importance of **placental examination**.

It is not possible to diagnose EHV abortion by serologic examination. Some mares do not have a significant antibody titer at the time they abort. Alternatively, a mare may have a significant antibody titer due to exposure to virus by vaccination or by a natural infection that did not induce abortion.

EHV infection in neonatal foals can be confirmed by the isolation of virus from a nasal swab or heparinized blood. Serologic examination is not a suitable means of diagnosis.

Neurologic disease

As the nervous signs do not manifest for about 10 days post infection, the majority of horses suffering from EHV neurologic disease have high antibody titers against the virus. Thus, the examination of a **single serum sample** is often a useful diagnostic aid. Some mares are slow to seroconvert and examination of paired sera is necessary in a minority of cases.

In the case of an outbreak of the neurologic form of the disease, it is usually possible to isolate EHV-1 from the nasal secretions and leukocytes of some of the affected horses. **Heparinized blood samples** (a minimum of 20 mL per horse) are particularly useful as many horses experience prolonged viremia.

If horses die or are euthanased, a diagnosis can be made by **pathologic investigation**. EHV-1 antigen may be detected using immunoperoxidase or immunofluorescence techniques and virus can be isolated from the brain or spinal cord.

Coital exanthema

EHV-3 can be isolated from swabs of the ulcerative lesions. The virus usually only grows in cells of equine origin.

Antibodies against EHV-3 can be measured by complement fixation or serum neutralization. Most affected horses have significant antibody titers against the virus.

Management and control

Respiratory disease

Both killed and live attenuated EHV-1 vaccines were widely used for many years to protect horses against equine herpesvirus respiratory disease, but their use met with only limited success. More recently, **vaccines** containing **both EHV-1 and EHV-4** (e.g. Duvaxyn EHV 1,4 [Fort Dodge Animal Health] and Resequin [Intervet], available in Europe, and Prestige [Intervet] and Equi Guard [Boehringer Ingelheim] available in the USA) have been introduced and although they reduce virus shedding, they **do not necessarily offer complete protection** against clinical disease. However, regular use of such vaccines at strategic times in a training program (such as prior to or when there is a break in intensive training periods and attendance at race meetings) appears to lessen the effects of virus challenge and decrease the recovery time.

The **serologic monitoring** of horses on a regular basis serves as a useful aid to the early detection of EHV in a yard. If EHV is detected, it is of the **utmost importance** to have the virus type determined in a **specialist laboratory** by PCR or other reliable method.

It is rarely practical or advisable to close a yard with an EHV-4 problem, but it is usually possible to control the disease by **careful monitoring** of all the horses and identification and isolation of those that are affected. Horses with clinical respiratory disease and those that show signs of depression or inappetance should be **isolated** from healthy horses and adequately **rested** before a gradual return to full work. The use of antibiotics, mucolytics and bronchodilators may be indicated in horses with **secondary bacterial infection**.

Return to work too soon may result in **chronic respiratory problems** or the **reactivation and shedding** of latent virus. Because the virus usually spreads

quite slowly in a group of horses it is not unusual for some horses from an infected yard to continue to perform well. However, care must be taken not to over-stress subclinically infected animals. Serologic testing will help to identify these horses.

EHV-1 respiratory disease constitutes a greater threat to a training yard than EHV-4. Because of the abortigenic potential of the virus, no horse should be allowed to move from an infected yard to one that contains brood mares. When deciding whether or not to close the yard it should be remembered that EHV-1 can cause **paralysis** and that there is some evidence to suggest that stressing animals that are incubating the virus may precipitate this condition.

Abortion

A combination of good management and vaccination helps to reduce the threat of EHV abortion. The regular use of a **vaccine of proven efficacy**, preferably containing both EHV-1 and EHV-4 (e.g. Duvaxyn EHV 1,4 [Fort Dodge]), during each gestation period is recommended. There are many vaccines on the market but only one product, Duvaxyn EHV 1,4, is currently licensed in the EU for use in the prevention of EHV-1 associated abortions. Similarly, only Pneumabort K + 1B (Fort Dodge) and Prodigy (Intervet) have an abortion claim in the USA. A live temperature sensitive EHV-1 vaccine has recently been developed in the UK and the experimental data look promising. This vaccine protected pregnant mares for up to 6 mo after a single intranasal inoculation. In comparison the inactivated vaccines need to be administered at 5, 7 and 9 mo of each gestation.

Properly vaccinated mares rarely abort due to EHV infection unless they are **stressed** or exposed to a **large virus challenge** and multiple abortions on studs with a stringent vaccination policy are uncommon. Commercial studs should be advised not to accept unvaccinated pregnant mares or, if this is not possible, to keep them isolated (i.e. in a separate field or barn) from other mares.

Wherever possible, brood mares should not be kept in close proximity to other horses such as racehorses, showjumpers, yearlings and children's ponies. If mares are kept on **mixed premises** they should always be handled **before** other horses. Horses returning from sales, race meetings and competitions should be **isolated** from the brood mares.

It is important to **minimize stress** to pregnant mares. There is a risk in transporting heavily pregnant mares over long distances. All pregnant mares, particularly those that have traveled long distances and those from sales yards, should be **isolated** on arrival at a stud. Horse boxes should be regularly cleaned and disinfected with a product which is active against herpesviruses.

All cases of abortion, stillbirth or foal death within 14 days of birth should be treated as suspect virus abortion. The fetus and the placenta should be submitted to a recognized diagnostic centre for pathologic investigation. The mare should be placed in isolation in case she is shedding virus. If she aborted in a stable, the bedding should be sprayed with disinfectant such as Virkon (Antec International) at a dilution of 1:100 and left for 48 h, after which it can be removed and burned. If she aborted in a field in the company of other mares, these mares should be isolated until further investigation is completed. No horse should be removed from the premises until the possibility of virus abortion has been excluded.

Common **Codes of Practice*** exist for the control of contagious equine reproductive diseases in the United Kingdom, Ireland, France, Germany and Italy. It is likely that these Codes will extend to all member states of the European Community in the future.

The correct procedure for the management of herpesvirus abortion is documented in the Code and is applicable to any premises where the owner is concerned to reduce the spread of the disease. The major points in the Code concern the **movement of horses from the infected premises**. All pregnant mares must remain on the infected stud **until they foal**. All other horses must remain on the stud until 1 mo after the last abortion. At this time, the infected stud's own non-pregnant mares, including those that aborted, can visit other studs to be covered subject to the full agreement of the receiving stud. The receiving stud should keep these mares isolated from pregnant mares.

The sampling of horses on infected premises for virus isolation and serologic examination for evidence of exposure to virus will assist a breeder in making decisions about the movement of horses within the stud farm. The cohorts of the mare that aborted should be isolated from other pregnant mares. Pregnant mares should be divided into small groups to minimize the spread of virus. If possible, each pregnant mare should be allotted a separate field or paddock so that if she aborts, her fetus does not serve as a source of virus for other pregnant mares.

Neurologic disease

If the neurologic form of EHV disease is confirmed, **no movement** should be allowed on or off the infected premises. All horses should be **rested** immediately as stress exacerbates the condition. In the case of a stud farm, **covering should cease** and because of the abortigenic potential of the virus, pregnant mares should be divided into small groups and kept on the premises until they have foaled.

The **treatment** of the neurologic disease is predominantly supportive and with good nursing care the majority of affected horses will recover. **Ataxic horses** (*q.v.*) should be stabled with deep bedding. **Recumbent horses** should be propped up in the sternal position if possible. Horses in **lateral recumbency** should be rolled frequently. **Abdominal slings** are useful to decrease muscle damage and the development of decubital ulcers.

Inappetant horses may need to be fed by stomach tube. Manual emptying of the rectum and bladder catheterization may be necessary. Immunosuppressive doses of corticosteroids have been administered during some outbreaks on the basis that this might prevent immune-mediated vasculitis. Neither the efficacy of this therapy nor that of anti-inflammatory drugs (flunixin meglumine, DMSO), vitamin E and aciclovir has been determined. Mildly uncoordinated

**Codes of Practice on Equine Venereal Diseases* available from: The Thoroughbred Breeders' Association, Stanstead House, The Avenue, Newmarket, Suffolk CB8 9AA, UK; Welfare and Breeds Department, British Horse Society, British Equestrian Centre, Stanely Deerpark, Kenilworth, Warwickshire CV8 2X2, UK; Syndicat des Eleveurs de Chevaux de Sang de France, 257 Rue du Jour se Leve, 92100 Boulogne, France; Direktorium fur Vollblutzucht und Rennen EV, Rennbahnstrasse 154, 5000 Koln 60, Germany; The Irish Thoroughbred Breeders Association, Greenhills, Kill Co. Kildare, Ireland; Associazione Nazionale Allevatori Cavalli Purosangue, Via del Caravaggio 3, 20144 Milano, Italy.

horses often recover within a few days, but horses that become recumbent usually take much longer and may never recover completely.

The decision to allow movement on and off the premises should only be taken when there is no evidence by serologic examination or by virus isolation that the virus is still circulating. This may take several months.

Coital exanthema

Aciclovir is not licensed for use in horses but is efficacious at the concentrations used in ointments for herpetic ulcers in humans. Antimicrobial ointments may also be applied to the affected areas to control secondary bacterial infection. Covering should cease until the lesions have healed.

EQUINE INFLUENZA

Etiology

Equine influenza viruses are RNA viruses of the orthomyxovirus group. They are categorized as **type A** on the basis of the antigenicity of their internal proteins and are divided into two subtypes on the basis of the antigenicity of the surface proteins **hemagglutinin (H)** and **neuraminidase (N)**. H and N account for 25% and 10% of the viral protein mass respectively.

Influenza viruses are codified according to their type, host species, subtype, and place and year of isolation. This is often followed in parentheses by the H and N subtypes. Thus the prototype of equine 1 influenza viruses is designated A/equine 1/Prague 56 (H7N7) and the prototype of equine 2 influenza viruses is designated A/equine 2/Miami 63 (H3N8).

The genes encoding H and N frequently mutate giving rise to **antigenic drift**. Influenza viruses are also subject to major changes in antigenic composition known as **antigenic shift**. This can occur due to reassortment of the H and N genes.

Equine influenza viruses are very labile and show **very little resistance to disinfectants** customarily used for viral infections.

Epidemiology

Although equine influenza is often associated with disease epidemics, it also causes sporadic outbreaks of disease in populations that are partially immune and is a persistent problem in parts of Europe and North America. Outbreaks of disease have been reported in South America but the disease has not yet been recorded in Australia, Iceland or New Zealand.

Equine influenza is contracted by **inhalation**. There is no evidence that horses become chronically infected with the virus. Epidemics often start at equestrian events where horses congregate in large numbers. The disease is then disseminated over a wide area following the dispersal of horses after the event. The incubation period varies from 1 to 5 days and depends primarily on the size of the virus challenge. The virus is **extremely contagious**. The short incubation period and persistent coughing, which releases large amounts of virus into the atmosphere, contribute to the rapid spread of the disease.

In a susceptible group of horses, morbidity can be as high as 100%. Mortality is usually low but can be as high as 10% in **foals, donkeys and affected horses that are not adequately rested**. The severity of the disease depends primarily on the immune status of the horses at the time of exposure, the environment and the amount of stress to which the animals are subjected.

Antigenic variation and **failure to vaccinate** are major contributing factors to influenza epidemics in countries where the disease is endemic but the most devastating epidemics occur when influenza virus is introduced into an immunologically naïve population. In India in 1987, over 27 000 Equidae were affected and several hundred animals died. In South Africa in 1986 race meetings were canceled for over 5 mo because of the influenza epidemic that resulted from the introduction of the virus into the country for the first time. In the 1989 epidemic in northeastern China, the overall morbidity rate was 80%; the mortality rate was 20%, but rose to 35% in certain groups.

Equine 1 influenza virus was first isolated in Czechoslovakia in 1956 and was subsequently detected in several European countries and in America. Although two international surveys have indicated that no equine 1 influenza viruses have been isolated anywhere in the world for more than a decade, there is some serologic evidence to suggest that they still persist. A/equine 1/Prague 56 or similar H7N7 virus is still included in influenza vaccines in many countries.

Equine 2 influenza virus was first isolated in Miami in 1963 and has continued to cause outbreaks of disease in Europe and North America ever since. Type 2 influenza viruses are less stable than type 1. Antigenic variants can give rise to **large-scale disease epidemics** such as occurred in 1979–1981 in Europe and in North America. The antigenic variant responsible for these epidemics was subsequently incorporated into the vaccines and annual vaccination for racehorses and competition horses became mandatory in several European countries.

Following the implementation of a mandatory vaccination policy in 1980, equine influenza was not diagnosed in Ireland and the UK for almost a decade. In 1989 both countries experienced an influenza epidemic. Genetic analysis of one of the viruses isolated in the UK, A/equine 2/Suffolk 89, demonstrated that it was significantly different from the prototype strain of the previous epidemic, A/equine 2/Fontainbleau 79. This led to a recommendation that A/equine/Suffolk 89 or similar isolate be included in influenza vaccines.

Further analysis of influenza A H3N8 viruses isolated in different continents demonstrated that there was an acceleration of H evolution in the late 1980s and that **two separate lineages** evolved. These have been designated European and American, based on the predominant geographic origin of the viruses. Co-circulation of viruses from both lineages can occur; for example, in the UK a European strain A/equine/Newmarket/2/93 was isolated at the same time as A/equine/Newmarket/1/93—an American strain from horses in the same yard. There is some evidence to suggest that the differences between the American and European lineages are sufficient to compromise cross-lineage protection after vaccination or infection.

Equine influenza viruses appear to be more stable than their human counterparts and no antigenic shift due to reassortment has been described in influenza viruses isolated from horses. Only viruses with the combinations H7N7 and H3N8 have been described in horses. However, shifts may occur not

only by genetic reassortment but also by mutation of an avian virus or other mammalian virus so that it becomes infectious for horses. The 1989 epidemic in northeastern China appears to have been caused by a virus that is more closely related to the influenza viruses of **aquatic birds** than to other equine influenza viruses. The prototype virus from this epidemic, A/equine 2/Jillin 89 (H3N8), is thought to be the latest mammalian influenza virus to emerge from the avian influenza gene pool, although it is no longer infectious to ducks which reduces the possibility of spread by aquatic birds during migratory flights. In 2004, there was a suggestion from the University of Florida that a strain of equine influenza virus may have infected dogs.

Clinical signs

Both subtypes of equine influenza viruses produce similar clinical signs in horses, but equine 2 infections are usually more severe. The first sign is an elevation in body **temperature** (up to 41°C) which is usually **biphasic**. This is followed within a few hours to a maximum of 2 days by a **dry deep cough**.

The other most commonly observed clinical signs are a **serous nasal discharge**, which may become mucopurulent due to secondary bacterial infection, myalgia, inappetance and enlarged mandibular lymph nodes. Edema of the legs and scrotum is sometimes observed and spasmodic and impaction colic (*q.v.*) have been reported.

Horses usually recover clinically from uncomplicated influenza within 10 days but coughing may persist for longer. **Secondary bacterial infection** prolongs the recovery period. Pneumonia (*q.v.*) may occur in foals, horses that are stressed by strenuous exercise, and **donkeys**, which are more susceptible to influenza than horses.

Equine 2 viruses are more pneumotropic than equine 1 viruses and have also been associated with **myocarditis** (*q.v.*). Pregnant mares may **abort** or resorb the fetus as a result of fever. Sequelae of equine influenza can include chronic pharyngitis, chronic bronchiolitis, alveolar emphysema which can contribute to chronic obstructive pulmonary disease (COPD), sinusitis and guttural pouch infections (*q.v.*).

Equine influenza may be **mild or even asymptomatic** in horses protected by recent or regular vaccination or by previous exposure.

Pathogenesis

The virus infects the **ciliated respiratory epithelial** cells, which become vacuolated, edematous and lose their cilia before being desquamated. This impairment of the clearance mechanism **increases the susceptibility** of the respiratory tract to **secondary bacterial invasion**. Damage to the respiratory epithelial cells can occur within 1 day after the onset of symptoms. Regeneration may begin a few days later but complete resolution may take up to a month, long after the horse appears clinically normal.

Diagnosis

The classical signs of influenza that are seen in unvaccinated horses are easy to recognize. The two major features of the disease are its **rapid spread** and the **dry deep cough**.

Diagnosis of equine influenza in a vaccinated population is more difficult as the clinical signs may resemble more closely those caused by other pathogens such as equine rhinovirus, equine herpesvirus or bacterial infection (*q.v.*) than classical influenza. A definitive diagnosis can only be made by **isolation or detection of the virus** from/in nasopharyngeal swabs or by **serologic examination**.

To isolate virus, **nasal secretions** collected in virus transport medium during the **acute phase** of infection should be kept cold **but not frozen** and transported to a specialist laboratory as quickly as possible. The samples are inoculated into the allantoic or amniotic sacs of 8–12-day-old chick embryos. After incubation at 33°C for 3 days the amniotic or allantoic fluids are harvested and tested for hemagglutinating activity. Some laboratories also isolate influenza virus using cell monolayers.

The presence of influenza virus can be confirmed and its antigen type determined by hemagglutination inhibition (HI) using **specific antisera**. Faster ELISA such as the Directigen Flu A (DFA) test have been developed for the detection of **influenza antigen**. The DFA takes approximately 15 min and is simple to perform. It requires no specialized equipment and can be performed by personnel that are not specially trained in virologic techniques. However, it is less sensitive than PCR; PCR requires a longer time to get a result than DFA but is considerably faster than virus isolation. **Virus isolation** remains essential for ongoing **strain surveillance**. In a recent study evaluating different viral detection methods in nasal secretions collected after experimental challenge, viral isolation and RT-PCR proved to be the most sensitive methods. The DFA test was the least sensitive method.

Clotted blood samples are required for serologic examination. Using the HI test, a sample taken in the acute stages of the disease can be compared with a sample taken 10–14 days later and a significant rise in type-specific antibodies will be readily detectable. Seroconversion can also be detected by single radial hemolysis (SRH). The HI test is simpler and less time consuming but the SRH is easier to standardize between laboratories.

Management

The standard recommended time for the management of equine influenza is **1 wk of complete rest for every day of elevated temperature** followed by a **gradual return to full work**. Some clinicians like to administer a course of antibiotics or sulfonamides to prevent secondary bacterial infections. Others, wary of the development of antibiotic resistance, prefer to treat secondary bacterial infections as they arise. A non-steroidal anti-inflammatory drug (NSAID) can be used in cases with high fevers to prevent excess pulmonary inflammation and abortion in mares.

In racing stables, the size of the yard, the vaccination history of the horses and the severity of the challenge should be taken into account when deciding whether or not to **close the yard** temporarily. Because of the **highly contagious** nature of the virus it is often advisable to close smaller yards, as the majority of horses will be exposed to the virus within a week. Moreover, resting the horses will reduce the severity of the clinical signs, decrease virus excretion, prevent the build-up of a large virus challenge in the yard, reduce the recovery period and minimize chronic sequelae.

In a larger yard with an intensive vaccination policy it may not be economically feasible to close the entire yard. In such a yard, virus spread will be slower, some of the horses will be asymptomatic and some remain capable of running good races. However, the trainer should always be warned that influenza virus is **pneumotropic** and that **working infected horses** will exacerbate the disease. It will also increase **virus shedding** which will serve as a risk to other horses.

Vaccination

Vaccinated horses are less susceptible to the disease than unvaccinated or inadequately vaccinated horses. During an extensive outbreak in Sweden in 1979, 1000 of 1300 horses under surveillance developed clinical signs, but whereas only 3% of horses that had received two or more doses of vaccine developed clinical signs, 98% of unvaccinated horses developed influenza.

In recent outbreaks, resistance to the disease has been shown to correlate well with the vaccination history and the antibody titers at the time of exposure. Young horses that have never been vaccinated or have only had a primary course and one or two boosters show classical signs of influenza, whereas in the same yards older competition horses that have been vaccinated regularly show no clinical signs. Racing yards that vaccinate every 4–6 mo are **less affected** than yards that vaccinate annually.

The majority of equine influenza vaccines that are currently available are **inactivated**. These vaccines contain either whole or subunit viral antigens, usually combined with an adjuvant such as aluminum hydroxide or carbomer. Equine influenza vaccines containing immune stimulating complexes (ISCOMs) are also available. These vaccines contain virus proteins attached to a matrix comprised of a glycoside Quil A extracted from the bark of a South American tree, *Quillaja saponaria molina*.

In North America a cold-adapted, temperature sensitive, **modified live vaccine** is available. This vaccine is administered **intranasally**. A single dose provides complete protection against challenge with homologous wild type virus for up to 3 mo and partial clinical protection for 6 mo or longer, in the absence of high titers of induced antibody. The vaccine does not provide sterile immunity and the mechanism of protection is not fully understood.

A **canarypox vector vaccine** expressing the H of a representative of both the European and American lineages has recently been licensed in Europe and may prove to be more effective than inactivated vaccines. It should stimulate cell-mediated immunity as well as humoral immunity.

Given that antigenic drift can compromise vaccine efficacy, vaccines need to be updated regularly to include virus strains that are representative of those circulating in the field. Since 1995, the recommendations of the World Organization for Animal Health, the Office International des Épizooties (OIE) have been to remove ancient isolates (for example Miami/63) and introduce recent isolates representative of the American and European lineages. Only **vaccines that have been updated in line with these recommendations should be used**.

It is advisable to vaccinate young horses, particularly racehorses and other competition horses, at **6 mo intervals** for several years after the primary course of three vaccinations. An annual booster will usually suffice for older

horses such as showjumpers and brood mares that have been vaccinated regularly since they were foals. Brood mares should be vaccinated in the **latter stages of pregnancy** but not later than 2 wk prior to foaling. This will ensure a good supply of colostral antibodies for the foal. Maternal immunity can last up to 6 mo.

Vaccination in the presence of **maternal antibodies** is not recommended as they interfere with the immune response. Furthermore it has been suggested that **repeat vaccination** in the face of maternal antibodies may be detrimental and interfere with the humoral response to vaccination many months after these antibodies have waned. It is advisable to monitor the antibody titers of foals and start the vaccination program when the maternal antibodies have declined to a negligible level.

Annual vaccination for racehorses and competition horses is mandatory in several countries. Although this helps to reduce the risk of influenza epidemics (it is estimated that >70% of the population need to be fully vaccinated to prevent epidemics) **annual vaccination in a training yard is unlikely to protect against clinical influenza**. The majority of horses in a yard need to have high antibody titers against influenza to withstand virus challenge. Such titers can be achieved by more regular vaccination (*q.v.*).

Serologic monitoring of the horses enables a clinician to decide on the most appropriate vaccination regimen. There are frequently a small number of horses in a yard that respond poorly to vaccination and have persistently low antibody titers. Such horses are often instrumental in starting an influenza outbreak in a yard.

Most influenza vaccines are marketed with and without **tetanus toxoid** (*q.v.*). The immune response elicited by tetanus toxoid is much more durable than that induced by influenza antigen. It is inadvisable to administer tetanus toxoid more frequently than the vaccine manufacturers recommend. In an intensive influenza vaccination program, vaccines containing **influenza virus alone** should be routinely administered and a tetanus toxoid booster administered at intervals of not less than 12 mo and preferably at 24–27 mo intervals. Horses should always be rested for a few days after vaccination.

EQUINE RHINO/RHINITIS VIRUSES

Equine rhinitis viruses, formerly known as equine rhinoviruses, belong to the family Picornaviridae, as do human rhinoviruses, frequently associated with the common cold. Serologic studies indicate a **high prevalence** of these viruses worldwide and it is likely that the majority of horses are exposed to rhinitis viruses at some stage in their lives.

Several different types of equine rhinitis viruses have been identified of which the virus formerly known as equine rhinovirus 1 appears to be the most clinically significant. This virus has recently been renamed **equine rhinitis A virus (ERAV)** and on the basis of its close relationship to foot-and-mouth disease virus (FMDV) has been classified as an Aphthovirus.

Equine rhinovirus 2 has been renamed **equine rhinitis B virus 1 (ERBV1**) and reclassified as the sole member of a new genus **Erbovirus**. It has been suggested that **equine rhinovirus 3** should also be assigned to this genus and renamed **ERBV2**.

Most of the clinical information available concerns ERAV, which is spread by **aerosols** and by **direct contact**. The incubation period is 2–8 days. Viremia is a regular feature and usually persists for 4–5 days. Virus is shed in **urine** for prolonged periods of time and this has led to the suggestion that the urinary tract may become persistently infected.

ERAV can cause **upper respiratory tract** disease characterized by fever, inappetance and **a copious nasal discharge**. There is a greater incidence of colds in children than in adults and similarly ERAV is more likely to cause disease in **young horses**. Upper respiratory tract disease due to ERAV infection is a significant problem in 2-year-olds in training. It is most prevalent in the autumn/fall and winter months. The virus appears to circulate constantly in most racehorse populations and the disease often occurs when horses are **stressed by intensive work** such as before their first race. Infection with another agent such as equine herpesvirus can also predispose a horse to ERAV infection.

ERAV spreads quite slowly and active cases of disease may occur in a training yard for several months. The lower respiratory tract does not seem to be very susceptible to rhinitis viruses and horses will usually recover from an uncomplicated ERAV infection within a week. However, **inadequate resting** of horses with ERAV disease increases their susceptibility to **secondary bacterial infection** that prolongs the recovery period. Rhinoviruses have been isolated from sinus fluids collected from people with acute sinusitis and it is possible that ERAV infection may contribute to the development of **sinusitis** (*q.v.*) in the horse.

ERAV infection in older horses is often subclinical but may contribute to a **loss of performance**. A high incidence of significant ERAV antibody titers is a common finding in yards presented to the clinician with problems of loss of performance.

People working with horses can be infected with ERAV but clinical signs have not been documented.

The laboratory diagnosis of ERAV is routinely based on **serologic examination** by CFT or by serum neutralization test (SNT) but the virus can sometimes be isolated from nasal swabs, blood, feces or urine. Detection of virus by PCR in nasal swabs has proven to be more sensitive than virus isolation.

Equine rhinitis viruses, like human rhinoviruses, are quite stable and can survive for weeks on a variety of surfaces in the environment. Management of the disease should include attention to stable hygiene and the use of a disinfectant with proven efficacy against rhinitis/rhinoviruses. None of the vaccines currently available contains equine rhinitis viruses.

EQUINE ADENOVIRUS

Serologic surveys for equine adenovirus indicate that infection is widespread but that the majority of infections do not result in clinical disease. However, **adenovirus pneumonia** is well documented in Arabian foals and the virus has been isolated from foals of other breeds with respiratory disease and from clinically normal foals.

Adenovirus infection is the most prevalent cause of death in Arabian foals with **combined immune deficiency** (CID) (*q.v.*). The disorder is inherited as an autosomal recessive trait and is characterized by the absence of functional

B and T lymphocytes. The foals are very susceptible to adenovirus, as well as to bacteria such as *Streptococcus zooepidemicus, Corynebacterium pyogenes, Escherichia coli, Staphylococcus aureus, Actinobacillus equuli, Pseudomonas* spp. and *Bacillus* spp. and to the protozoan *Pneumocystis carinii* (*q.v.*), and usually die before reaching 5 mo of age.

Adenovirus infection in foals with immunodeficiency is characterized by intermittent fever, rhinitis, conjunctivitis, pneumonia and, less frequently, diarrhea. Foals appear normal at birth but develop clinical signs between 2 and 6 wk of age and usually die within 2 wk. Hematologic examination reveals severe lymphopenia.

At **necropsy**, necrotizing bronchitis, bronchiolitis, interstitial pneumonia, as well as fibrin and hyalin membranes within the alveoli, are observed. Foci of abscess formation due to bacterial infection are frequently present. The lymph nodes, spleen and thymus are small with virtually no germinal centers. Large basophilic intranuclear inclusion bodies occur in respiratory epithelial cells and sometimes in the epithelial cells of the salivary glands and ducts, the conjunctiva, the pancreas, the bladder and the small intestine. Adenovirus can usually be isolated from the lung tissue. Primary equine kidney cells are the cell line of choice for virus isolation.

Several virus challenge studies have illustrated that immunocompetent foals exposed to adenovirus by the respiratory route develop respiratory disease. **Colostrum-deprived foals** are more susceptible to pneumonia. Post mortem lesions in such foals are similar to those in the CID foals described above but their lymphoid systems are normal.

Immunocompetent foals exposed to adenovirus by natural infection may develop conjunctivitis, dyspnea, fever, coughing and diarrhea. Uncomplicated adenovirus is rarely fatal but deaths due to combined infections of adenovirus and various bacteria have been recorded.

Adenovirus infection does not appear to be a significant problem in adult horses but it has occasionally been associated with upper respiratory tract disease, ocular discharge and soft feces in racehorses. In such cases a diagnosis may be confirmed by isolation of virus from nasal, ocular or rectal swabs and by serologic examination of **paired blood samples** collected 10–14 days apart. Hemagglutination inhibition is probably the most widely used serologic assay for the detection of equine adenovirus.

EQUINE VIRAL ARTERITIS

Introduction

Serologic surveys indicate that the equine arteritis virus (EAV) is widely distributed throughout the world. However, clinical disease is a relatively rare occurrence. It is the **abortigenic potential** of the virus that causes international concern and often leads to restrictions on movement of seropositive horses. The 1984 outbreak in Thoroughbreds in Kentucky led to a temporary embargo on the export of horses of all breeds from the USA to the tripartite countries (UK, France and Ireland). However, current international movement restrictions relate primarily to carrier stallions and infected semen.

Etiology

EAV is an enveloped spherical RNA virus of the genus Arterivirus, family Arteriviridae, order Nidovirales. Porcine reproductive and respiratory syndrome virus (PRRSV), another important veterinary pathogen, has been classified in the same genus. Only one serotype of EAV has been identified but genetic heterogeneity among strains has been detected by the determination of their nucleotide sequences.

Epidemiology

The first recognized outbreak of equine viral arteritis (EVA) occurred on a Standardbred stud in Bucyrus, Ohio, in 1953 but descriptions of the disease "**epizootic cellulitis-pinkeye**" in the veterinary literature date back to the late nineteenth century. In spite of the apparent worldwide distribution of EAV, disease outbreaks appear to be infrequent and sporadic in nature. Serologic evidence of exposure has been reported in America, Africa, Australia and Europe. Evidence of exposure to EAV has been reported in Standardbreds, Thoroughbreds, Quarter Horses, Arabians and Warmbloods.

Considerable variation in the prevalence of seropositive horses occurs between certain breeds within a country. In America, Australia and New Zealand, EAV is endemic in Standardbred horses but rare in Thoroughbred horses. Serologic surveys in the USA indicate that 70–90% of Standardbred mares but only 3% of Thoroughbred mares are seropositive. In Australia, 73% of Standardbred stallions tested seropositive compared with 8% of Thoroughbred stallions and 1% of Thoroughbred mares and racehorses.

The reason for the high prevalence of serologically positive horses in the Standardbred population is unknown. Experimental infection does not suggest that Standardbreds are more susceptible than Thoroughbred horses and in France there is a similar prevalence of EAV antibody in Thoroughbred and Standardbred horses.

The disease has not been recorded in a clinical form in Japan or Iceland but outbreaks have been recorded in several European countries including Switzerland, France, Poland and Spain, as well as in the USA and Canada. The first recorded outbreak of clinical EVA in the UK was reported in 1993. The first in Thoroughbred horses in North America occurred in Kentucky in 1984 and was a source of major international concern throughout the industry.

The virus is transmitted by the **respiratory** and **venereal** routes, and to a lesser extent by indirect contact with **fomites**. Virus may be shed for up to 16 days in nasal secretions and respiratory transmission can lead to widespread dissemination of virus, particularly where large numbers of horses are congregated together, for example, at race tracks, stud farms or sales. **Aborted fetuses** are heavily contaminated with virus and are a source of infection.

Carrier stallions play a critical role in the spread of the virus. A high proportion of EAV-infected stallions (1:3) may become long-term carriers and shed virus constantly in the sperm-rich portion of their semen. The establishment and maintenance of the carrier state appears to be **testosterone dependent**. The carrier state has not been identified in the sexually immature colt. The virus persists in the accessory sex glands and is eliminated within 26 days of castration. Although some carrier stallions spontaneously cease to shed

virus, others may continue to shed for their lifetime. Such stallions do not appear to be viremic nor do they shed virus in nasal secretions or urine.

It appears that **all susceptible mares bred to chronic carrier stallions become infected with virus** and outbreaks frequently start when a carrier stallion covers a susceptible mare. Initial **venereal transmission** is followed by **lateral spread** of virus via the **respiratory route**. The incubation period after venereal exposure is usually approximately 1 wk. The incubation period after respiratory exposure varies from 3 to 14 days.

There is no evidence of a carrier state in mares although virus shedding from the vagina of experimentally infected mares has been reported. Foals born to mares that were exposed to EAV when pregnant do not appear to become carriers.

The virus remains **infective in frozen semen** and artificial insemination (AI) has proved to be a highly effective mechanism of virus transmission. In the outbreak in the UK in 1993 mares inseminated artificially exhibited more severe clinical signs than those bred naturally. Some outbreaks have been due to the international trade of incorrectly certified semen.

The mortality rate in natural outbreaks of EAV is very low; mortality has only been reported in young foals. The ratio of clinical to subclinical infection, when infection was acquired following venereal exposure, has varied from 1.4:1 to 1:6 in different outbreaks. The highest morbidity rates have been reported where large numbers of horses are stabled together in the same air space.

The protective immune response elicited by natural infection with EAV appears to be very durable, perhaps permanent. Maternal immunity in foals born to immune mares declines after 2–6 mo.

Clinical signs

Clinical signs of EAV infection are extremely variable and the majority of infections appear to be **subclinical**. The most common clinical signs are fever, depression, inappetance, limb edema especially of the hindlimbs, stiffness in gait, inflammation of conjunctivae ("pink-eye") and nasal mucous membranes, urticarial rashes and edematous plaques, ocular and nasal discharge, palpebral edema and edema of the orbital fossa. Edema of the mammary gland is frequently seen in mares and the majority of stallions develop scrotal edema. All or any combination of these clinical signs may occur in different outbreaks.

The predominant clinical signs in an outbreak may depend on the virus strain. For example, in 1993 conjunctivitis was a primary feature of an outbreak of EVA in the UK but in the same year urticaria was the main clinical sign observed in a major outbreak in North America.

Abortion may occur in mares in mid to late gestation. Stallions may experience a temporary decrease in fertility due to pyrexia and scrotal edema. This **sub fertility**, which is associated with both a reduction in the sperm count and morphologic changes, has been demonstrated to persist for up to 17 wk in experimentally infected stallions.

The most severe form of natural infection described occurred in the 1953 outbreak in Bucyrus, Ohio, when there was a 50% abortion rate in pregnant mares. Abortions occurred 10–34 days after exposure to virus and in 33% of cases were not associated with any other clinical abnormality. There were no

confirmed cases of EAV abortion during the 1984 outbreak in Kentucky but abortion has been a feature of subsequent outbreaks in the USA and Canada. Abortion rates of up to 50% have been reported during outbreaks of EVA on stud farms in Europe.

Post-mortem findings

The gross and microscopic lesions associated with EVA are consistent with the predilection of the virus for the media of the arteries. In the original Bucyrus outbreak, edema, congestion and petechial hemorrhages of the lymph nodes, the subcutaneous tissues and many of the organs were noted. The predominant microscopic lesion was a **widespread necrotizing arteritis**.

Pathologic examination of the aborted fetuses revealed edema of the lungs, increased pleural fluid and petechial hemorrhages of the pleural and peritoneal surfaces. Cardiac myodystrophy and hemorrhages and edema of the brain have been observed in fetuses from other outbreaks. A severe necrotizing arteritis in the placenta was described during an outbreak of EVA in Thoroughbred mares in Oklahoma in 1987. Fetuses aborted as a result of arteritis are often partly autolyzed.

Diagnosis

The diagnosis of EVA cannot be made based solely on the clinical signs without corroborative virus isolation and/or serology. The variability in pathogenicity among strains of EAV means that the absence of clinical signs cannot be taken as evidence of the absence of virus infection.

The detection of EAV in some equine populations, for example, in Irish Thoroughbreds in 2003, relied solely on serology. **Serologic diagnosis** of EAV infection is based on seroconversion. A **clotted blood sample** should be collected during the acute stages of the disease and a second convalescent sample should be taken 14–28 days later. Samples should be submitted to a reputable laboratory where the SNT is carried out in accordance with OIE standards. The SNT is the internationally recognized test but ELISA and CF tests have also been developed. ELISA tests are more rapid than the SNT but appear to have some specificity problems.

The virus can be isolated from nasal secretions, semen, urine, buffy coats and fetal tissues using a variety of cell lines including rabbit kidney cells (RK13). Nasal swabs and fetal tissue should be placed in **virus transport medium**, which is available from most specialist diagnostic laboratories. All samples should be kept cool and transported to the laboratory as quickly as possible. Recovery of virus from experimentally infected horses rarely presents a problem but it is sometimes difficult to isolate virus from naturally infected horses.

Virus isolation from the sperm rich fraction of **ejaculates** is an effective means of detecting a shedding stallion, as is test breeding. The isolation rate from dismount samples is not of equivalent accuracy and the testing of the pre-sperm fraction is likely to lead to false negative results.

The **shedding status** of a putative carrier stallion can also be determined by breeding him to **two seronegative test mares**. The mares are bled 14 and 28 days after covering and the sera checked for the presence of antibodies against EAV.

PCR can be used to amplify EAV nucleotide sequences to facilitate their detection in seminal plasma. Some laboratories have found PCR to be more sensitive than virus isolation. All shedding stallions identified to date are seropositive by the SNT.

Management and control

Adequate rest, with supportive therapy if necessary, allows the majority of horses to make a speedy and uneventful recovery. To minimize the risk of the development of **chronic carriers** it is particularly important that affected stallions are allowed several weeks of sexual rest. It is also important to control pyrexia in the stallion as this may lead to a temporary loss of fertility. Gonadotropin-releasing hormone (GnRH) antagonists (*q.v.*) have a potential role in the treatment of carrier stallions but a causal relationship between treatment and permanent cessation of shedding has yet to be established.

The spread of EAV can be limited by **restriction of movement** of horses from affected premises until there is no virologic evidence of active virus infection. Carrier stallions should only be allowed to breed under very restricted circumstances. In Kentucky, carrier stallions are kept physically isolated and bred only to mares that are seropositive to EAV as a result of previous exposure to virus by vaccination not less than 3 wk previously or by natural infection. Similar control programs are conducted in New York State, France and New Zealand.

A **modified live EAV vaccine** Arvac (Fort Dodge) is available in North America and a killed vaccine Artervac (Fort Dodge) is available in some European countries. The live vaccine has been used extensively in the Kentucky and New York Thoroughbred EVA control programs. It is derived by serial passage of the prototype Bucyrus strain in a variety of different cell lines and is not recommended for use in pregnant mares or in foals less than 6 wk of age but is considered safe for use in stallions and in barren mares. Safety studies have shown that vaccinated stallions may experience a temporary reduction in the percentage of sperm with normal morphology 2–3 wk after vaccination but no other significant effects on semen quality were observed. Vaccine virus can be isolated sporadically from the blood and nasopharynx of some stallions but it does not appear to be shed in the semen. The vaccine appears to protect horses against clinical disease but does not prevent virus infection, replication or shedding. **Vaccinated mares can be covered by a carrier stallion and are protected against clinical disease**.

The killed EAV vaccine is available in the UK for use in all horses and in France, Germany and Ireland where it is only permitted for use in stallions. In countries where the vaccine is available it is recommended that all stallions be vaccinated annually.

All stallions should be serologically tested immediately prior to and 2–3 wk after vaccination in order to be able to prove that their antibody titer is a consequence of vaccination and not natural infection. The keeping of adequate **records** obviates the need for investigations into the carrier status of the horse at a future date, particularly if the owner wishes to sell or export the horse.

Within the EU, the common **Codes of Practice** (*q.v.*) for the control of equine reproductive diseases in the UK, France, Germany, Ireland and Italy recommend that all mares be serologically tested within 28 days prior to covering and

that all imported animals be subjected to a serologic test for EVA. Any seropositive stallion must be isolated and his carrier status established. Seropositive mares should be subjected to two serum neutralization tests not less than 14 days apart. Their antibody titers should be stable or falling prior to release from isolation. Because of the lack of carrier status in the mare, a barren mare with stable or falling titers does not represent a significant risk to other horses and can be covered. Pregnant seropositive mares should be kept in isolation until they foal unless it can be established that they are seropositive as a result of exposure to virus prior to the pregnancy.

Breeders who practice artificial insemination of non-Thoroughbred mares should only use semen from stallions that are seronegative for EAV or that have been shown conclusively not to be shedding virus at the time of semen collection.

AFRICAN HORSE SICKNESS AND EQUINE ENCEPHALOSIS

Introduction

African horse sickness (AHS) is a **highly fatal**, infectious, arthropod-borne disease of horses, mules and donkeys. There are four recognized forms of the disease but most of the clinical signs and lesions result from impairment of the respiratory and circulatory systems.

African horse sickness virus (AHSV) is enzootic in most of Africa south of the Sahara. It occasionally spreads to other areas with devastating effects on the susceptible equine population. The disease appears to be capable of persisting anywhere in the world when the climatic conditions favor the multiplication of the vector and its survival during the winter months. Epidemics have occurred in the Middle East, Asia and the Mediterranean countries including Spain, Portugal and Morocco.

Etiology

AHS is caused by a double-stranded, RNA icosahedral virus belonging to the Reoviridae family, genus Orbivirus. It is related to bluetongue and Ibaraki viruses. **Nine different serotypes** of AHSV have been identified. They can be attenuated for use as vaccines by passage in mice and in tissue culture.

The virus is destroyed by heating it to 70°C for 5 min or 50°C for 10 min or by treatment with acetic or citric acid. However, it can persist for **several months** in putrefied blood. Equine encephalosis viruses (EEV) constitute a serogroup of the genus Orbivirus.

Epidemiology

In **endemic areas of Africa**, AHS occurs periodically during hot weather following heavy rains. The disease was confined to the African continent until 1944 when it spread to Palestine, Syria and Jordan. In 1959 there was a major epizootic in Iran, West Pakistan and Afghanistan that spread eastward to India and westward through Turkey to the eastern Mediterranean including Cyprus. The fatality rate among affected animals was nearly 90% and an estimated total of 300 000 Equidae died of the disease. In 1966 and 1967, AHS spread up to Northern Africa and into Spain but was controlled by slaughter of infected

animals and by an extensive vaccination program. All of these outbreaks outside Africa and an outbreak in Saudi Arabia in 1989 were due to AHSV type 9.

An outbreak in the Iberian Peninsula in 1987 was due to AHSV type 4 and was the first time this virus type had been recorded outside Africa. The outbreak began in August after the importation of **zebras** from Namibia to a safari park near Madrid. Zebras are quite resistant to AHS and may serve as a source of infection for more susceptible Equidae. The disease affected eight premises and 146 Equidae died or had to be destroyed. Approximately 36 000 animals were vaccinated. More than a year after the last death, however, a new outbreak of AHS was detected over 600 km away in Andalusia. Approximately 18 000 Equidae were vaccinated but the disease recurred again in the summer and autumn of 1989 in the same area causing the death of more than a thousand Equidae. It spread to the Algarve in Portugal and to Morocco. Mandatory vaccination of all Equidae was implemented in Portugal and no subsequent cases of AHS have been identified since 1989. The disease persisted in Morocco where outbreaks were reported in 1990 and 1991. In Spain, compulsory vaccination of all Equidae in Andalusia was begun in 1990 and the last positive case was recorded in November of that year.

Until recently *Culicoides imicola* (*C. imicola*) was considered the only field vector for AHSV but it now appears that *Culicoides bolitinos* (*C. bolitinos*) may be a significant vector in certain high-lying regions of South Africa.

The **seasonal nature** of AHS reflects the activity of the biting midge. The midge becomes infected by feeding on a viremic animal. The virus localizes in the salivary glands and is transmitted when the midge feeds on susceptible animals. The midge remains infected for life.

The life cycle of the *Culicoides* is divided into four stages: egg, larva, pupa and adult. The adult midges live for approximately 21 days during hot, wet months and feed on horses and other large animals from dusk until just after dawn. The midges are weak fliers but they can be carried for long distances in the **wind**. Outbreaks of AHS usually cease after a spell of cold weather, which kills the midges. New cases rarely appear more than 10 days after frost.

Culicoides overwinters in the larval stage but there is no evidence that transovarial and transtadial transmission of AHSV takes place. This suggests that there is another as yet **unidentified reservoir** in enzootic areas that serves as a source of infection for adult midges when they appear in the spring. Antibodies against AHSV have been detected in a variety of domestic and wild animals in Africa including elephants, sheep and goats but the virus has never been isolated from these species. AHSV has been isolated from dogs and camels in Egypt. It has been suggested that donkeys may have been responsible for the persistence of AHS in Spain between 1987 and 1988. Donkeys are less susceptible to the disease than horses and can experience persistent viremia.

The virus has also been isolated from other species of *Culicoides* that are more common in northern Europe and the UK than *C. imicola* and *C. bolitinos.*

C. pulicaris, *C. obsoletus* and *C. nubeculsus* species, which are prevalent in the UK, can be **experimentally infected** with AHSV and *C. nubeculsus* can transmit the virus. It is possible that these species could play a role in the transmission of virus if it were introduced into the UK or other northern European countries. The primary vector of bluetongue virus in the USA, *C. variipennis*,

has been shown experimentally to transmit AHSV. The virus has also been isolated from mosquitoes and ticks, which may play a role in the transmission of the disease.

EEV also appears to be transmitted by *Culicoides* midges and to date has only been identified in South Africa.

Clinical signs

Four forms of the disease have been described; acute or pulmonary, subacute or cardiac, mixed, and a mild form known as horse sickness fever.

The **acute or pulmonary form** is usually seen in susceptible animals during severe epizootics. After a 3–5 day incubation period the horse experiences an acute febrile reaction that may last only 24–48 h with temperatures as high as 40°C. The fever is followed by respiratory signs associated with pulmonary edema, which include tachypnea, paroxysms of coughing and frothy nasal discharge. The horse may experience great difficulty in walking and lower its head after the slightest exertion.

In the agonal stage the white, sometimes blood-tinged nasal discharge is voluminous and at the time of death a frothy liquid may flow from the horse's mouth. The total course of the disease is 4–5 days and the animal literally drowns in its own fluids. The mortality rate is approximately 90%.

The **subacute or cardiac form** of the disease is more common in enzootic areas. The incubation period lasts 5–20 days and is followed by a febrile reaction for about 5 days. Characteristic edematous swellings develop in the head region especially in the supraorbital fossa and the eyelids. The edema frequently extends to the neck and chest but is not gravity dependent. Petechial hemorrhages may develop on the ventral surface of the tongue and on the conjunctiva. Abdominal pain often results from hemorrhage in the gastrointestinal tract. Dyspnea may be observed but horses rarely present frothy nasal discharge. The mortality rate is approximately 50%.

The **mixed form** of AHS is a combination of the cardiac and pulmonary forms. The outbreaks in Spain and Portugal in the late 1980s were characterized by the mixed form in which either the cardiac or pulmonary form prevailed. Clinical signs were consistent with cardiorespiratory failure with progressive pulmonary edema.

Horse sickness fever is the mildest form of AHS. It is observed in donkeys, zebras and immunized horses. It presents as a febrile response sometimes accompanied by slight dyspnea.

It is thought that infection is usually subclinical but pyrexia, enteritis, abortion, jaundice and death due to cerebral edema and myocarditis have been recorded.

Post mortem findings

In the majority of field cases of AHS the gross lesions are consistent with both cardiac and pulmonary involvement. However, there are certain lesions that characterize each form of the disease. The **pulmonary form** is characterized by edema of the lungs and hydrothorax. It is possible to find 3–5 L of fluid in the chest cavity. The lungs are hypertrophic with interstitial and alveolar edema. The lumen of the trachea usually contains froth and a whitish or

yellowish foam is almost invariably present in the nostrils. Other lesions may include submucosal congestion of the fundus of the stomach and slight ascites.

The **cardiac form** is characterized by a yellow gelatinous edema of the supraorbital fossa, the intermandibular space and along the fascia of the muscle bundles in the frontal, cervical and sternal regions. There is marked hydropericardium. The pericardial sac may contain more than 2 L of yellowish fluid. Hemorrhages of the epicardium and endocardium are common and the lungs may be congested. Hydrothorax and ascites are sometimes present. Hyperemia of the glandular fundus of the stomach, perirenal edema, hyperemia and hemorrhages in the mucosa and serosa of the large and small intestines, subcapsular hemorrhage of the spleen and hypertrophy of the mediastinal and mesenteric lymph nodes are also commonly seen.

Diagnosis

In enzootic areas, familiarity with the disease may permit a presumptive diagnosis on the basis of clinical signs and gross lesions. However, because of the various forms in which the disease appears and the potential to confuse some of the clinical signs and lesions with those of equine infectious anemia, piroplasmosis, purpura hemorrhagica (*q.v.*) or poisoning, a confirmed laboratory diagnosis is essential.

Virus can be isolated from heparinized blood samples collected from the live animal or tissues collected at post mortem examination. The **spleen** is the tissue of choice but virus has been isolated from lung, liver and bone marrow. In the outbreak in Spain, AHSV was isolated from the **bone marrow** in the tail of a carcass that had been buried for several weeks. However, to maximize the chances of isolating virus, tissue samples should be placed in **virus transport medium** and kept cool while they are transported as quickly as possible to a virology laboratory.

Isolation of AHSV is achieved by intracerebral inoculation of suckling mice or by inoculation of monkey kidney cell lines (VERO and MS) or embryonated hen eggs. Virus isolation can be a slow process necessitating several passages in tissue culture or mice. An **indirect sandwich ELISA** that allows the identification of AHSV antigen within a day or two has been developed.

Virus isolation should be performed in parallel with the ELISA, as it is necessary to isolate the virus to determine its antigenic type. Isolates are typed by virus neutralization with type-specific antisera.

Clotted blood samples should be submitted to the laboratory for serologic examination. Serologic tests for the detection of antibody against AHSV include immunoblotting, CFT, the SNT and ELISA. At present the CFT and an indirect ELISA are the prescribed tests for international trade. The majority of countries require that Equidae from a country that has experienced an outbreak of AHS test negative prior to importation.

A high CF antibody titer is a good indication of fairly recent exposure to virus by natural infection or by vaccination because CF antibodies are not particularly durable and often start to decrease after 6 or 7 wk. SN antibodies take longer to rise but they are more durable. Horses with a negligible titer by the CFT are often positive by SNT and ELISA.

Horses that have been exposed to virus by natural infection mount a greater and more durable antibody response than those exposed to virus by vaccination. Approximately 7.57% of horses do not mount a detectable antibody response when they receive their first dose of vaccine. However, when a booster is administered an anamnestic response is elicited and they usually seroconvert within a week.

If EEV is suspected, virus can be isolated from blood or tissue samples on baby hamster kidney (BHK) cells or detected using a group-specific ELISA. A CFT and an SNT have been developed for measuring antibodies.

Control and eradication

Eradication of AHSV in enzootic areas is not feasible as it is impossible to control the vector and the reservoir host has not been identified. However, it has been possible to control and eradicate the virus outside Africa. Stringent management procedures must be implemented to prevent the spread of AHS in susceptible populations, requiring the cooperation of all sections of the community.

When the disease is confirmed there must be a **total ban on the movement** of Equidae including the cancellation of all horse shows, sales, race meetings and other gathering of Equidae. Strenuous efforts must be made to identify all infected animals and slaughter them. Horse owners should be advised to **stable** their horses from early evening until morning when the *Culicoides* are most active and to spray horses and stables with appropriate **insect repellents** and insecticides. The closing of stable doors and the gauzing of windows have been shown to lead to a 14-fold reduction in numbers of *C. bolitinos and C. imicola* entering stables.

Immediate vaccination of all Equidae and proper identification of vaccinated animals must be undertaken to control an outbreak of AHS. Before the viral serotype is identified it is necessary to use a polyvalent vaccine but a monovalent vaccine can be employed when the virus has been typed. An inactivated vaccine appears to be effective but is more expensive than the traditional live attenuated vaccines.

A **control program** is essential to verify that the virus has been eradicated from an affected area. The main features of such a program are the regular clinical examination of sentinel horses, the investigation of deaths among Equidae and the monitoring of the *Culicoides* population.

EQUINE INFECTIOUS ANEMIA

Introduction

Equine infectious anemia (EIA) occurs in horse populations worldwide and is characterized by antigenic variability of the causal virus and by persistent infection. Affected animals remain viremic and often suffer irregularly recurring episodes of disease. They become lifelong carriers of the virus. EIA is sometimes referred to as **"swamp fever"** as most outbreaks occur in warm wet areas where hematophagous insects that transmit the virus are abundant.

Etiology

The EIA virus belongs to the Retroviridae family that includes the human T lymphotropic virus (HTLV) and the human immunodeficiency virus (HIV)

or AIDS virus. It is a lentivirus and, like other members of this subfamily such as maedi visna virus and caprine arthritis virus, is associated with persistent and debilitating infections. Persistent replication of the virus within the host leads to the periodic emergence of **novel antigenic strains** of EIA. The virus is stable in refrigerated serum but is inactivated by heat (56°C), detergents and organic solvents such as ether.

Epidemiology

EIA was first described in France in 1843 and has subsequently been reported in horses, mules and donkeys in Asia, Africa, North and South America, Australia and occasionally in many European countries including the UK, France and Italy.

The virus is **mechanically transmitted** by biting flies or by contaminated needles, teeth rasps, stomach tubes and any other instrument that may cause abrasion. Several outbreaks due to contaminated sampling equipment have been recorded in **serum production horses**.

All infected horses serve as a potential source of virus for other susceptible horses. Viremia peaks when horses are pyrexic and is usually low when horses appear healthy, thus the role of inapparent carriers in perpetuating the disease may not be very significant.

Horseflies (*Tabanus* spp.), deer flies (*Chrysomyia* spp.), stable flies (*Stomoxys* spp.) and mosquitoes transmit the virus but, because of their large mouthparts, **horseflies** are the most effective natural vectors of EIA. Transmission of EIA is dependent on the interrupted feeding of the vector because the virus does not remain viable in the arthropod for more than 4 h. Horsefly bites are painful which increases the likelihood of interrupted feeding. Although most horseflies interrupted when feeding will return to the same horse unless there is another horse in close proximity, cases of EIA sometimes occur at a considerable distance from an initial outbreak as this vector can travel several miles in a very short period of time.

As few as 10 horsefly bites are sufficient to transmit EIA from infected horses to susceptible cohorts and a single horsefly has transmitted EIA from an acutely infected pony to a susceptible pony. Because of the prevalence of insect vectors, natural outbreaks of EIA usually occur during the summer and early autumn in low-lying marshy areas and river valleys.

Transmission of EIA can occur **transplacentally** but this is more likely if a mare is clinically ill during the gestation period than if she is an inapparent carrier. Foals may become infected after birth by ingesting **virus-contaminated colostrum or milk**.

When conditions are ideal for spread, the morbidity of EIA can approach 100% in a group of horses and the mortality may be as high as 30%.

Clinical signs

The disease may take an acute, chronic or subclinical course. The incubation period varies from a few days to more than 3 mo. The **acute form** is usually associated with the introduction of the virus into a susceptible herd. However, the emergence of a new antigenic variant can give rise to acute clinical signs in a carrier. Characteristic features of the disease are fever, edema of the

dependent parts, hemorrhagic diarrhea, jaundice, petechial hemorrhage on the mucous membranes, anemia and death.

Symptoms of the **chronic form** include progressive anemia, loss of condition, weakness and tachycardia after exercise. Typically, the affected horse suffers recurrent episodes of fever, weakness, anemia, weight loss and edema that may last only a few days or persist for weeks. Sometimes the anemia and edema become more pronounced with succeeding episodes of disease. Recurrences are often stress related and may be provoked by malnutrition, overwork or surgery. The majority occur within the first 3 mo after initial infection. The frequency and severity of the clinical episodes of disease usually decrease with time and most horses become inapparent carriers.

Pathogenesis

The periodic nature of EIA appears to be due to **antigenic change** of the surface glycoprotein of the virus and the periodic release of new strains that evade the host's immune system. In general there is no cross-neutralization between different variants. When a new variant is released there is some delay before the horse adapts and produces antibodies that neutralize the virus.

The virus appears to have a predilection for macrophages and monocytes that provide a vehicle for dissemination to a variety of organs including the liver, kidney, adrenal, brain and heart. The **anemia** in EIA results from hemolysis of erythrocytes to which the virus has adhered and from impairment of bone marrow function. The **glomerulitis** (*q.v.*) of horses with acute EIA appears to be due to the deposition of circulating virus–antibody complexes in the kidney. These complexes may also be responsible for damage to the reticuloendothelial system leading to hemorrhage and edema.

Post mortem findings

The gross lesions commonly seen include enlargement of the liver with accentuated lobular structure, enlargement of the spleen, lymphadenopathy, anemia, jaundice, emaciation, edema and serosal hemorrhages. In chronic cases, emaciation and anemia may be the only gross findings. Lesions are difficult to find in inapparent carriers.

The most characteristic microscopic lesions are **interstitial mononuclear cell infiltrations** in the liver, kidney and spleen. These are most prominent in the periportal areas of the liver. The severity of the hepatic lesions is usually related to the frequency of recurrences of disease. The infiltrates increase when the clinical signs are severe and as much as one third of the liver may be comprised of mononuclear cell infiltrates. The Kupffer cells become enlarged and laden with hemosiderin. These lesions frequently disappear in inapparent carriers.

Generalized **hemosiderosis** (*q.v.*) is common as is glomerulitis. Virus is present in greatest concentration in the liver, spleen and bone marrow.

Diagnosis

Hematologic tests such as a platelet count, a differential white blood cell count, the determination of packed cell volume and a sideroleukocyte count may be helpful indicators in EIA diagnoses but are not pathognomonic.

The virus can be isolated in equine macrophages or equine dermal cells or detected by PCR but the **Coggins test** (*q.v.*), an agar gel immunodiffusion test, has since its development in 1970 formed the basis of most control programs for EIA. The antigen used in the Coggins test, the p36 viral core protein, is very stable and reacts with serum from horses infected with different variants. False negatives have been recorded in a small number of inapparent carriers. Also, although the precipitating antibodies detected by the Coggins test are usually present at the time of onset of symptoms, sometimes they may not be at a detectable level until later (up to 10 days).

More recently developed tests include an **ELISA** that appears to be more sensitive than the Coggins test. However, at present the Coggins test is regarded as the most reliable serologic test for EIA and although some countries will accept a negative ELISA, most countries require a horse to have a negative Coggins test result prior to importation.

Management and control

The antigenic variation of the virus presents a major obstacle to the development of an efficacious vaccine. **No vaccine** of proven efficacy is currently available. Blood transfusions and fluid therapy may assist in recovery from clinical disease but there is no effective means of eliminating EIA virus from an infected horse. The prevention of EIA is based primarily on the detection of infected horses by the Coggins test and their **isolation** from other horses. Since infected horses are the only known reservoir of the virus it is quite feasible to eradicate EIA from an area by testing and slaughter of reactors. The testing of all incoming horses will help to maintain the disease-free status. **Control of vectors** by drainage of swampy areas and by the strategic use of insecticides may help to limit the spread of the disease.

EIA is a **notifiable disease** in many countries including those in the EU, Canada, Sweden and certain states in Australia. Seropositive horses are destroyed in some countries including France and Germany. There is a voluntary control scheme in operation in Canada where horse owners receive financial compensation for slaughter of infected horses. In the USA, the slaughter of infected horses is not compulsory but there is a requirement for a negative test prior to interstate movement of horses. By contrast, within the EU, testing for EIA is only compulsory for horses moving from premises where the disease has occurred. However, all horse owners should be advised to have horses tested prior to introduction to their premises.

EQUINE RABIES

The incidence of rabies in horses, compared with that in many other animals, is low but the disease is of importance because rabid horses may serve as a source of infection for humans. Infected horses may become aggressive and although there are few reports on virus shedding by rabid horses the death of humans infected by rabid horses has been reported. Risks to veterinarians, handlers and other exposed people and animals should always be considered.

Etiology

Rabies is caused by a neurotropic rhabdovirus that belongs to the genus Lyssavirus. Several strains of rabies virus have been identified using

monoclonal antibodies, and non-pathogenic variants can be selected by growing virus in the presence of neutralizing monoclonal antibodies. The virus is **quite fragile** and is readily destroyed by heat, desiccation, ultraviolet light and most disinfectants. It can, however, survive in a refrigerated carcass for several days.

Epidemiology

Rabies occurs throughout most of the world including South America, the USA, Canada and Continental Europe. It is absent from Australia, Japan, Scandinavia, the UK, Ireland and some other countries.

Most warm-blooded animals are susceptible to rabies. Enzootic dog rabies is a major problem in developing countries. The incidence of rabies in people is far higher in these countries than in developed countries where wild animals are the main reservoir of virus.

Horses are moderately susceptible to rabies and usually become infected by the bite of a rabid animal. Infection by inhalation, such as may occur in a cave inhabited by rabid bats, or by the oral or transplacental route is unlikely to play a significant role in the epidemiology of the disease in horses. Rabid dogs and cats are a threat to horses and other domestic animals but **wild animals** are the most likely source of virus in many countries. **Foxes** are the most common reservoirs of the virus in Europe. **Skunks and raccoons** are a major source of infection in parts of the USA and **vampire bats** infect horses in South America. There is some evidence to suggest that the use of a modified live virus rabies vaccine was associated with the induction of rabies in horses during 1981–1982 in the USA. Live rabies vaccines are no longer recommended for use in horses.

Pathogenesis

Rabies virus enters the body by salivary contamination of a bite wound. The virus replicates in the muscle at the site of the bite before invading the **axons** of the peripheral nerves and spreading centripetally to the brainstem and spinal cord. Once the virus enters the **spinal cord** it spreads rapidly throughout the CNS. It is thought that the cerebrospinal fluid may be involved in the spread of the virus at this stage. The virus replicates in the CNS and spreads centrifugally along peripheral nerves to other parts of the body. High concentrations of virus are shed in the **saliva**.

As the virus is present in the nervous system for much of the course of the disease the immunologic response to infection is often minimal.

Clinical signs

The incubation period usually varies from 2 to 9 wk but can extend to 15 mo. The clinical signs are extremely variable and rabies should be considered in the differential diagnosis when a horse is presented with rapidly progressive neurologic disease, especially in countries where rabies is endemic.

Terminally, the signs are those of **diffuse CNS disease** but documented cases indicate that the early signs differ greatly between individuals. They include lameness, pyrexia, anorexia, muscle tremors, colic, ataxia, profuse salivation, teeth grinding and frequent whinnying.

Two clinical forms of rabies are recognized in the horse as in other species: the dumb or paralytic form due primarily to damage to the spinal cord, and the furious form due primarily to damage to the brain. This categorization refers only to the major manifestations of the disease and many cases exhibit clinical features of both types.

Horses that develop the **dumb form** often have ascending paralysis, ataxia and fecal and urinary incontinence. They have difficulty standing, become recumbent, make paddling movement with their forelegs and die. Horses that develop the **furious form** of the disease behave erratically and may attack and bite humans, other animals and inanimate objects. They may bite themselves at a particular site of the body. Such cases usually deteriorate rapidly and paralysis, convulsions and death ensue.

Equine rabies usually has a short course. It is rarely longer than a week and sometimes death occurs as early as 12 h after onset. Rabies is virtually always **fatal in unvaccinated horses** although there is one report of a donkey that recovered from an experimental infection after an illness lasting 11 days.

Diagnosis

Ante mortem laboratory examinations are of limited diagnostic value. Measurement of antibody titers against rabies in serum or cerebrospinal fluid, or examination of skin biopsies or corneal smears by immunofluorescence may give a diagnostic positive result but a negative result does not preclude rabies as a possible diagnosis.

The post mortem diagnosis of rabies can be made from examination of the **brain** using fluorescein-conjugated rabbit antiserum raised against the rabies virus. This test is reported to identify at least 98% of positive cases but testing of sections of the spinal cord is sometimes indicated, especially in horses that had the dumb form of the disease. Histologic examination for the presence of **Negri bodies**, the characteristic large eosinophilic cytoplasmic inclusions that occur in ganglion cells and neurons, is reported to identify 85% of positive cases.

Prevention and control

Countries that are free of rabies maintain this status by the rigorous enforcement of import regulations. The elimination of stray dogs and cats, together with the immunization of pets, plays a major role in the control of the disease in developing countries. In South America, immunization of cattle and the killing of vampire bats by the intraruminal administration of anticoagulants to cattle are widely practiced. In North America and Europe, wildlife control is being replaced by immunization of wildlife as a more humane way of controlling the disease. Baits impregnated with vaccines have been used successfully to vaccinate foxes in Europe.

Several killed rabies vaccines are approved for use in horses in the USA and annual vaccination is recommended. If a **vaccinated horse** is bitten by an animal that may be rabid, it should be **revaccinated immediately** and kept under observation for 90 days.

If an **unvaccinated horse** is bitten it should **not** be vaccinated immediately but isolated for 6 mo and vaccinated 1 mo before the end of quarantine. If at

any stage exposure to rabies is confirmed **the horse should be euthanased immediately**.

People caring for a suspect case should be immunized against the virus. Immunization should also be considered for anyone who has had contact with the horse in the recent past. Veterinarians should take particular care in endemic areas when conducting oral/dental treatments. If a person is bitten by a rabid horse the wound should be thoroughly scrubbed with soap and water and both rabies immune globulin (RIG) and human diploid cell vaccine (HDCV) should be administered as soon as possible.

VESICULAR STOMATITIS

Vesicular stomatitis is characterized by the development of vesicles on the feet and mouth. In horses it is associated with a **very painful lameness** and in cattle and swine it can be confused clinically with foot and mouth disease.

Etiology

Vesicular stomatitis virus (VSV) belongs to the same family as rabies virus, the Rhabdoviridae. Two serotypes have been associated with disease in horses in the USA: the New Jersey type and the Indiana type. There is extensive genetic diversity of viruses within these serotypes but the diseases they induce appear to be clinically indistinguishable.

The majority of outbreaks of vesicular stomatitis (VS) in the USA have been associated with the New Jersey serotype. Many virologists believe that there are additional serotypes of VSV but others maintain that these are variants of the Indiana type. High temperatures (50–60°C) rapidly inactivate the virus, as do common disinfectants such as phenols, formalin and quaternary ammonia compounds.

Epidemiology

Horses, cattle and pigs are susceptible to vesicular stomatitis. Sheep and goats are much more resistant. The disease may be transmitted to people.

The disease occurs in the Western hemisphere and is endemic to Central America, the southern USA and Colombia, Peru, Ecuador and Venezuela. It occurs seasonally every year in Mexico, Central America, northern South America and Ossawa Island, Georgia, in the USA. Major outbreaks in the USA occur irregularly. Outbreaks associated with the New Jersey type have occurred in the southeastern states and outbreaks associated with both the New Jersey type and the Indiana type have occurred in the southwestern states. The 1995 and 1998 outbreaks occurred in the western States and affected 365 and 380 ranches respectively. In 2004 an outbreak was confirmed in horses in Texas. Horses are more susceptible to New Jersey and Indiana type VS than cattle and in one large outbreak 44.7% of horses were infected compared to 4.5% cattle on affected farms.

The **mode of transmission** of the virus is not fully understood. The virus cannot penetrate intact skin but can enter through abrasions, wounds and mucous membranes, thus the feeding of poor quality rough forage that causes abrasions in the mouth facilitates virus spread.

Transmission may occur by **direct contact**, and **saliva and vesicular fluid** from clinically affected animals are highly infective. However, several outbreaks have occurred in horses that have had no contact with infected animals and it is widely believed that the virus is transmitted by **insect vectors**. In support of this theory the virus has been isolated from sand flies, horn flies, black flies and mosquitoes, and experimental evidence exists that VSV can be transmitted by black flies to swine. Disease outbreaks usually occur in August and September when these insects are abundant. Very few outbreaks have been recorded after the onset of cold weather with frost.

The disease is prevalent in low-lying wooded areas with heavy rainfall. In a survey in Utah in 1982 it was shown that horses stabled in an environment with some type of insect control were much less likely to contract the disease than horses kept on pasture near a river. Trajectory analysis of winds suggests that carriage of infected insects on the **wind** may play a role in the spread of the disease.

The **reservoir** of the virus is unknown although there is serologic evidence of infection of many wild mammals including elk, deer, feral pigs, skunks and raccoons. It has also been suggested that the reservoir may be a plant or insect and that vertebrates are only accidental hosts. There is a spatiotemporal association between grasshopper outbreaks and VS epizootics and cattle fed VSV-infected grasshoppers can develop VS.

People who have contact with infected animals, particularly those who routinely examine the mouth of infected animals, who have abrasions on their hands or arms and who have exposure to infected saliva through the eye or skin, are at risk of contracting the disease. A higher risk is associated with examining horses than cattle. Since the disease in humans resembles **influenza**, many rural cases are probably never diagnosed. Serologic studies in Georgia, New Mexico and Panama have revealed that 25–90% of farmers in some areas have antibodies against VSV.

Pathogenesis and clinical signs

Following a 2–8 day incubation period, there is pyrexia and inflammation of the mucosa of the mouth and tongue with the formation of vesicles. The vesicles rupture and leave **ulcers**. The resultant irritation leads to **salivation** and a reluctance to eat. This can result in considerable loss of condition. This is frequently the stage at which the clinician is consulted, i.e. vesicular lesions are not observed but the horse is anorexic and salivating excessively and the lesions are ulcerated or crusted.

In severe cases, ulcers may develop on the nasopharynx, larynx and turbinates, resulting in **epistaxis and respiratory distress**. Lesions may also be found on the mammary glands of lactating mares and the prepuce of male horses. Ulceration of the coronary band is common and results in lameness, which in severe cases may culminate in the sloughing of the hoof.

Unless complicated by secondary bacterial infection the oral lesions usually heal within a couple of weeks. Lesions on the feet may take longer because of secondary infection and trauma. Lameness may persist if a horse develops a severe coronitis and cracked hoof walls. Mortality is rare but may occur if there is severe secondary bacterial infection of the mouth, which prevents the animal from eating or drinking.

Diagnosis

A definitive diagnosis of vesicular stomatitis can be made by isolating the virus from the **vesicular fluid** or by **serologic examination** of two blood samples collected 10–14 days apart. Seroconversion can be detected by the ELISA, CFT or by SNT.

Management and control

Vesicular stomatitis is a notifiable disease in the USA and in the EU. Infected horses should be **isolated** and supplied with ample water and soft palatable feed. The use of systemic antibiotics may be indicated if the horse has secondary bacterial infection. Fluid therapy and nasogastric tube feeding are indicated if the horse is unable to eat or drink. During an outbreak care should be taken to avoid any injury or abrasions to the hoofs. Involvement of the feet may necessitate treatment similar to that employed in cases of laminitis (*q.v.*).

The disease is rarely fatal and usually runs its course in a couple of weeks. If VS is present in an area, insect control, the removal of animals from wooded pasture and their confinement in stables will help to curtail the spread of the virus. In the USA all livestock on affected premises are quarantined for several weeks until they no longer pose a threat to other livestock.

VS has been classified by the OIE as a list A disease because it is clinically indistinguishable from foot and mouth disease. Thus, VS is subject to stringent control measures wherever it occurs and can result in trade restrictions.

TOGAVIRAL AND FLAVIVIRAL ENCEPHALITIDES

Etiology

The togaviruses are small, enveloped RNA viruses. Within the family **Togaviridae**, viruses of the alphavirus genus including **eastern encephalitis virus (EEV), western encephalitis virus (WEV)** and **Venezuelan encephalitis virus (VEV)** are associated with encephalitis in horses.

Japanese encephalitis virus (JEV) and **West Nile virus (WNV)** are members of the genus Flavivirus of the family Flaviviridae. The flaviviruses are small, enveloped RNA viruses that were considered a genus within the Togaviridae family before they were reclassified because of lack of antigenic relatedness and differences in biochemistry and replication strategy.

The alphaviruses and most flaviviruses including JEV are classified biologically as arboviruses because they are transmitted by **arthropods**. These viruses are geographically restricted by the availability of appropriate vectors and reservoir hosts. They can extend to new areas, for example WNV in North America, by the emergence of more virulent or more efficiently transmitted strains.

Epidemiology

Alphavirus encephalomyelitis was first described on the eastern coast of the USA in 1931. The etiologic agent was not identified as a virus until 1933, the same year that it was shown that the diseases on the east and west coasts of the USA were produced by two antigenically distinct viruses. The virus isolated during an epizootic in California, when approximately 3000 horses died, became known

as WEV and the virus isolated during an epizootic along the Atlantic seaboard became known as EEV. These viruses have been responsible for devastating periodically recurring epizootics and sporadic outbreaks of disease in the Western hemisphere.

Eastern encephalitis (EE) occurs in the eastern half of North America but it is not, as originally thought, restricted to the Atlantic seaboard. Epizootics have occurred largely in the seaboard states, especially New Jersey and Massachusetts, but also in the southeastern states (Georgia, Florida and Louisiana), the Caribbean, Panama, Central America and South America.

The distribution of **WEV** is more widespread than that of EEV, encompassing virtually all of North and South America. Large-scale epizootics have occurred in Canada and in western and central USA. It is estimated that over 180 000 horses died in a series of outbreaks in California in the 1930s. A few cases, but no epidemics, have occurred in eastern USA. A variant of WEV, the Highland J virus, has been reported in Florida.

VEV was first isolated in Venezuela in 1936 and has been shown to be antigenically distinct from WEV and EEV. Subsequent large outbreaks of disease were reported in Venezuela, Colombia, Ecuador, Peru, Trinidad, Central America and the USA.

JEV is a major problem in most of Asia. Epizootics are most commonly encountered in China, Korea, Japan and the eastern province of the Soviet Union. The virus has been found in the Western Province of Papua New Guinea and northern Australia.

WNV was first isolated in 1937 in Uganda and was subsequently identified in birds, humans and horses in Africa, Asia, the Middle East and the Mediterranean region. In 1999, WNV was isolated for the first time in North America. Clinical cases and deaths associated with WNV infection were confirmed in humans, horses and birds in a limited geographic area extending from New York. Within three years there was complete transcontinental movement of WNV. The means by which WNV was introduced into the USA is unknown but American isolates are closely related to a virus isolated in Israel in 1998.

The virus is now permanently established in the Western hemisphere. In 2003, almost 10 000 human cases were reported to the Centers for Disease Control (CDC). In 2002, there were 14 717 equine cases, and over 5000 equine cases were reported in 2003. Outbreaks have occurred in Europe. In Tuscany, Italy, in 1998 there were 14 clinical cases in a wetland area that is a breeding ground for migratory birds. In the Camargue, a similar environment in France, there were 58 cases of equine encephalitis in 2000. However, the virus has not become endemic in Europe.

WEV, EEV, VEV, JEV and WNV have **sylvatic life cycles**, involving bird and rodent reservoirs and insect vectors. Transmission of these viruses to the horse is nearly always by the bite of an infected **mosquito**. The mosquito ingests infected blood from the amplification host. The virus replicates in the cells of the mid-gut and travels via the hemolymph or nerves to the salivary glands. This extrinsic incubation period varies from 3 days to 2 wk. The mosquito remains infected for life and its longevity does not appear to be affected by the presence of the virus.

Culex tarsalis mosquitoes, which maintain WEV, breed prolifically throughout the summer in flood pools, rice fields, lake sides and irrigated places. They

feed readily on birds, horses and, to a lesser extent, people. In contrast, *Culiseta melanura*, which transmits EEV from bird to bird, breeds in saltwater swamps and does not travel far from its habitat. It rarely feeds on horses or people. EEV is transmitted from birds to humans and horses by other species of mosquitoes. These factors may explain in part why EEV is less prevalent than WEV.

There are many different subtypes and strains of VEV, some of which (the sylvatic viruses) appear to be non-pathogenic for horses while others (the epizootic viruses) can cause disease epizootics. Different strains of sylvatic VEV replicate in specific types of *Culex* mosquitoes which breed in swamps and have only limited movement. Epizootic strains of VEV are transmitted by many species of mosquitoes and other hematophagous insects including black flies (*Simulium* spp.). The diverse feeding preferences of the many vectors of epizootic strains of Venezuelan encephalitis (VE) contribute to the **widespread dissemination** of the virus.

JEV is transmitted by *Culex tritaeniorhynchus* and other related mosquitoes.

Over 40 mosquito species are competent vectors for WNV. *Culex* mosquitoes, particularly *Culex pipiens*, appear primarily responsible for epizootic transmission. **Ticks** may also serve as vectors for WNV.

The distribution of togaviruses and flaviviruses is governed by their transmission cycles. Epidemics occur at irregular intervals. In temperate zones they usually occur in mid to late summer and in the tropics they occur during the wet season. High humidity and moderately warm temperatures favor the long life and mobility of mosquitoes. Epizootics usually halt if the weather becomes cold or if there is a drought. Thus, in northern temperate regions if the first cases of encephalitis are diagnosed in late September a full-scale epizootic is unlikely to occur. Overwintering mosquitoes contribute to virus maintenance. Vertical transmission of WNV has been demonstrated in some species of mosquitoes.

Alterations in the environment and human behavior contribute to changing patterns of disease. Mosquitoes can be carried on **surface winds** at temperatures of 13°C or higher. They land when they encounter a cold front or rain. In this way climatic change leads to variation in the location and timing of outbreaks from year to year. Similarly **human management** of land affects the incidence of the disease such that clearance of land and drainage of marshes and swamps can destroy mosquito habitats while poorly managed irrigation systems can create new mosquito breeding sites. Periods of drought often lead to an increase in the amount of **stagnant water** available as breeding sites.

The distribution of the viruses is also governed by the **movement** of the amplification or reservoir hosts. Swamp-dwelling birds such as the red-winged blackbird are the reservoirs for EEV although passerine birds that fly into the swamps may also become infected. The passerine birds such as swallows, sparrows and blackbirds that amplify and transmit WEV may transport the virus over considerable distances. The sylvatic varieties of VEV are amplified in rodents such as the rice rat, the spiney rat and the cotton rat. Natural wildlife reservoirs for the epizootic varieties have not been identified.

Horses and people are **dead-end hosts** for WEV and usually EEV. They do not develop significantly high viremias to infect mosquitoes and to maintain the cycle. This is also true of the sylvatic varieties of VEV but not of the epizootic varieties. Horses experience high titer viremias when infected with an epizootic strain of VEV and play an important role as amplification hosts. They shed

virus in **nasal and ocular secretions, saliva and milk**. Virus transmission can occur by **aerosol**.

During an epizootic of VE large numbers of horses become infected within a short space of time. The disease can spread up to 32 km per day and epizootics usually cease when **susceptible horses** are no longer available to support the disease.

The major amplification hosts of JEV are water birds, such as the black crowned night heron and egrets. Pigs also serve as efficient amplifying hosts and the spread of the virus in the last three decades is thought to be due, at least in part, to the expansion of the pig breeding industry in Asia. **Horses and people appear to be dead-end hosts**.

WNV is amplified by both wetland and terrestrial birds and has been isolated from crows, cranes, mallards, doves, eagles, robins and many other species in the USA. Crows appear to be highly susceptible and thousands of deaths in crows and other wild birds have been recorded in the USA since the introduction of WNV. Recent European outbreaks differ in that they do not appear to have been preceded by notification of any increase in deaths among wild birds. The first report of such deaths concerned the 1998 outbreak in storks in Israel and it has been suggested that European birds may have adapted to certain strains of WNV and that the epidemic nature of the disease in the USA may have been due to the lack of avian adaptation or to a more virulent virus strain.

The comparison of the amino acid sequence of the envelope protein of the European WNV isolates and viruses from Israel in 1998 and the USA in 1999 showed only two amino acid changes that are linked to attenuation in other flaviviruses. WNV has been associated with illness and death of mammals such as reindeer, mountain goats, squirrels, seals, sheep, new world camelids and dogs but these animals are not thought to play a significant role in the maintenance and amplification of the virus.

Like horses, humans are usually infected by a bite from **mosquitoes**. Horses and humans are considered incidental hosts and horse to human transmission has never been recorded. Also, like horses, humans only appear to experience a **transient viremia** but intrauterine transmission and transmission via blood donation and organ transplants have been reported.

Clinical signs

It is not possible to differentiate between EE, Western encephalitis (WE), VE or Japanese encephalitis (JE) on the basis of clinical findings. Infection with any of these viruses can result in subclinical disease, a generalized febrile illness with depression, anorexia and tachycardia or encephalitic disease, which can be fatal. The initial signs may go undetected and **sudden death** of apparently healthy horses has been reported with VEV infections.

The typical signs of **encephalitic disease** begin with fever and depression. Inappetance and reluctance to drink can result in dramatic weight loss. Hematologic examination often reveals a severe leukopenia. It may take from 12 h to 5 days before the neurologic signs develop. Some horses exhibit **transient excitement** and restlessness. They may walk in circles, press their head against fixed objects and chew aimlessly. Intense pruritus has also been recorded. Such horses can be **aggressive**.

This period of hyperactivity is followed by a period of **profound depression**. Typically the horse is unwilling to move and stands with its legs apart, its head drooping or supported on a fixed object. The lower lip becomes pendulous and the tongue may hang out. There may be tremors of the facial muscles and dysphagia. The horse appears to suffer from **faulty perception** and becomes incoordinated and has difficulty in maintaining its balance. Progressive ataxia and weakness result in recumbency. Seizures may occur with spasmodic movements of the legs.

EEV and VEV are typically **more virulent** than WEV, JEV or WNV. Approximately 80% of horses with EE die less than 5 days after the onset of neurologic signs. Those that survive frequently have residual CNS damage such as visual deficits and behavior and learning disabilities. The fatality rate among horses with epizootic VE may reach 80%. The fatality rate of WE is approximately 25% but it can be as high as 50% during some outbreaks. If the clinical course is not prolonged or complicated and the horse does not become recumbent complete recovery is often possible.

Horses that survive paralysis and recumbency are more likely to have **neurologic sequelae**. The fatality rate among horses with JE has been reported as 5% in endemic areas, rising to up to 40% in seasonal epidemics in Japan. Mortality rates of 33% to 45% have been reported among horses in WNV outbreaks in the USA and Europe.

Pathogenesis and pathology

The virus replicates at the site of infection and in the regional lymph nodes. This is followed by a period of **extraneural amplification**, when the virus spreads via the blood to organs such as the liver and spleen. At this time the horse may experience a generalized febrile illness and in many cases the disease is self-limiting. If the virus is not successfully cleared by the reticuloendothelial system it may cross the blood–brain barrier and encephalitis ensues. The gray matter, including the pons, medulla, spinal cord, cerebellum, thalamus and olfactory bulbs are most often affected. The most common post mortem findings are edema and hemorrhage of the brain and spinal cord. Histologic examination reveals neuronal lysis, gliosis, neuronophagia and focal perivascular round cell infiltration. These lesions are not pathognomonic for any of the encephalitis viruses.

Diagnosis

Clinical diagnosis of togaviral or flaviviral encephalomyelitis is based on the clinical signs, the geographic location, the season, a history of contact with vectors and knowledge of other cases in the area. However, **clinical differentiation** from other conditions causing multifocal neurologic defects such as trauma, hepatoencephalopathy, rabies, verminous encephalitis, protozoal myeloencephalitis and bacterial meningoencephalitis may be difficult. Definitive diagnosis of viral encephalomyelitis and identification of the etiologic agent requires **laboratory testing**.

Viruses can be isolated from brain, blood and cerebrospinal fluid. They are also isolated without difficulty from avian blood and mosquitoes. They produce a **cytopathic effect (CPE)** in nearly all vertebrate cells. Baby hamster

kidney cells (BHK-21) and African green monkey kidney cells (VEROs) are widely used. Embryonated eggs are also highly susceptible. Different strains of these viruses may differ in growth characteristics in tissue culture. For example, virulent strains of VEV produce larger plaques in VERO cells than naturally attenuated strains. Viruses can also be detected and typed by PCR. When submitting blood samples to a virus isolation laboratory clinicians should be aware that there is a greater likelihood of isolating virus from a horse in the **early febrile stage** of the disease because viremia has often terminated by the time the nervous signs are manifested.

Serologic diagnosis is based on a specific rise in antibody titer in paired, acute and convalescent samples. Tests used for this purpose include HIT, CFT, virus neutralization (VN), immunodiffusion and ELISA. Because the antibody titers against these viruses rise quite quickly (VN antibodies are often detectable within 7 days post infection) and it may take several days, particularly with VEV, for the horse to exhibit signs of neurologic disorder, it is advisable during an outbreak to collect an **acute serum sample** from any horse with an elevated temperature. Then if the horse shows neurologic signs the second convalescent sample can be collected to confirm the diagnosis. An IgM capture ELISA technique has been developed for some of the encephalitis viruses and permits diagnosis with a single serum sample.

Some sylvatic and epizootic strains of VEV are antigenically closely related and caution should be exercised when interpreting serology results in an area where **sylvatic VE viruses** are endemic, for example in the Florida Everglades. Conclusive virus typing requires PCR or antigenic characterization of an isolate using monoclonal antibodies.

Treatment

Before initiating intensive nursing and treatment, it is wise to evaluate the chance of survival and the possibility of residual CNS damage. The prognosis for a horse with EE or VE is poor. The prognosis for a horse with WE, JE or WN encephalitis is better; with **intensive nursing** many affected horses recover.

In the absence of antiviral agents, supportive measures and symptomatic therapy are the primary modes of therapy. Throughout the therapy it is important to **minimize self-inflicted trauma** by using heavily padded bedding, a padded stall, leg bandages and a padded helmet. Every effort should be made to maintain the horse in sternal recumbency. Slinging will restrain the affected horse and prevent the problems associated with prolonged recumbency. If it is not possible to maintain the horse in sternal recumbency or in slings it should be turned on the opposite side every 2 h.

Supportive measures include feeding by stomach tube, the administration of balanced fluid solutions and the administration of **cold water** or alcohol baths to decrease pyrexia. It may be necessary to **catheterize the bladder** and to empty the rectum manually. **Secondary bacterial infections** should be treated with appropriate antibiotics. Corticosteroids are sometimes administered to decrease inflammation of the CNS but may make the animal more susceptible to secondary bacterial infection. Osmotic diuretics may decrease intracranial edema in cases with severe progressive depression. The administration of barbiturates, chloral hydrate or diazepam may be indicated to control seizures.

Control

Control of alphavirus and flavivirus can be achieved by **vaccination** and **vector control**. Mosquito habitats can be destroyed by drainage and by the elimination of **stagnant water**. Individual horses can be protected using insect repellents and screens. The incidence of alphavirus and flavivirus encephalitis is much lower in stabled horses than in horses on pasture. Major epizootics sometimes necessitate massive aerial spraying of insecticides. However, this raises environmental concerns and insect resistance may result.

Bivalent (WEV and EEV) and trivalent (WEV, EEV and VEV) **formalin-inactivated vaccines** are available for intradermal and IM administration. A live attenuated VEV strain TC-83 vaccine has proved very effective in the past but has the potential to **revert to virulence**. Thus killed virus vaccines are preferable. Initial vaccination schedules for the inactivated vaccines vary according to manufacturers' recommendations and are followed by annual revaccination prior to the mosquito season. However, in areas with a long mosquito season twice-yearly vaccination is strongly recommended to ensure complete protection. Vaccinating mares during the last month of pregnancy will increase the antibody titer of the colostrum. Because the duration of maternal immunity is very variable and can interfere with the foal's ability to mount an antibody response to vaccination, it is advisable to check the antibody titer of the foal before beginning its vaccination program.

An inactivated vaccine for JE produced by Kaketsuken and Nisseiken is available in many Asian countries where there is mass vaccination of racehorses. A live attenuated vaccine has been used in China. In some areas of Japan, pigs have been vaccinated against JE to reduce their threat as amplification hosts.

In 2002, an inactivated WNV vaccine, West Nile-Innovator (Fort Dodge), was licensed in the USA. It is recommended that horses receive two initial doses 3–6 wk apart before the mosquito season and thereafter an annual booster. However, many clinicians administer more than one booster per year. A booster should always be given just prior to the start of the mosquito season. More recently a **canarypox virus vector vaccine** for WNV (Recombitek) was approved by the United States Drug Administration (USDA) for use in horses. The manufacturers, Merial, have demonstrated that two doses at 5 wk intervals conferred significant protection to horses against WNV viremia.

A good **surveillance system**, including surveys of the size of the mosquito populations, the detection of virus in vectors and in reservoir hosts and the close monitoring of strategically situated sentinel flocks of domestic birds, is an invaluable aid to the prediction and prevention of epizootics. Such a system is in place in several states in the USA for WEV, EEV, VEV and WNV where it facilitates strategic vaccination and vector control. A sentinel pig surveillance system is in place for the detection of JEV in Australasia.

Human health considerations

EEV, WEV, VEV, JEV and WNV cause **encephalitis in humans**. Outbreaks of encephalitis in horses usually precede outbreaks in humans. Thus, it is important that cases of equine encephalitis are rapidly diagnosed and that state officials and the medical profession are alerted to the likelihood of an outbreak in

humans. Veterinary clinicians, like the rest of the public, should be aware of the possibility of contracting encephalitis from mosquitoes during epizootics and from contact with infected horses in the case of VE.

Horses with EE, WE and JE experience low titer viremia and thus are unlikely to transmit the disease to humans via mosquitoes. Horses with VE can serve as an indirect source of infection.

There are numerous reports of laboratory workers contracting encephalitis by aerosol. When performing a post mortem on a suspected case extreme precautions should be taken not to create an aerosol when removing the brain and spinal cord and to avoid puncture wounds with contaminated bones. Laboratory workers should be adequately vaccinated against the type and strain of virus that they are handling.

ROTAVIRUS

Rotaviruses are a major cause of diarrheal illness in infants and young animals in most areas of the world. It is estimated that equine rotavirus is responsible for more than 25% of cases of **foal diarrhea**.

Etiology

Rotaviruses are classified as a genus of the family Reoviridae. Equine rotaviruses belong to group A and are further subdivided into serotypes by neutralization with hyperimmune guinea pig or rabbit antiserum. The rotavirus genome contains 11 segments of double-stranded RNA. These segments are easily visualized by polyacrylamide gel electrophoresis (PAGE) and this procedure has served as a useful epidemiologic tool to differentiate strains. However, some viruses that belong to different serotypes are indistinguishable by PAGE. There is no in vitro marker for virulence.

It appears that cross infection from other species is rare but the genetic relatedness of equine rotavirus strain H-1 to porcine rotaviruses has led to the suggestion that transmission from pigs to horses may occur.

Epidemiology

Rotavirus disease is characterized by high morbidity and low mortality. The virus is highly contagious and is transmitted by the fecal–oral route. The incubation period can be as short as 18 h. The first signs are often **depression** and **failure to suck**. Diarrhea commences between 1 and 5 days post infection.

On affected stud farms the morbidity in foals is usually less than 100% and there is marked individual variation in the severity of the disease. Some foals remain **asymptomatic** while their cohorts become **severely dehydrated**. Foals younger than 4 mo are most susceptible, and foals born to mares that have recently been introduced to a stud farm are often more severely affected than the foals of resident mares. The offspring of some mares appear to be particularly vulnerable each year suggesting that the mare does not have a protective immunity against rotavirus or that there is poor concentration of maternal antibodies against the virus in her colostrum.

Some studs have **recurrent problems** with rotavirus infection. This can be due to **poor hygiene** and bad management or more usually to a **dense stocking**

rate which facilitates a build-up of virus. Rotavirus is frequently detected in the feces of foals that are clinically normal and it appears that the infective dose is an important determinant of the disease. Large quantities of the virus, up to 10^8 infective doses per gram of feces, are shed by affected foals. Virus may be shed prior to onset of diarrhea and after recovery. Other factors that influence the outcome of infection are strain virulence and the age and immune status of the foal.

Rotaviruses are highly resistant and can survive up to 9 mo in a contaminated environment. Thus, they can survive on **contaminated premises** from one breeding season to the next, causing a recurrent disease problem.

Clinical signs

The clinical signs are depression, inappetance, diarrhea, mild colic and dehydration. Pyrexia is not a major feature. Both increased and decreased borborygmi have been reported. In young foals the **dehydration** can be fatal. Older foals may not exhibit the typical profuse watery diarrhea but show signs of abdominal pain.

Pathogenesis

Rotavirus infects the enterocytes primarily of the jejunum and ileum and causes atrophy of the proximal third of the villi. This leads to **impairment of digestion** and absorption of nutrients. The crypt cells are not infected and secretion progresses normally or is increased as they proliferate in an attempt to replace the damaged cells.

The undigested material results in an **osmotic drain** of body fluid into the intestinal lumen. The osmolarity of the intestinal contents is increased by **bacterial fermentation** of unabsorbed materials. The colon in the foal does not have a fully functioning microflora and is unable to absorb the excess fluid. The result is **profuse diarrhea** and subsequent dehydration.

Duodenal infection has been demonstrated and it has been suggested that mucosal damage combined with altered blood flow and a decrease in the number of goblet cells may cause ulcers. However, a consistent relationship between gastroduodenal ulcer disease (*q.v.*) and rotavirus antigen in the feces has not been demonstrated.

Diagnosis

Rotaviruses are fastidious and difficult to isolate routinely in tissue culture. Infectivity is enhanced if samples are pretreated with trypsin and the cell monolayers propagated in roller tubes in maintenance medium supplemented with trypsin. Diagnosis usually depends on the detection of virus or virus antigen in the **feces**. Two grams of feces should be collected from the rectum if possible. Freshly voided feces can be submitted to the laboratory but rectal swabs are unsuitable. Samples should be kept cool **but not frozen** while they are transported to the laboratory. The samples can be examined for the presence of virus by electron microscopy, which is highly specific but rather insensitive. Other disadvantages of this method of diagnosis include the expense and the need for an experienced operator.

ELISA and latex agglutination kits designed primarily for the detection of human rotavirus provide a very useful means of diagnosing equine rotavirus. They are used extensively by people caring for sick foals who require a rapid diagnosis. It has been suggested that for maximum sensitivity and specificity the method of choice for equine rotavirus diagnosis is the detection of viral RNA by PAGE. However, this is a significantly more time consuming technique than the technically simpler ELISA and latex agglutination tests.

Treatment

Rotavirus enteritis is usually **self-limiting**, lasting a week or so, but it is essential to **replace fluids and electrolytes** lost because of diarrhea. The incorporation of electrolytes in the drinking water is adequate for mildly affected foals. If lactase deficiency is suspected it is important to **reduce milk intake**. Foals may need to be muzzled and fed mares' milk diluted with a glucose and electrolyte solution via a stomach tube. Balanced electrolyte solutions, for example **lactated Ringer's** solution, should be given IV in cases where severe diarrhea and systemic signs are present. One liter of Hartmann's solution (**lactated Ringer's** solution) can be given in a 50 kg BW foal prior to evaluating serum electrolytes and the initiation of a calculated fluid therapy regimen (*q.v.*).

Sequential blood samples should be collected for hematologic and biochemical analysis including an estimation of total plasma protein. The administration of plasma is recommended for foals in danger of circulatory collapse. Acid-base disturbance can be monitored by blood gas and blood pH estimations. IV administration of **sodium bicarbonate solution** will help to correct acidosis but care must be taken as overloading the system can have untoward effects (*q.v.*). Persistent diarrhea can lead to potassium deficiency, which can be corrected by the administration of 8 g/100 kg BW t.i.d. potassium chloride PO.

Intestinal protectants (*q.v.*) such as kaolin (4–8 mL/kg BW b.i.d.) or bismuth subsalicylate (0.5–1 mL/kg BW 3–4 times daily) and **anti-ulcer drugs**, e.g. ranitidine (6.6 mg/kg BW t.i.d. PO, or 2 mg/kg BW b.i.d. IV) or omeprazole (1 mg/kg PO s.i.d.), are sometimes administered to foals with rotavirus diarrhea but **broad-spectrum antibiotics should be avoided** as they inhibit the development of the large intestine microflora. **Probiotics** and **natural yogurt** may help to restore the normal intestinal flora. Dose rate is empirical. Hyperimmune plasma (*q.v.*) can be administered orally or IV in accordance with the producer's recommendations.

Control

Good management will help to prevent a build-up of virus in the environment and decrease the incidence of rotavirus-induced diarrhea. Mares and foals visiting a stud should be **isolated** from resident mares and foals.

Povidone or iodine scrubs should be provided for handwashing and disposable gloves should be worn by anyone handling a foal. The stud farm should supply **disposable protective clothing** for use by the veterinary surgeon.

Rotating mares through a foaling unit can lead to a build-up of virus unless strict attention is paid to cleaning and disinfection procedures. After each foaling, the **foaling box** should be thoroughly cleaned with a pressure spray

and detergent prior to disinfection with a product that is active against rotaviruses, e.g. **phenol** or iodine.

Foals suffering from rotavirus-induced diarrhea should be moved immediately with their dams to an **isolation facility**. The handler in the isolation facility should not be in contact with other healthy horses. Any barn where a case of diarrhea occurs should be **steam cleaned** and disinfected. **Feces should not be spread on pasture**.

Studies in other animals have indicated that antibody in the lumen of the small intestine plays a much greater role than systemic antibody in resistance to rotavirus disease. Thus vaccination against equine rotavirus is aimed at effecting adequate lactogenic immunity. An **inactivated oil adjuvanted vaccine**, Duvaxyn R (Fort Dodge), is available. It is administered by IM injection to mares at 8, 9 and 10 mo of pregnancy. The vaccine appears to be safe and observations in the field suggest that it reduces the incidence and severity of disease. The generation of efficacy data has been complicated by the absence of a challenge model for the virus. Thus the vaccine only has a conditional license in EU countries. Some clinicians administer additional doses of vaccine to mares post foaling and others vaccinate foals. However these vaccination regimens are not included in the manufacturer's recommendations.

HENDRA VIRUS

In 1994, a previously undescribed disease occurred in racing stables in Hendra, a suburb of Brisbane, Australia. One human and 14 horses died. The causal virus was known initially as equine morbillivirus but was renamed Hendra virus.

Etiology

Hendra virus (HV) is the type species of a new genus within the subfamily Paramyxovirinae. It is closely related to **Nipah virus (NV)**, a virus that emerged in 1998 in Malaysia causing fatal encephalitis in humans and respiratory disease in swine.

Epidemiology

The first identified outbreak commenced on the 9th September 1994, when a horse died from **hyperacute respiratory disease** in a Thoroughbred training yard. Within 20 days there were 13 further deaths. Ten in-contact horses died at the yard and a single horse on each of three connected properties died. The trainer of the horses died on the 27th September. He had been closely involved with the affected horses and had abrasions on his hands and arms. His assistant also suffered from respiratory disease but recovered.

In October 1995 the husband of a veterinary surgeon was referred to Brisbane Royal Hospital with encephalitis, paralysis and seizures. He had assisted his wife at the necropsy of two horses in August 1994. One horse died from acute respiratory disease and the other displayed neurologic signs. The horses died 10 days apart and neither gloves nor masks were worn at the necropsy. Subsequent to the necropsy the man contracted meningitis but recovered. He subsequently suffered from persistent fatigue before developing epileptic

seizures and becoming comatose. He was seropositive for Hendra virus and retrospective analysis of archived samples from the horses also demonstrated the presence of the virus. His wife tested seronegative. No direct link between these cases and the outbreak in Hendra was demonstrated.

In 1999 a Thoroughbred mare in Cairns died after an illness lasting 24 h. Another horse that had been her companion for the previous 2 mo remained seronegative.

In 1994 and 1995 over 4000 horses were serologically tested in Queensland. All were seronegative. Wildlife serosurveys of almost 50 species gave negative results with the exception of **flying foxes** (family Pteropodidae), also known as fruit bats. All four species of these Pteropus bats have been shown to be seropositive with over 20% of the population in eastern Australia showing evidence of exposure to HV. The virus has been isolated from the uterus of the bats. They give birth in autumn and were occasionally found in the trees in the paddocks grazed by the affected horses. No disease has been reported in fruit bats but vertical transmission has been demonstrated. Bats of the genus *Pteropus* also appear to be the reservoir for Nipah virus in Malaysia.

Virus was isolated from the **urine** and **oral cavity** of infected horses and from the kidney at necropsy. There was no evidence of virus excretion from the respiratory tract, feces or conjunctiva. Virus was also isolated from the kidneys of the trainer who died in 1994 and from the urine of cats and guinea pigs experimentally inoculated with HV. Although horse to horse transmission appears to have occurred in the training yard in Hendra, it would appear that the virus is not highly contagious and that aerosol transmission is inefficient.

The humans affected had very close contact with infected horses. In Hendra the trainer had tried to clear the air passages of the index case per os and the assistant had restrained the mare in the terminal stages of the disease. The veterinarian's husband in Mackay had not worn gloves or a mask at the necropsy. No bat to human transmission has been reported but it has been suggested that the **Australian paralysis tick**, *Ixodes holocyclus*, could play a role in the transmission of virus from bats to other mammals.

Clinical signs

The incubation period is usually between 8 and 11 days. An **acute respiratory disease** usually results in **death** within 1–3 days. Clinical signs include pyrexia, increased respiratory and heart rates, depression, anorexia and severe pneumonia. Subcutaneous edema, frothy nasal discharge and neurologic signs have also been observed. In the outbreak in Hendra, seven infected horses recovered and three of these showed virtually no clinical signs.

In the first outbreak the trainer and his assistant suffered an influenza-like illness with respiratory disease, fever and myalgia. The trainer died of kidney and heart failure. The man who died in 1995 showed primarily neurologic symptoms culminating in fatal encephalitis.

Pathology

In horses the most significant lesions are **pleural and pericardial edema** and **congestion and ventral consolidation of the lungs**. Hemorrhages are present in the lung parenchyma and in some cases the airways are blocked by foam.

Histologically, the main lesions are interstitial pneumonia and severe vascular degeneration leading to widespread edema. Syncytial giant cells with cytoplasmic inclusion bodies are present in the vascular endothelium.

Diagnosis

The virus can be isolated in cell cultures and immunoperoxidase and immunofluorescence tests exist for virus detection. PCR assays have also been developed. Serologic tests include an SNT and an ELISA.

Control

The virus does not appear to be very contagious. To date, outbreaks have been managed by slaughter of seropositive horses and movement restrictions of horses within a designated control zone surrounding the affected premises. The drug **ribavirin** has been shown to be effective against the virus in vitro and may have potential for use in humans.

BACTERIAL DISEASES OF THE NEONATE AND YOUNG FOAL

INTRODUCTION

Foals that do not receive a sufficient quantity of **colostral antibodies** are at risk from bacteria that can cause septicemia, respiratory, enteric, locomotor or articular disease or concurrent combinations of these conditions. The principal organisms involved are species of *Actinobacillus*, *Clostridium*, *Escherichia*, *Salmonella*, and *Streptococcus*. Infections with other organisms, such as *Klebsiella pneumoniae*, occur sporadically.

The **septicemias** of the newborn foal are largely indistinguishable clinically and have the common features of increasing lassitude, reluctance to stand or feed, hypo- or hyperthermia and the signs of metabolic disturbances and shock, with tachycardia and tachypnea (*q.v.*). A good laboratory can normally demonstrate that the plasma of affected animals is acidotic and hypoglycemic, with IgG level $\leqslant$800 mg/dL, and that the total and differential white count is abnormal. Determining which organism is producing the septicemia requires blood culture, the materials for which are readily available.

In the very young animal that does not die from septicemia (or severe bacteremia), many of the causal organisms tend to localize and persist, particularly in the joints and tendon sheaths. In the case of the foal, antimicrobial therapy needs to take this fact into account.

ACTINOBACILLOSIS (SHIGELLOSIS, EQUULOSIS)

Etiology

The cause of actinobacillosis is *Actinobacillus equuli*, a Gram-negative coccobacillus approximately 1.5 μm × 0.5 μm in size. The cells are arranged in smears of cultures or infected tissues with a typical "**Morse code**" appearance. A relative of *A. equuli*, *A. suis*, produces disease in pigs and has been encountered in normal and sometimes diseased foals and older horses. The two

organisms can be differentiated in the laboratory by their biochemical and other properties.

Epidemiology and pathogenesis

A. equuli is a commensal in the intestine of solipeds. The foal acquires the organism from its dam **in utero**, during or soon after birth, or from its surroundings. Post-natal infection usually occurs via the **umbilicus** or, less frequently, by the oral route. The disease recurs regularly on some premises. The offspring of some mares appear to be particularly vulnerable each year, which suggests that their dams may have a persistent cervical infection. In older foals migrating strongyles may provide a vehicle of entry for *A. equuli*.

Clinical signs

The disease takes either a peracute or an acute course. In peracute cases foals become depressed and drowsy 12–24 h after birth. They show a **reluctance to suck**, become severely dyspneic, collapse and die within hours. The rectal temperature may be elevated (41°C or more) but becomes subnormal before death. There are few distinctive clinical signs.

In **acute cases**, the foal becomes **depressed** and reluctant to suck 24–72 h post partum. Clinical signs may include pyrexia (40°C or more), inflammation of the conjunctivae, an unwillingness to move, diarrhea, hyperpnea and dehydration. Purulent glomerulonephritis (*q.v.*) may result in a **coma** and subsequently sudden death. Localization of the organism in the synovial membranes results in painful swellings in the joints and lameness. All joints can be affected but gonitis and tarsitis are common. Inflammation of the atlanto-occipital joint may result in extension and drooping of the head.

Pathologic findings

There are few distinctive lesions in peracute cases although pulmonary edema, petechial hemorrhages and yellow discoloration of skeletal musculature may be observed. **Miliary pinpoint abscesses** in the renal cortex and adrenals are characteristic of subacute cases. Similar abscesses are sometimes observed in the lungs as is a purulent exudate in affected joints, synovial sheaths and bursae.

Diagnosis

A. equuli can be isolated by blood culture from the septicemic foal. After death the organism can be isolated from the umbilicus, kidney and the musculoskeletal lesions. It can also be isolated from the cervix of some mares by the use of guarded swabs.

Treatment

Affected foals should be provided **aggressive antibiotic therapy** and supportive nursing care including **plasma** if the immunoglobulin level is low, plus nutritional support. Affected foals may be hyperglycemic. It is essential that antibiotic therapy with a broad-spectrum drug be instituted as soon as **bacterial**

septicemia is suspected. These conditions progress extremely rapidly and it is inadvisable to wait for the causal organism to be identified by the laboratory.

If **actinobacillosis** is suspected the therapy of choice is a combination of full doses of penicillin (or potentiated penicillin) and an aminoglycoside (gentamicin [7 mg/kg IV s.i.d.], amikacin [15 mg/kg IV s.i.d.]). Therapy should be continued for at least 2 wk and for 4 wk (or more) if the infection has localized in the joints or lungs. If an aminoglycoside is used, renal function should be monitored because the toxicity of the drug is enhanced in young animals with renal damage.

Control

Attention to hygiene and ventilation of stables is very important. Overcrowding should be avoided. **Foaling areas should be thoroughly cleaned and disinfected between foalings**. *A. equuli* is readily destroyed by the common disinfectants.

The umbilical cord should be allowed to sever spontaneously and the stump should be treated with **antiseptic** as soon as this occurs. The foal should obtain an adequate intake of colostrum during the first day of life. If colostrum is not available, 1 L of plasma should be administered.

Prophylactic antibiotics (gentamicin [7 mg/kg IV s.i.d.], amikacin [15 mg/kg IV s.i.d.]) can be administered to newborn foals on premises where there is a disease outbreak.

COLIBACILLOSIS

Etiology

The cause is ***Escherichia coli***; these Gram-negative rods are morphologically typical enterobacteria. Like many other bacteria, *E. coli* can be divided into serogroups on the basis of the specific antigenicity of their somatic and flagellar proteins. Some strains possess **virulence factors**, and it is on these factors that pathogenicity depends.

Epidemiology and pathogenesis

The organism is a notable pathogen of many species of domesticated animals although it is also an inhabitant of the normal gut. Particular serotypes tend to be predominantly associated with particular species of domesticated animal, but can infect other species. The virulence factors of the *E. coli* strains recovered from foals and adult horses have not been identified but the **enteropathogenicity** of some strains of *E. coli* that infect other species of domestic animals and humans has been conclusively linked to the expression of adhesins and cytotoxins by plasmids within the bacteria. In other pathogenic *E. coli* strains, virulence factors, also capable of damaging the enterocyte, are known, although the prevalence, or even the occurrence of such strains in the horse, has yet to be determined.

Approximately 25% of cases of **septicemia** in the foal are caused by *E. coli*. The foal presumably acquires the bacteria from its immediate surroundings at birth. The relative importance of the probable routes of infection (umbilical, oropharyngeal or enteric) remains to be established.

Once access to the host has been gained, most of the pathogenesis in the septicemic disease is probably attributable to **shock** (*q.v.*) induced by endotoxin released from disintegrating bacteria. The main manifestations of endotoxic shock are pyrexia, hypotension and neutropenia.

Clinical and pathologic findings

The disease is very sudden in onset. In foals that are 3–4 days old the disease may take a 1–2 day course but it is usually more rapid still in foals that are less than 2 days old. Severe disease may be present before any clinical signs are observed.

Pyrexia may occur in the very early stages of the disease but the temperature is usually subnormal when the foal undergoes a collapse. The clinical signs are those of septicemia. They include depression, a reluctance to suck, petechiation of mucous membranes, respiratory distress, a progressively weakening pulse and colic.

If the foal survives for a few days individual bacteria and bacterial emboli can localize in the lungs, joints, bones or elsewhere in the body. The long-term prognosis for future athletic performance should be considered guarded for cases with involvement of the joints or bones, particularly if multiple joints are involved. Pathologic findings are typical of septicemia and reflect the time span of the infection.

Diagnosis

A definitive diagnosis can be made by **blood culture**. *E. coli* rapidly invades the carcass from the gut, so post mortem specimens should be taken for bacteriologic examination no later than 1 h after death.

Treatment

Despite the use of antimicrobial drugs and supportive therapy, the prognosis for foals with colibacillosis is not good. *E. coli* strains exposed to selection pressure are often resistant to the well-established antibiotics used in veterinary practice, such as ampicillin, tetracyclines, neomycin and kanamycin. They may be sensitive to trimethoprim—sulfamethoxazole, gentamicin, amikacin, chloramphenicol, quinolones or cephalosporins. Bacterial sensitivities are very useful in determination of the appropriate antibiotic therapy. Aminoglycosides (gentamicin [7 mg/kg IV s.i.d.], amikacin [15 mg/kg IV s.i.d.]) are the drugs of choice but they are nephrotoxic and **renal function** should be monitored.

In some equine neonatal intensive care units (*q.v.*) where *E. coli* is the leading cause of infection, amikacin in combination with penicillin is used if neonatal infection is suspected. This approach is adopted because of the prevalence of resistant organisms in nosocomial infections. Newer antimicrobial molecules, such as the highly active fluoroquinolones (enrofloxacin 4–5 mg/kg PO b.i.d. or 7.5 mg/kg PO s.i.d.), are becoming available for therapy in some countries.

Control

The same measures apply as in the control of actinobacillosis.

SALMONELLOSIS

Etiology

Salmonellosis is a **septicemic or bacteremic enteritis** of the foal that usually appears a few days later than other infections such as actinobacillosis or colibacillosis. The disease is caused by *Salmonella* spp., which are Gram-negative, facultative anaerobic, non-spore-forming rods typical of the enterobacteria.

Epidemiology and pathogenesis

A variety of species of salmonellae are involved in producing disease in the very young foal but currently *S. typhimurium* is most common. The most likely sources of salmonellae for the very young foal are the **dam** (which may be ill or seem entirely normal) or the **immediate surroundings**. The organism can be introduced by clinical cases, carrier animals, feedstuffs, water supplies, fomites, or other species of domesticated or wild animals, including birds. Salmonella may be a recurrent problem on some premises.

Carrier horses and other animals play a major role in the transmission of salmonellae. Between 10% and 50% of horses are silent carriers of these organisms. **Stress**, including illness and many veterinary procedures, provokes such animals into **active shedding** of salmonellae. This shedding only stops when the stress subsides and may recommence if the horse is again stressed. It is not clear whether salmonellae persist for the lifetime of the carrier.

The pathogenesis of salmonellosis is described in more detail elsewhere (*q.v.*). The normal flora has had little time to establish itself in the gut of the newborn foal and infection with salmonellae frequently results in septicemia in such animals. Even if septicemia does not occur, bacteremia is a feature of salmonellosis and the localization of the infection anywhere in the body is a common sequel to a diarrheal disease.

Clinical and pathologic findings

The onset is often **sudden** and very young foals may die from **septic shock** (*q.v.*) within hours before diarrhea develops. The initial features are depression, fever, reluctance to suck, weakness, dehydration and cyanotic mucous membranes. Neutropenia and toxic degeneration of lymphocytes are consistently seen. A **persistent watery fetid diarrhea** appears as the disease progresses and some cases develop **purulent bronchopneumonia** with loud rales. The spread of infection to other tissues can result in clinical pyoarthritis, nephritis or meningitis (*q.v.*).

Post mortem findings include severe visceral congestion and petechial hemorrhage in the serosae. A **catarrhal enteritis**, particularly of the ileum, is often seen. The synovias of foals with pyoarthritis contain floccules of pus and those with pneumonia may have minute pulmonary abscesses together with a generalized pulmonary edema.

Diagnosis

Definitive diagnosis of septicemic salmonellosis in the living animal depends on isolating the agent from cultures of the blood and feces. Fecal material should be obtained directly from the rectum. It is important, for epidemiologic

reasons, to determine which serotype (and phage type) is involved, so that the source(s) from which the agent emanated can be established and dealt with or avoided in future.

Treatment

Treatment consists of **maintaining hydration** by the IV and oral administration of fluids containing electrolytes and an energy source such as glucose (*q.v.*), long-term antibiotic therapy based on sensitivity assays, and the administration of intestinal protectants (*q.v.*) such as bismuth. Non-steroidal anti-inflammatory drug therapy, for example flunixin meglumine 1 mg/kg IV s.i.d. or b.i.d., may reduce the signs of endotoxemia.

Some salmonellae (especially *S. typhimurium*) are often **resistant** to several antibiotics simultaneously so antimicrobial sensitivity testing of isolates is imperative. In general, *Salmonella* spp. are sensitive to amikacin, gentamicin, ceftiofur (and other third generation cephalosporins), chloramphenicol, trimethoprim–sulfonamide, and fluoroquinolones.

The ubiquity of salmonellae, their pathogenicity, and the existence of the seemingly normal carrier, all contribute to the difficulty of controlling the disease. The management of the septicemic foal should include **strict isolation** of the foal and its dam and **vigorous disinfection** (sodium hypochlorite, phenols or quaternary ammonium compounds) of their surroundings.

The ability of salmonellae to infect other animals and humans needs to be considered when practical measures to control spread are chosen. The personnel caring for the affected animals should wear disposable overalls, boots and gloves and, if possible, they should not have contact with healthy horses. The equipment, bedding and feedstuffs, etc. for the sick animals should be kept separate from those for healthy horses.

In other species of domesticated animals, **vaccination** with salmonellae of modified virulence has been practiced in some countries and has a welcome degree of success in controlling acute disease. Pregnant mares on premises where there is a disease outbreak or where there is a recurrent problem can be vaccinated 8 wk and 4 wk pre partum. Such vaccines are not universally available, nor will they always protect the newborn animal from an infection leading to septicemia. In addition, the ability of the vaccines to affect the carrier state, or modify its prevalence, is uncertain.

ENTEROTOXEMIA

Clostridia are serious pathogens of the horse. Enterotoxemia in the newborn foal associated with either *Cl. perfringens* type B or type C is reported occasionally but the exact prevalence of the disease is unknown. The specific clostridial enterotoxemias are easier to suspect and confirm in a group of animals of similar age than in an individual.

Etiology

Cl. perfringens is a ubiquitous, large (approximately 4–8 μm long and 1 μm wide) and strictly anaerobic Gram-positive rod, which grows easily in the laboratory if its requirement for anaerobic conditions is met.

Epidemiology and pathogenesis

All the clostridia live in the soil (especially **well-cultivated soil**) and, by extension, in the gut. Animals naturally acquire the vegetative organisms or the spores orally at birth. Pathogenic clostridia have in general two striking characteristics. They release exceptionally **powerful toxins** into their surroundings, and they form **highly resistant spores**.

An imbalance in the relationship between the normal flora of the gut and normal enteric function in the newborn foal may allow an **explosive multiplication** of *Cl. perfringens* B or C so that they reach numbers far in excess of normal. This exceptional occurrence leads to the release of overwhelming amounts of **necrotizing toxin** and subsequent enterotoxemia.

Whereas other pathogenic bacteria tend to produce disease more readily when the newborn animal is compromised for some reason, the pathogenic clostridia tend to affect the animal that is progressing very well. Foals cease to be susceptible to clostridial enterotoxemia when they reach a few weeks of age.

Clinical and pathologic findings

Enterotoxemia in foals a few days old is rapid in onset. The animal quickly enters a state of **profound depression** and very soon has a markedly subnormal body temperature, tachycardia and tachypnea and great abdominal pain. These clinical signs are the consequence of, firstly, a **hemorrhagic, ulcerative necrosis**, most marked in the terminal ileum and, secondly, absorption through the mucosa of the powerfully cytotoxic beta toxin, which is produced by *Cl. perfringens* types B and C. If **death** does not occur quickly, the animal experiences severe diarrhea or, more probably, **dysentery**.

Diagnosis

An overwhelming abundance of *Cl. perfringens* is demonstrable in the **feces** from the diseased foal or in the luminal contents and mucosa at post mortem by staining smears by Gram's method or with specific fluorescent antibody.

The beta toxin can also be demonstrated in the gut contents. A piece of small gut (about 5 cm long) with its cut ends tied off to conserve the contents should be **refrigerated or frozen** as it is transported to the diagnostic laboratory. The toxin is labile and digestible by trypsin.

The smears and gut samples should be collected as soon as possible after death. It should be remembered that clostridia reside in the intestinal tract of normal animals and that merely finding *Cl. perfringens* or beta toxin in the gut or fecal material does not of itself constitute a definitive diagnosis of enterotoxemia.

Treatment and control

The course of enterotoxemia in the foal lasts usually no more than a few hours. Oral or parenteral administration of an antibiotic (such as **metronidazole** 15–20 mg/kg PO t.i.d. or q.i.d.) active against Gram-positive bacteria will usually sharply diminish the numbers of *Cl. perfringens* B or C in the gut. However, it will not decrease the prospectively **fatal quantity** of the beta toxin perhaps already absorbed from the gut.

Attempts can be made to **neutralize** the damaging effects of the beta toxin by the speedy and repeated administration of large doses (exact doses depend on formulation) of appropriate **antitoxin** in the form of an antiserum to either *Cl. perfringens* type B or type C.

In other species of domesticated animals, licensed preparations containing approximately 1200 IU of **anti-beta toxin** are said to be therapeutically effective if given in large doses (e.g. 30 mL per 75 kg). This antiserum can also be used prophylactically to provide passive immunity to a foal that is known to be at risk of contracting the disease. The same end can be achieved by vaccinating the mare a few weeks before foaling with vaccine known to contain *Cl. perfringens* type B or C toxoid. However, the low prevalence of *Cl. perfringens* enterotoxemia in the newborn foal does not justify a general vaccination program in mares.

LISTERIOSIS

Listeria monocytogenes (and *L. ivanovii*) are short Gram-positive rods (approximately 1–2 μm long) that can be grown fairly readily in the laboratory. The organism is ubiquitous in the soil and in the gut of mammals and birds. It has been found in diseased individuals of some 60 species of animal, including humans. The agent is classifiable into serotypes and subtypes, of which 1/2a, 1/2b and 4b appear to be the most pathogenic, as they are regularly isolated from diseased material. *L. monocytogenes* persists in animal or vegetable material at a low pH and multiplies at temperatures from 4°C to 39°C.

The pathogenesis of the various forms of listeriosis is poorly understood but climatic conditions, stress and other concurrent disease all play some part in allowing infection with *L. monocytogenes* to become established in the individual. Multiplication of the organism in the body is cell associated. Typically, ingestion of the organism leads to penetration of the alimentary mucosae and then to one of several possible states, including **subclinical** infection with prolonged excretion of the bacteria in the feces, **bacteremia**, accompanied by localization in various tissues, and **fatal septicemia**.

The **gravid uterus** is particularly susceptible. In early pregnancy, infection simply leads to **abortion** whereas in late pregnancy the fetus is **stillborn** or has a **congenital septicemia** and/or other lesions in the major viscera. In **visceral listeriosis** the liver and cardiac muscle in particular contain multiple, small necrotic foci that are readily visible to the naked eye as whitish specks. Otherwise, in the newborn animal, the disease is a typical **septicemia**, and the rate of recovery depends on the speed with which diagnosis is made and treatment applied.

L. monocytogenes is, for the most part, not particularly susceptible in vitro to many of the common antimicrobial agents but penicillin (40 000 IU/kg IM daily for up to 2 wk) is the drug of choice. Early treatment is most important. *L. monocytogenes* is also susceptible to streptomycin and the tetracyclines. The value of vaccination with either killed or attenuated material is inconclusive. As the disease in the horse is sporadic, most likely to manifest itself as a septicemia in the foal, and, as the protection conferred by infection or vaccination is strongly cell mediated, vaccination of the dam does not appear to be an effective or practical control measure.

BACTERIAL DISEASES OF THE OLDER FOAL AND ADULT

INTRODUCTION

Bacterial infections like salmonellosis or actinobacillosis (*q.v.*) may not arise in foals until they are some weeks or even months old. In such instances the pathologic events in the disease and its clinical course differ from those seen in the youngest animals. Septicemia becomes much less common whereas clinical evidence of alimentary or respiratory involvement is much more marked. Some other bacterial infections also become more prominent at this stage in the foal's life. These infections include those with *Rhodococcus equi, Clostridium piliformis, Clostridium perfringens* type A, and the putative pathogens, *Cl. difficile* and *Bacteroides fragilis* (*q.v.*).

RHODOCOCCUS EQUI

Rhodococcus equi is a common pathogen of **foals**. The organism can localize in many organs; however, the respiratory tract is most commonly involved. A severe pyogranulomatous pneumonia may ensue.

Etiology

The causative organism was initially isolated from foal lungs in 1973. DNA sequencing identified the genus *Rhodococcus* to be an accurate classification for this bacterium. *R. equi* is a facultative, Gram-positive, pleomorphic rod.

Epidemiology

R. equi has a worldwide distribution and equine disease is common in areas with large horse populations. It is a **soil inhabitant**. Reports of increased incidence of *R. equi* in warm, wet years suggest that moisture may be important for bacterial multiplication.

Heavily stocked horse farms may develop large numbers of organisms in pasture soil. Oral ingestion of the bacterium with multiplication in the gastrointestinal tract adds to the concentration of the bacterium in the environment. On farms with a history of *R. equi* problems, the organism is found not only in soil, but also in barn dust, cobwebs and air. Where weather conditions are appropriate (i.e. dry and windy), a situation exists in which overwhelming exposure to **aerosols** can occur.

The mode of transmission of this disease was originally thought to be solely through oral ingestion, with the consequent development of local ulceration, abscessation and subsequent dissemination to other organ systems. Experimental oral inoculation with large numbers of organisms has not reproduced significant respiratory disease whereas experimental exposure by inhalation has reproduced severe pulmonary disease. Therefore, it is likely that **inhalation** is the mode of transmission of the respiratory disease, and that oral ingestion may result in gastrointestinal lesions or dissemination to lymph nodes, joints or both.

Yearly recurrence of the disease is common, with the number of foals affected on a particular farm ranging from a few to more than 50%. The rate of occurrence is likely to be dependent upon environmental factors, gastrointestinal multiplication, dissemination and host resistance factors. A mortality rate of 80% was not uncommon formerly but improvements in the comprehension, recognition and treatment of the disease have greatly decreased the rate of mortality.

R. equi is most common in foals that are from 2 to 4 mo of age, but it can occur in younger and older foals. The age-related occurrence of the disease is probably related to the decreasing maternally derived immunity of the foal and the fact that the majority of foals reach 2–6 mo of age during the warm, dry months of the year when aerosol exposure is likely to occur. Disease in adults is rare, but has been reported in immunosuppressed individuals. Adult resistance to this disease is likely to be related to the development of an adequate immune response.

Pathogenesis

The pathogenesis of the disease is not completely understood. However, the scavenging of large numbers of organisms by alveolar macrophages and the ineffective killing of the bacteria is integral to the pathogenesis of *R. equi*. Although initial hypotheses regarding the pathogenesis of the disease focused on defects of the cellular immunity of the horse, it now appears that humoral factors play an important role.

The presence of antibodies is important for the process of opsonization. Neutrophils in the presence of *R. equi* antibody result in 95–100% bacterial killing. In the absence of antibody, neutrophilic killing is inadequate. This feature would explain the increased incidence of disease during the period of **decreasing maternal antibodies**. Organisms that escape neutrophilic killing may be ingested by macrophages, where bacterial multiplication may occur. An absence of protective antibody or a massive exposure that overwhelms humoral immunity may lead to disease. **Specific immune plasma** has been shown to reduce the severity of the disease in pony foals that were experimentally infected with *R. equi*.

Clinical findings

The most common clinical picture of the disease is of a progressive pneumonia, the development of which may be acute or gradual. A combination of any of the following signs may be present: pyrexia, depression, anorexia, tachypnea, mucopurulent nasal discharge, cough and abnormal thoracic auscultation. Auscultation varies from marked diffuse crackles and wheezes to minimal cranioventral auscultatory changes and is dependent upon severity and progression of the disease. These signs of lower respiratory disease do not differentiate *R. equi* from other causes of pneumonia. Joint effusions may be identified in conjunction with pneumonia. Lameness is usually absent and synovial fluid analysis is compatible with an immune-mediated synovitis (*q.v.*).

The gastrointestinal form of the disease presents as chronic weight loss or as an unthrifty foal. Diarrhea or abnormal feces can be present. Other forms of the disease that have been reported include septic arthritis, abscessation

(integumentary or abdominal), meningitis, osteomyelitis, pleuritis and valvular endocarditis (*q.v.*).

Clinical pathology

Clinicopathologic findings are generally **non-specific**. Evidence of inflammation is represented by a leukocytosis and a variable elevation in fibrinogen. Some practitioners have reported that elevations in white blood cell (WBC) counts may precede clinical signs of the disease and may be used as an aid to early diagnosis on problem farms. An absence of a leukogram indicating inflammatory processes should not, however, preclude diagnosis in clinically ill foals.

Post mortem findings

The characteristic gross post mortem findings of respiratory disease include **bilateral abscessating bronchopneumonia**. Cranioventral, irregular and multifocal involvement is typical. Abscesses range from millimeters to several centimeters in diameter. A generalized multifocal distribution of abscesses is not uncommon. Abscesses may be present in the bronchial and mediastinal lymph nodes. Pleural empyema may occur, but it is not common. Lesions within the gastrointestinal tract can be located in sites ranging from the stomach to the large colon. Villous atrophy, mucosal necrosis, diphtheritic membranes, ulcerative enterocolitis and abscessation in the mesenteric lymph nodes may be identified. The histologic response is primarily pyogranulomatous. A central core of necrotic debris is surrounded by necrotic neutrophils, with the surrounding tissue infiltrated by macrophages.

Diagnosis

The diagnosis of *R. equi* pneumonia is based on the evidence of clinical respiratory disease, history (including age of onset), confirmed diagnosis in other foals on the farm and the presence of the disease previously.

Transtracheal aspirates are critical to the differentiation of *R. equi* from other causes of pneumonia. Cytologic examination can be very useful in the early recognition of the disease, as cultures require a 48 h growth period. The characteristic, Gram-positive pleomorphic rods may be identified in the aspirate. Bacteriologic examination provides a more definitive diagnosis. Such examinations of peritoneal fluid, feces or both can also be beneficial in the detection of the gastrointestinal disease.

Serologic procedures (ELISA) can be useful; however, a positive reaction is not diagnostic, as normal, exposed foals may have antibodies against *R. equi* antigen. Foals with active *R. equi* infection should be serologically positive.

Radiology and ultrasonography may be useful aids to diagnosis. Pulmonary abscessation may be identified. However, the absence of abscess formation does not rule out the disease.

Treatment

The treatment of *R. equi* pneumonia consists of **specific antibiotic therapy**. In vitro sensitivity results often suggest a wide range of antibiotic sensitivity.

However, in vivo success is achieved only with those antibiotics that reach adequate intracellular levels. A **combination of rifampicin** (5 mg/kg PO b.i.d.) **and erythromycin** (20–30 mg/kg PO q.i.d.) has proved to be a very effective treatment of *R. equi* pneumonia. These antibiotics can be administered orally and attain excellent tissue and intracellular levels. A combination of antibiotics is used because a rapid development of resistance to rifampicin when used alone has been reported. Erythromycin can occasionally produce diarrhea and has been associated with hyperthermia in foals kept outdoors.

Trimethoprim–sulfonamide combinations (5 mg/kg of the trimethoprim portion, b.i.d.) have been suggested in combination with rifampicin when problems are encountered with erythromycin. Two newer generation macrolides have been used—azithromycin (10 mg/kg orally s.i.d. for 5 days followed by q 48 h therapy) or clarithromycin (7.5 mg/kg b.i.d. PO).

In addition to antibiotic therapy, **supportive care** can improve the outcome for the foal, particularly one that is critically ill. Air conditioning can provide relief in hot, humid climates. Nasal insufflation of oxygen, bronchodilators and anti-inflammatory drugs can be considered in specific cases.

Control

An approach to the prevention of the disease should include basic management and health programs. A **reduction in stressful conditions** such as overcrowding, excessive handling, and dust exposure, should be attempted. Adequate stall ventilation is imperative. Appropriate **vaccination programs** may reduce viral infections and subsequent secondary bacterial infections. A reduction in dust exposure may be achieved by watering down or changing the composition of the soil by adding gravel to areas around gates, feeders and waterers.

The use of bacterins has not been universally successful. These results may be influenced by bacterin preparation or by the type of adjuvant used. In addition, the immunologic response to a bacterin may not provide the cellular immunity or local immunity needed for adequate protection. Hyperimmune serum has been shown to reduce the severity of the disease in experimental infections. Boosting a foal's humoral immunity may prove to be beneficial for farms with *R. equi* problems; however, immunoprophylaxis and immunotherapy are expensive and clinical efficiency has not been definitely proven.

TYZZER'S DISEASE

Etiology

The cause of Tyzzer's disease, *Bacillus piliformis*, is the only Gram-negative spore bearing, obligate intracellular bacterium known. The properties of *B. piliformis* have been poorly characterized because it cannot be propagated in artificial media. The organism has been cultivated successfully in the chick embryo and in primary monolayers of hepatocytes. Recently this organism has been reclassified to the *Clostridium* species and now is known as *Clostridium piliformis*.

Epidemiology and pathogenesis

Tyzzer's disease is recorded mainly in populations of laboratory or wild rodents, especially mice, which may constitute the essential reservoir of this

agent. Fatal disease from infection with *Cl. piliformis* has, however, also been noted in the young of many other species, including the horse. The mode of transmission is unclear. It may be that adult horses serve as carriers and shed the moderately resistant bacterial spores. Foals may become infected by ingestion of materials contaminated with infected feces.

Clinical and pathologic findings

The disease occurs sporadically and with low prevalence in foals usually 7–40 days of age. The onset is abrupt and the brief course (1–2 days) is characterized by fever, prostration and finally coma, although some cases also exhibit severe diarrhea, which may be hemorrhagic, and jaundice. These signs, which reflect the presence of a **catarrhal colitis**, enlarged liver and hepatitis with a focal necrosis, are accompanied by marked increases in glutamic oxalacetic transaminase (SGOT), glutamic pyruvate transaminase (SGPT) and lactic dehydrogenase (LDH) in the plasma and a profound leukopenia.

Diagnosis

Confirmation of Tyzzer's disease depends on demonstrating the agent in suitably stained preparations (with Giemsa or Warthin–Starry) made from the **liver or intestinal epithelium**. Histologic examination of the hepatocytes or intestinal epithelium near the necrotic lesions typically reveals bundles of beaded rods with subterminal spores.

Treatment and control

Cl. piliformis is sensitive to all the common antimicrobial drugs used in veterinary practice; aminoglycosides (gentamicin 7 mg/kg IV s.i.d. or amikacin 15 mg/kg IV s.i.d.) may be the most useful for therapy. Since the mode of transmission is unclear, developing a strategy for control of the disease is difficult.

INFECTIONS WITH *CLOSTRIDIUM PERFRINGENS* TYPE A, *CI. DIFFICILE* AND *BACTEROIDES FRAGILIS*

Each of these bacteria is encountered in diarrhea in younger and older foals. *Cl. perfringens* A and *Cl. difficile* both produce **exotoxins** which damage the gut wall and produce acute diarrhea in other species. The conclusion that they are associated with a comparable syndrome in the foal rests principally on the evidence that these organisms are present in higher numbers in diarrheic foals than unaffected animals, and that the toxins are demonstrable in the feces or gut contents. A similar argument is advanced for implicating *B. fragilis*.

Overgrowth in the gut of the clostridia in question occurs **spontaneously** or can be promoted by many factors including an imbalanced or abruptly altered diet, administration of drugs (especially antimicrobial substances) or the activity of other infectious agents, including other bacteria, or even helminths or viruses. The need for therapeutic intervention in diarrheic foals depends on **clinical assessment**. Many foals have a largely self-limiting episode of diarrhea at the time of the mare's first heat after parturition.

DERMATOPHILOSIS

Dermatophilosis (**subcutaneous streptothricosis**) is an exudative dermatitis of animals and, very occasionally, humans. It is most prevalent in ruminants and only occurs sporadically in horses. With the possible exception of sheep, animals in the tropics are more often and more severely affected than those in temperate areas. The condition is sometimes referred to as **rain scald, mud fever** or **greasy heel**.

Etiology

The disease is produced by the penetration of *Dermatophilus congolensis* into the epidermis. *D. congolensis* belongs to a large, heterogeneous group of bacteria, the actinomycetes, whose main habitat is the soil. However, *D. congolensis* lives only in the **living tissue of the epidermis**. It is a Gram-positive organism that grows as branching filaments, the hyphal cylinders of which condense in two planes at right angles to each other to give rise to coccoid bodies. These coccoid bodies eventually become highly motile zoospores $\leqslant 1\,\mu m$ in diameter and are the essential means of dissemination of the pathogen. The filamentous mass—the mycelium—readily fragments.

Epidemiology

The only known **reservoirs** of *D. congolensis* are chronically affected animals. The organism may be present in a quiescent state in the epidermis until local climatic conditions, specifically a period of warm, wet weather, promote further multiplication of the mycelium and the formation of the zoospores. To establish infection in new areas of skin in an infected animal, or in a previously uninfected animal, the motile zoospores, responding to carbon dioxide diffusing through the skin, must penetrate the sebaceous layer and enter the epidermis. They germinate in the epidermis, producing a hypha and ultimately a mycelium.

Minor abrasions of the superficial layers of the skin make an animal more susceptible to infection. The disease is more common in **younger animals** because their sebaceous layer is thinner and can be more readily weakened by prolonged wetting. Biting arthropods such as ticks and flies, which are more prevalent and active in warm, humid conditions, play a part in the mechanical transfer of zoospores. The extent to which sweating by horses favors infection does not appear to have been investigated.

Clinical findings and pathogenesis

Foals and young horses are the most susceptible. Any part of the integument may be involved although the back, shoulders and flanks are usually the most affected. Instances in which the pasterns and coronets were the main areas involved have also been described (**mud fever**).

In the early stages after infection, influxes of neutrophils into the affected skin, inflammatory reactions and the resultant serous exudation mat the hairs of the coat together and produce the characteristic, so-called "**old paintbrush**" **appearance** of the lesions. These lesions, which are scattered over the skin, coalesce with others to produce circular, raised crusts or scabs up to 2 cm

in diameter. They do not itch and most heal spontaneously within a few weeks though a few may persist indefinitely. The factors that govern the curtailment of spread and subsequent healing of the lesions in about 3 wk or less are imperfectly understood.

Diagnosis

The appearance of the lesions in a clinically affected animal is highly suggestive of **streptothricosis**, which requires differentiation only from the lesions of the early stages of ringworm or pyoderma (*q.v.*).

The diagnosis is easily confirmed by observing the unusual morphology of *D. congolensis* in smears of exudate or scabs that have if necessary been moistened, crushed and teased and stained with methylene blue or Giemsa. Preparations stained by fluorescent antibody are useful when the characteristic sporulating structures are scarce, as they are in material from chronic lesions. Isolation of the organism from affected skin is also comparatively simple if attempted from specimens that contain affected epidermis. Growth of *D. congolensis* in the laboratory is rather slow (taking 2–3 days) but the distinctive colonies, which are often surrounded by a zone of hemolysis, are easily recognized.

Treatment and control

The lesions of streptothricosis usually heal spontaneously, and therapy is required only for severe cases. **Procaine benzylpenicillin** (18 000 IU/kg IM b.i.d.) is the drug of choice.

Since cases of cutaneous streptothricosis in the horse are largely sporadic and much dependent on weather conditions, there has been no requirement for protection by immunologic means. In any case, variability among the antigens of the flagella of the zoospores of *D. congolensis* makes the prospects for a universally applicable vaccine unlikely.

SALMONELLOSIS

Etiology

As in the younger foals, an extensive variety of *Salmonella* spp. (serotypes) can be encountered in the adult horse (including *S. heidelberg, S. eimsbuttel, S. ohio, S. senftenberg*, and *S. enteritidis*) but *S. typhimurium* is still the **most common** salmonella recovered from the horse.

S. abortus equi is a very host-specific organism that historically caused abortion in mares, but which is no longer isolated in either North America or Western Europe, although it is still encountered in horses in Eastern Europe.

Epidemiology and pathogenesis

A horse may be exposed to salmonellae from its ingesta, its surroundings, or from other animals. If the organism succeeds in establishing itself, it may do so sufficiently to create a carrier state or colonize so effectively that enteric and even systemic disease results.

In most cases the infection is confined to the intestine but bacteremia is a feature of the more severe infections. Acute, severe disease can be precipitated

in **latently infected** animals by early weaning, by transportation or hospitalization, overworking or other stresses. On abatement of the stress, excretion of salmonellae normally ceases but resumes if the animal is subjected to further stress. Between 10% and 50% of horses in some populations may be **carriers** of salmonellae. Outbreaks of salmonellosis in transported or hospitalized horses constitute a major problem.

Colonization of the terminal small intestine, the cecum and the colon by salmonellae is greatly favored if peristalsis is poor and if the normal flora (including fusobacteria, *Bacteroides* spp. and lactobacilli) fails to produce acids that inhibit the attachment of the salmonellae to the enterocytes. After attachment, salmonellae enter the epithelial cells, multiply and pass to other cells in the lamina propria. Inflammation and cell damage induce release of prostaglandins, which activate adenyl cyclase, leading to the secretion of excessive volumes of ion-rich fluid into the gut. Continued multiplication of the salmonellae in the mucosa produces a **necrotic enteritis** and diarrhea.

During the course of infection salmonellae multiply in macrophages and enter the lymphatics, lymph nodes, reticuloendothelial system and blood. **Septicemia** ensues in cases of severe infection or where resistance is lacking. If this process is not **rapidly fatal** the agent may localize in other tissues including the lungs and synovia. Infection of the gravid uterus leads to death of the fetus and abortion.

Clinical and pathologic findings

Salmonellosis is a good example of the need to distinguish clearly between infection and disease. Infection with salmonellae can result in a **necrotizing colitis** with bacteremia or in a **carrier state** that can persist for years without overt disease.

Mild attacks of disease in the horse last no more than a few days and are characterized by depression, unwillingness to eat and the passage of soft feces. The acute form is marked by fever, depression, anorexia and severe enteritis, with the passage of fluid and **foul-smelling feces containing casts**. A pregnant mare often aborts. Acute cases die if inadequately treated. Usually, the duration of the clinical disease is approximately 3 wk and, if the horse survives, it may remain a carrier or experience intractable diarrhea for several months. When the diarrhea subsides the horse commonly remains a carrier.

Acidosis, electrolyte imbalance and protein loss from the gut, along with a profound neutropenia, are the prominent clinicopathologic findings. At death the large gut is severely and extensively necrotic and has pseudomembranes. The lumen may contain casts.

Diagnosis

The clinical signs are distinctive but not diagnostic. Bacteriologic confirmation, involving isolation of the salmonellae, **sensitivity testing plus phage typing** of the serotype involved, is necessary not only for clinical but also for epidemiologic reasons as already noted. In the laboratory, culture of a specimen of fecal material is always more likely to lead to the isolation of the organism than the examination of mere rectal swabs. This is true of clinical cases and suspected carriers.

Treatment and control

Clinical cases should be kept in **strict isolation**. The facilities need to be thoroughly disinfected and extreme care must be taken to prevent cross infection of other animals and man. Effective disinfectants include cresols, phenols, sodium hypochlorite and quaternary ammonium.

The prognosis for horses with the acute disease is not good. Supportive treatment, including the parental administration of fluid and electrolytes (*q.v.*), is essential. **Antimicrobial therapy** is complicated by differing resistance patterns, and sensitivity testing of all isolates is **essential**. Currently most *Salmonella* spp. are sensitive to amikacin, ceftriaxone, ciprofloxacin, imipenem, and trimethoprim–sulfamethoxazole.

The efficacy of antimicrobial therapy is, however, controversial as **disturbances of the normal flora** in the gastrointestinal tract may enhance the ability of salmonellae to grow and prolong the course of diarrhea. Many clinicians believe that antimicrobial therapy is of little benefit to horses with diarrhea but may be useful in preventing or counteracting bacteremia.

Attempts should be made to identify the source of the agent, especially if a group of horses is affected. **Detecting the carrier state** in the horse is difficult since many animals affected in this way shed the organism quite erratically and in very low numbers. The bacteriologic examinations may need to be repeated at intervals. Routinely, swabs or fecal material collected from the rectum are incubated in selenite enrichment broth prior to streaking on selected agar. Once isolated, the serotype of an isolate is identified in the laboratory by its biochemical and antigenic properties. Isolates are commonly submitted to specialized laboratories for corroborative identification by antigenic analysis and phage typing.

CLOSTRIDIOSIS

Epidemiology and pathogenesis

Clostridium perfringens is ubiquitously distributed in its vegetative form or as spores in soil and is part of the normal intestinal flora of animals. However, *Cl. perfringens* type A seems best adapted to survive in the soil and forms a very minor part of the normal clostridial flora of the gut of the horse. Nevertheless, in some circumstances, many still unclear, these bacteria can flourish in the equine intestine to form a **major proportion** of the bacterial flora. In that instance, through an abundant production of alpha toxin (and probably other aggressins or toxins), type A can cause acute disease.

As well as severely damaging the **mucosae of the cecum and colon** in horses of all ages, the alpha toxin (a phospholipase C) hydrolyses lecithin in mitochondria and cellular membranes including those of endothelial cells and erythrocytes. **Toxemia** results from absorption of the toxin from the intestinal lumen.

Cl. difficile (*q.v.*) also inhabits the intestinal tract of normal horses and can lead to **enterocolitis** (*q.v.*).

Clinical and pathologic findings

In adults there is an abrupt onset of fever with the production of a profuse, watery and foul-smelling diarrhea or dysentery, severe depression and

dehydration, pallor, jaundice and even hemoglobinuria. The course is rapid and death usually occurs within 48 h of the development of clinical signs. At necropsy there is hemorrhagic typhlitis and colitis. The kidneys are dark, swollen and may have infarcts. The liver is swollen and friable and the lungs are hyperemic, edematous and hemorrhagic. The myocardium contains areas of degenerated muscle that are detectable histologically.

Diagnosis

The involvement of *Cl. perfringens* type A can be confirmed by demonstrating the presence of the **toxin** in abundance in the **fecal excreta** or **gut contents**. As *Cl. perfringens* type A is not commonly isolated from the feces in normal horses, high counts ($\geqslant 10^4$/g of fecal material) suggest its predominance in the flora of the small and large intestines and therefore its association with disease. The bacteria can be observed microscopically in suitably stained smears of the fecal excreta or of the luminal contents at post mortem.

Treatment and control

Oral administration of an antibiotic (apart from the aminoglycosides, which do not affect the clostridia) might reduce the number of type A in the gut but therapy requires the administration of **antisera** prepared against *Cl. perfringens* type A, B, C, D or E, all of which produce the alpha toxin. Large volumes of antiserum (approximately 250 mL per dose) are needed, **diluted with a balanced salt solution** and given by slow IV injection to avoid shock.

Because of the **myocardial damage** caused by the alpha toxin, rest for at least a month after recovery is advised. The disease is sporadic and does not seem to warrant prophylactic vaccination with the appropriate toxoid.

CLOSTRIDIAL NECROTIZING CELLULITIS/MYOSITIS

The descriptive but pathologically antiquated terms **wound gas gangrene** and **malignant edema** are still in general use and refer to the activity of clostridia which, given the opportunity, will penetrate and multiply in tissues and produce toxin(s) that exacerbate the spread of the organism. Since this clostridial invasion gives rise to peracute or acute toxemia and/or septicemia, the survival of the affected animal is usually threatened.

Etiology

The clostridia chiefly responsible for necrotizing cellulitis/myositis in the horse are *Cl. perfringens, Cl. novyi* and *Cl. septicum*. These clostridia gain access to the subcutis or skeletal musculature or both, anaerobic conditions arise and toxin is produced. The toxin kills incoming neutrophils and so prevents phagocytosis of the rapidly multiplying bacteria.

Epidemiology and pathogenesis

In the horse, **cellulitis/myositis** (*q.v.*) is usually associated with lacerations, abrasions or surgical or inoculation procedures. Instances have been recorded, however, where there is at least circumstantial evidence to suspect the activation

of dormant spores at or near the site where the lesion forms. This phenomenon suggests that the pathogenesis of some equine cases resembles that of blackleg in cattle.

Clinical findings

The extent of the inflammatory damage at the site can become astonishingly extensive within a few hours. Tissue necrosis and vascular damage give rise to a **rapidly enlarging** and at first painful swelling with a **doughy feel**. Within 12–48 h of the start of the infectious process the lesion spreads and is infiltrated with a bloody gelatinous exudate or even gas.

Infections that occur at castration spread along the abdomen and the medial aspect of the hindlimbs. Infection acquired at parturition may also extend to the hindlimbs. Infection of the neck, for example after IM injection, may result in horses being unable to lift their heads and dependent edema of the head. Pyrexia, increased pulse rate, congestion of the mucous membranes, tachypnea, depression and other signs of toxemia and severe bacteremia/septicemia appear. The toxemia, if unchecked, is **lethal**.

Diagnosis

In clostridial cellulitis/myositis, large Gram-positive rods (3–10 μm long by 0.5–1 μm wide) lying singly, in pairs or in short chains among amorphous Gram-negative material from necrotized cells and exudate can be seen in smears of tissue deep within the lesion. No living neutrophils are seen in such aspirates. Immunofluorescent staining of the aspirates with specific antibody will help to determine the causal species.

Because of the propensity of clostridia to invade the carcass from the gut soon after death in any animal, no definitive diagnosis can be based solely on the isolation of the organism post mortem.

Treatment

As soon as the condition is suspected **massive antibiotic and supportive therapy** is needed to save the animal. Clostridia are almost always susceptible to **penicillins** (procaine benzylpenicillin 25 000–30 000 IU/kg IM q 8 h and crystalline benzylpenicillin 25 000–30 000 IU/kg IV q 4 h). Other antimicrobial drugs commonly available to the veterinarian are also efficacious, although as already noted, *Cl. perfringens*, the most common clostridium of wound gas gangrene in the horse, is inherently resistant to the aminoglycosides.

In severe cases, administration of fluids and analgesics is indicated. The identification of the clostridial species involved in producing the lesion is important as it allows for valuable additional therapeutic support to be given to the animal in the form of **specific antitoxin**. Horses infected with *Cl. perfringens* have a higher survival rate than those infected with *Cl. septicum*.

BOTULISM

Etiology

Botulism, a **non-contagious** disease of mammals and birds, is a **flaccid paralysis** of voluntary muscle produced by toxins of *Clostridium botulinum*. All six or

seven types of *Cl. botulinum* are relatively large (approximately 5 μm × 0.6 μm), motile Gram-positive rods. Like other clostridia, *Cl. botulinum* only grows in anaerobic conditions. The vegetative form of the organism is not notably resistant to chemical or physical agencies but the spore is reliably destroyed only by exposure to steam under pressure for at least 20 min.

Epidemiology and pathogenesis

The **neurotoxins** produced by the different types of *Cl. botulinum* are antigenically distinguishable but their action is the same regardless of source. The types also vary in their ecologic distribution. Types A, B, E and F are essentially dwellers in soils and alkaline muds and the vegetation associated with such places. By contrast, types C and D parasitize the gut of mammals and birds and are only coincidental inhabitants of soils, waters or decaying vegetation. **Types A and B** are involved in equine botulism.

All types of *Cl. botulinum* release toxin when their vegetative cells lyse. In at least some types, production of the toxin, a protein approximately 150 kDa in weight, depends on the presence of the DNA of a bacteriophage within the vegetative cell. The protein forms a complex with another large hemagglutinating molecule of bacterial origin, which may protect the neurotoxin from degradation by proteolytic enzymes in the gut. However, in some types, only exposure to proteolysis in the gut allows the fully active toxic principle to be formed. The toxin is **remarkably poisonous**; it provides some $10^{8.3}$ mouse LD_{50} per mg N_2. Although the vegetative cell of *Cl. botulinum* must have anaerobic conditions in which to multiply, anaerobic conditions are not necessary for the production of the toxin. It is produced at temperatures as low as 30°C.

Vegetative *Cl. botulinum* and its spores are much more widespread than botulism.

In most instances, botulism follows ingestion of **food contaminated** by toxin. Decomposing carcasses or meat products classically constitute the chief sources of the toxin, but the organism can grow in decaying vegetable matter or in silage or hay that has become spoiled at a stage that will allow *Cl. botulinum* to flourish. Vegetable products in bulk can also be vehicles for the toxin if they contain decomposing rodents. The feeding of brewers' grains contaminated by the toxin has produced the disease.

Although botulism in horses is also known as "**forage poisoning**", *Cl. botulinum*, like other clostridia, can in certain circumstances replicate and produce toxin either in the gut or in suitably anaerobic areas of necrosis in the living animal.

Toxicoinfectious botulism is known to occur in the horse as well as in humans. An association with grass sickness (*q.v.*) has been proposed but never confirmed.

On ingestion, the toxin is exposed to proteolytic enzymes in the gut but it is much less affected by these enzymes than is tetanospasmin, the principal toxin of *Cl. tetani*. It is also partially protected by the hemagglutinin. Because of its potency, only a small quantity of the toxin needs to survive for **lethal amounts** to be absorbed across the alimentary mucosae into the circulation. The toxin is distributed by that route to all parts of the body except the CNS; it cannot pass the blood–brain barrier. The toxin binds to gangliosides at the neuromuscular

junctions of the skeletal muscles. There it prevents the release of acetylcholine in cholinergic nerves, thus preventing transmission of impulses to the muscles. Consequently, affected voluntary muscles remain in a state of continuous, **flaccid paralysis**. The absorbed toxin **continues spreading** in the blood and the animal dies when the muscles required for respiration can no longer contract.

Clinical and pathologic findings

Botulism is a non-contagious disease that occurs sporadically and usually affects **individual** animals. However, large groups of animals are sometimes affected when they are all concurrently exposed to contaminated feed or other similar vehicles of the toxin.

The incubation period (3–17 days) depends on the quantity of toxin in the foodstuff and how much of it is absorbed from the gut. A large dose produces death in 2–3 days, with often no premonitory signs apart from reluctance or failure to eat or drink. In its less peracute form, the disease is characterized at first by tremors and vague weakness, then by the flaccid motor paralysis that involves first the hindlimbs, then the forelimbs, and latterly the head and neck. The affected animal has no fever and is **fully conscious** until it dies 1–4 days after the first appearance of the clinical signs.

When the effective amount of toxin acquired is small the disease can be much milder in nature and its course is more protracted. The animal spends most of its time lying down and eats and drinks with difficulty. Respiration is labored but these cases have much the best prognosis. Mildly affected animals can recover spontaneously after 3–4 wk if tended carefully to prevent respiratory failure and by taking steps to counter the adverse effects of inanition and recumbency.

The **shaker foal syndrome**, which occurs in the USA and the UK in animals 2–8 wk old, is probably a form of **toxicoinfectious botulism**. Experimentally, the administration of *Cl. botulinum* type B toxin produces a similar syndrome in foals.

The condition arises infrequently; even on premises known to be prone to annual recurrence it affects only one or two foals each year. Foals in good condition appear to be most prone to the disease. The onset of marked muscular trembling and weakness of the affected animal is abrupt and eventually the fallen shaker foal can no longer rise unaided, although it is conscious, afebrile and responsive to stimuli. Death from respiratory failure occurs approximately 3 days after the onset of clinical signs. Acidosis has been reported as a feature of the disease and enlargement and mottling of the liver may be evident at post mortem. *Cl. botulinum* may be recovered from gastric ulcers and umbilical and pulmonary abscesses.

Spontaneous toxicoinfectious botulism in adult animals is believed to arise also as a consequence of multiplication of *Cl. botulinum* in **necrotic lesions** or **wounds** in the body. Unlike the case in infants, multiplication of *Cl. botulinum* in the gut of the horse alone does not lead to the toxicoinfectious form of the disease.

Diagnosis

The damage produced by the neurotoxin is a simple biochemical malfunction and there are **no characteristic lesions** at post mortem. Botulism is easier

to suspect and diagnose clinically than bacteriologically, especially when a group of animals are affected. Verification of the true cause in a case of botulism is difficult. It can only be made categorically by demonstrating the toxin in the circulation of the affected animal or, failing that, in the food the animal ate or in the contents of its gut. Mice are susceptible to the toxin and its clinical effect in them can be abolished with the appropriate antitoxin. However, since the mouse is less susceptible to the effect of the toxin than the horse, this biological test can give false negative results. The presence of toxin can also be demonstrated in suitably arranged **immunosorbent assays** in a specialist laboratory. Their sensitivity in the case of the horse is unknown.

The presence of the vegetative forms or the spores of *Cl. botulinum* in a foodstuff or in any part of the carcass of even a suspected case is not by itself adequate evidence of botulism. In an animal that has died from other causes, *Cl. botulinum*, like other clostridia, can rapidly invade the rest of the body from the gut.

Treatment and control

Where *Cl. botulinum* types A and B are predominant as the cause of equine botulism, the disease is sporadic and unpredictable. Routine mass vaccination against this intoxication is not warranted. If the condition is suspected in one of a group of animals, the other members should be **vaccinated** immediately by administering the appropriate **toxoids**.

Clinically affected horses can be slung, purged, fed by stomach tube and given antitoxin. These procedures are more likely to be effective in the milder case. The therapeutic effectiveness of administering **antitoxin** is directly related to the ratio of free to bound toxin in the body. Antitoxin cannot reverse the effects of toxin that has already bound to motor endplates. The prognosis for severe cases is poor.

TETANUS

Etiology

Clostridium tetani is a Gram-positive rod (approximately 2–5 μm long and 0.5 μm wide) and is typical of the toxigenic, sporulating bacteria that comprise this genus of anaerobes. When sporulating, the vegetative organism develops a spherical spore at one end of the cell, giving rise to the characteristic morphologic appearance of "**drumsticks**" in smears. The spores are very resistant to chemicals; even acidified phenol takes 2 h or more to kill them under the most favorable circumstances. Oxidizing disinfectants, such as solutions of iodine, are faster and more reliable but steam under high pressure is the surest method of destroying spores.

Epidemiology and pathogenesis

Cl. tetani is often abundant in **equine feces** but it occurs in the gut of other herbivores and in the soil. The numbers in soils vary greatly, but the organism is especially abundant in warm areas with **rich, well-cultivated soils**.

Tetanus occurs sporadically throughout the world, the prevalence in unprotected populations correlating with the numbers of spores in the soil.

Mammals in general are susceptible to tetanus but, for reasons yet to be determined, the horse is the most susceptible animal and hence at greatest risk of developing the disease. **Humans are also highly susceptible**.

Cl. tetani cannot multiply in any normal tissue, or even in damaged tissue provided an oxidation-reduction potential equal to that of normal blood remains extant. In **damaged tissue**, where necrosis and lowered oxygen tension combine to create a sufficiently anaerobic state, the organism multiplies and toxin is released. So although deep, penetrating and heavily contaminated wounds produce the most favorable circumstances for the organism to flourish, tetanus can develop after even **minimal superficial damage** provided an anaerobic state develops in the infected area. In addition, one component of tetanus toxin—the hemolysin—is itself a necrotizing substance which contributes to the development of the conditions necessary for the replication of the agent and release of the neurotoxin, **tetanospasmin**, the major component of the toxin. The interaction between tetanospasmin and nervous tissue and the way it is distributed in nerves is responsible for the development of the clinical signs of tetanus.

In *Cl. tetani* the gene coding for tetanospasmin is part of a plasmid residing in the cytoplasm of the vegetative cell. The gene product is a polypeptide, which is resistant to heat but readily cleaved by some proteases, including those in gastric juices. Since the peptide is also poorly absorbed from the alimentary tract, ingesting tetanus toxin is harmless, a feature not shared with the toxins from *Cl. botulinum*. To produce tetanus, tetanospasmin must adsorb to the gangliosides that are present in nervous tissue. Once this has occurred, the binding is virtually **irreversible**, which explains why tetanus antitoxin is much more effective prophylactically than therapeutically, even when given in large doses.

When tetanospasmin is released by the organism multiplying in a wound, it enters the local motor and sensory nerves. If the production of toxin is abundant, free toxin also enters the capillary vessels and lymphatic channels. The organism itself does not spread from the site of injury. Tetanospasmin can reach the CNS via the nerves or through the blood. These two possible routes of distribution of the toxin in vivo give rise respectively to: (1) **ascending tetanus**, in which the movement of the toxin is along the motor nerve trunks to the cord, and (2) **descending tetanus**, in which toxin distributed by the vascular system affects the voluntary muscles of the head and subsequently those of the trunk, forelimbs and then hindlimbs. The skeletal muscles of the side of the body with the wound are affected before those of the opposite side.

The action of tetanospasmin in nervous tissue is multiple but its principal activity is to inhibit the release of the neurotransmitters. This feature among other things permits all muscle groups to contract simultaneously when stimulated, in contrast to the normal state where contraction of one muscle is accompanied by relaxation or inertia in its counterpart.

Clinical and pathologic findings

The incubation period in tetanus is very variable. It generally ranges from 1 to 3 wk after the time of the injury, although some cases have been attributed to

wounding that occurred months previously. Usually, the longer the incubation period the more favorable is the prognosis. There is no incontrovertible evidence in the horse that tetanus can occur following activation of latent spores in tissue, as is the case in some other clostridial diseases in domesticated animals.

The clinical signs of tetanus are similar in all susceptible species. The horse usually suffers from **descending tetanus**, which is marked by an inability to retract the **nictitating membranes** and continual spasms in the facial muscles, producing in the affected animal an appearance resembling the lockjaw and the risus sardonicus seen in tetanus in humans. Premonitory signs include continuously pricked ears, stiffness, trembling and increasing difficulty in eating, chewing, and making other natural movements.

As the disease develops **all** muscular responses become exaggerated. Hyperesthesia increases so that the slightest sensory stimulus provokes violent contractions of the skeletal muscles. The limbs are rigid; the forelimbs stick out forward and the hindlimbs back. Sweating is profuse, the heart rate increases and the repeated, uncontrollable spasms interfere with breathing. The body temperature rises in the later stages of the disease when the horse experiences spontaneous convulsions. Eventually the muscular contractions are **violent and continuous** and can be provoked by the most minor external stimulus.

Once the first signs appear, the course is short and these distressing events last no more than about a week before death supervenes. The mortality rate is approximately 80%. Since the disease is produced entirely by biochemical changes in the neurologic control of skeletal muscle, there are no macroscopic or microscopic lesions detectable post mortem in the fatal case apart from the wound. The wound is not always discernible in the carcass.

Diagnosis

The clinical disease is remarkably distinctive. Only eclampsia in the mare (*q.v.*) and laminitis (*q.v.*), in which there is **no prolapse of the nictitating membrane**, are likely to be confused with tetanus. The assistance of the bacteriology laboratory is only required if an attempt is made to culture the organism from deep within the wound, given that it can be discovered, or it is known that surgical interference has recently taken place. The organism can be easily grown and identified in the laboratory. However, the isolation of *Cl. tetani* should be interpreted in relation to the clinical signs. The mere presence of the organism is not irrefutable proof of tetanus.

Treatment and control

Despite the virtually irreversible effect of the toxin on nervous tissue, antitoxin (20 000–50 000 IU, SC or IM s.i.d. or as needed) may parenterally prevent more nervous tissue being drawn into the pathologic process and neutralize all the toxin in the vascular system. Any good effect obtainable from antitoxin is likely to be limited to the earlier stages of the disease. The precipitating wound, if found, should be drained and infused with penicillin. **Penicillin** should also be given repeatedly in large doses (22 000 IU/kg IV q.i.d. or IM b.i.d.) to kill the organism and prevent yet more toxin being released.

The risk of tetanus is so great after wounding or surgery that **immunoprophylaxis** against the disease is essential in horses. Boosting dams with tetanus toxoid approximately 6 wk before parturition enhances the immunity acquired by foals in the colostrum. Foals can also be protected passively by giving antitoxin (approximately 3000 IU) parenterally which protects for approximately 2 wk and can be repeated until the foal is competent enough immunologically to respond actively to tetanus toxoid, as it is when 2–3 mo old.

Tetanus toxoid with adjuvant is a highly potent antigen which induces a durable, active immunity even if given simultaneously with antitoxin, provided separate sites are used for the respective injections. Despite the marked immunogenicity of tetanus toxoid, two doses approximately 4–6 wk apart are needed to produce adequate active immunity against the tetanospasmin. Solid immunity is usually established approximately 2–4 wk after the course is completed.

The immunity created by a course of toxoid also needs to be reinforced at **regular intervals**, these being determined principally by the degree of risk and the immunologic responsiveness of the individual horse. One year after the primary course a boosting dose of toxoid should be given and followed by further doses every 18–36 mo, the timing being dependent on the perceived risk. If required, the laboratory can determine the amount of antibody in the circulation. The minimum level of antitoxin in the circulation deemed to be protective is approximately 0.02 IU/mL.

Despite a satisfactory history of regular immunoprophylaxis in a horse, it is still sensible to administer antitoxin and/or toxoid (according to the known history of the animal) before surgery is attempted or after the occurrence of actual or suspected wounding.

ANTHRAX

The horse, like humans and the pig, is less susceptible to anthrax than ruminants. Nevertheless, when a horse is infected with *Bacillus anthracis* the course of the disease is acute and death usually occurs within days.

Etiology

B. anthracis is a large, non-motile, Gram-positive rod (approximately 4–8 μm long by 1 μm wide). It is a strict aerobe that grows well between 12°C and 44°C and freely produces its highly resistant spores between 15°C and 40°C. The square-ended vegetative cell is surrounded by a large capsule composed of a polyglutamic acid, which is induced by a plasmid. The capsule is always formed in vivo by virulent strains but only in special circumstances in vitro.

Vegetative cells sporulate in the presence of air. The production of spores in the diseased animal is inhibited by buffering and carbon dioxide. Unlike the vegetative forms, the spores are resistant to most disinfectants unless they are applied for lengthy periods at comparatively high temperatures. Peracetic acid is a useful sporicide but the spores are only readily killed by steam under high pressure.

The organism is readily cultivated in the laboratory and produces a highly distinctive growth. Each large, rough colony is non-hemolytic, looks like a piece of frosted glass and, because the bacilli grow in long whorls at the periphery, it has been likened to the **Medusa's head**.

Epidemiology and pathogenesis

The persistence of *B. anthracis* as a threat to animal health depends on a combination of environmental factors. There are well-recognized **enzootic zones** in the world (e.g. parts of the Indian subcontinent, Africa, North and South America) in which circumstances regularly favor the organism. In these areas, the existence of alkaline and calcareous soils with suitable amounts of nitrogen and a combination of a warm temperature (frequently ⩾15°C) with periodic wetness promotes abundant multiplication of the vegetative bacilli. Decreases in the humidity and temperature in these enzootic areas promote sporulation and the extensive contamination of the soil and vegetation is further augmented by spores from the carcasses of animals dying from the disease. The spores can survive in soil for more than **60 years**. Repeated, if unpredictable, epidemics of disease occur in these zones unless control measures are implemented.

Outside these zones anthrax is a much more **sporadic** disease, the occurrence of which depends either on exposure to the accidental introduction of spores on vegetable foodstuffs or animal products or to the disturbance of soil contaminated in the past by buried anthrax carcasses. These circumstances prevail in the UK and more generally in Western Europe.

Sometimes in the subtropics or tropics **biting flies** inoculate *B. anthracis* into the skin, but in general anthrax is contracted by **ingesting or inhaling the spores**. When ingested, the spores lodge in the pharyngeal or enteric mucosae, germinate and encapsulate. The capsule prevents phagocytosis and destruction of the cell. The vegetative cells begin to produce toxin. The complete toxin is a complex of substances, which are encoded by a plasmid. One component (Factor I) of the toxin is an adenyl cyclase, which provokes **massive edema** at the site of invasion. This event favors further multiplication and dissemination of the vegetative cells into the lymphatic system. Factor II is a substance for promoting the binding of Factors I and III (a lethal substance) to mammalian cells.

Bacteremia and septicemia occur when the lymphoid tissues can no longer contain the agent. Death usually follows within a few hours. The circulating toxin also produces general impairment of phagocytosis, capillary permeability, irreversible damage to the clotting mechanism, and shock with renal failure. It is important to appreciate that in acute anthrax the production of lethal amounts of the toxin **precedes** septicemia by several hours.

Clinical and pathologic findings

The onset of the disease in the horse is sudden and the course brief with few prodromal indications. Marked, **subcutaneous swellings** develop in the more dependent parts of the neck, thorax, abdomen and genitalia. Fever and extreme depression accompany severe colic and dysentery. Death follows these signs in a day or two. Rigor mortis is incomplete and unclotted, **tarry blood** oozes from the orifices of the body. The pathologic picture is one of hemorrhagic

edema and vascular damage throughout the body. There is hemorrhagic necrosis and gross swelling of all the lymphoid organs.

Diagnosis

In many countries anthrax is a **notifiable disease**, and even a suspicion of its possible occurrence must be reported to the appropriate authorities. Diagnosis in a freshly dead animal is made in the first instance by **microscopic examination of blood smears**.

The blood should be collected from a **small superficial vein** (such as the cephalic) that is likely to ooze little when opened. Swabs of this blood are also normally required. Any leakage from the vessel should be staunched with swabs soaked in strong disinfectant or the vessel should be cauterized. The smears should be reasonably thick and lightly fixed before staining with polychromatic methylene blue (or Giemsa). The slides should be handled with **caution** because spores are likely to be present. The presence of blue, square-ended bacilli surrounded by large pink capsules, which frequently have frilly edges, is conclusive. These bacilli are often in short chains. *B. anthracis* can readily be isolated from the swabs either directly or by scarifying the skin of a laboratory animal such as the guinea pig with the swab.

Treatment and control

B. anthracis is very sensitive to a wide range of antibiotics, including penicillin and the tetracyclines. Penicillin is curative if administered in **massive doses** (40 000–80 000 IU/kg IV q.i.d.) to an animal in the early stages of the disease, before the toxin has produced irreversible damage. They also prevent the development of the disease in other animals within a group deemed to be at risk from exposure to a common source of infection.

In areas where the disease is known to constitute a more or less continuous threat, **annual vaccination** of all grazers is necessary. The **Sterne vaccine** contains viable spores, which produce living cells of *B. anthracis* that lack the genes that encode the capsular material. They cannot therefore encapsulate when they germinate in vivo. Such cells survive only briefly when the spores are inoculated into animals but they live long enough to elaborate toxin. Both Factors II and III are immunogenic and stimulate antibody production. Antibody to the receptor-binding molecule (Factor II) prevents Factors I and III from acting on cells.

If there is even the slightest reason on clinical grounds to suspect anthrax, **great circumspection** is required in handling the case to minimize the risk to all the people and any other animals directly or indirectly associated with it. The carcass should not be the subject of a post mortem examination for this procedure favors a massive release of spores into the environment. Control measures vary in detail from country to country but always include prompt and effective disposal of infectious carcasses, disinfection of buildings, bedding and equipment, and quarantining of contacts, with additional controls on their produce.

STREPTOCOCCAL INFECTIONS

Etiology

Streptococci are probably the most frequently isolated bacterial pathogens of Equidae. The species and subspecies usually encountered are *S. equi* subspecies

equi, *S. equi* subspecies *zooepidemicus* and *S. dysgalactiae* subspecies *equisimilis*. These organisms belong to Lancefield group C, are beta-hemolytic and are readily distinguished by their fermentation behavior in lactose, sorbitol and trehalose as well as by the reactivities of their **M-like proteins** with specific antisera.

S. equi is the most host adapted and causes **strangles** (*q.v.*), a suppurative lymphadenitis of the head and neck of horses of all ages. It is also the most highly conserved with almost no variations in M (SeM) and other proteins. In contrast, strains of *S. zooepidemicus* have highly variable M-like (SzP) proteins and other characteristics, are not host adapted, and are identified from a variety of opportunist infections. *S. equisimilis* is the least commonly isolated equine group C streptococcus and is occasionally isolated from uterine or placental samples and from abscessed lymph nodes and arthritic joints. Equine strains show antigenic variation.

Alpha-hemolytic streptococci have been isolated from aborted fetuses and from lesions of funisitis and placentitis. *S. pneumoniae* capsule type III has been isolated from the airways of young horses in training.

Epidemiology

The highly host-adapted *S. equi* is maintained only in horse populations in which clinical disease is occurring. However, it survives in water for about 30 days and for extended periods in moist discharges. Nevertheless, persisting contamination of the environment is not an important source of the organism in outbreaks or in interepizootic maintenance. **Prolonged carrier states** associated with guttural pouch empyema (*q.v.*) are found in some herds, although the organism commonly disappears from horses in geographic regions for long periods of time only to reappear when an infected horse is introduced. Horses of all ages are affected but the disease is most common and most severe in **young horses**. Pre-existing immunity may ameliorate expression of the disease. *S. equi* is transmitted when discharges from the nose or abscesses contaminate feed or water or when affected foals suckle the mammary gland. Direct nose to nose contact may also result in transmission and contributes to the **highly contagious** character of strangles.

In large groups of horses on breeding farms the most severely affected age groups are foals, weanlings and yearlings. Morbidity in this age group may be up to 100% with a mortality of 1–5%. Older animals show a lower morbidity and mortality.

S. zooepidemicus occurs widely as a mucosal commensal of the nasopharynx and **external genitalia** of the horse and other host animals. An **opportunist pathogen**, it invades mucosal and epithelial surfaces damaged by virus infection or injury. It is the most commonly encountered pyogen in the horse and is isolated frequently from infected wounds and injection sites of older horses and from the **umbilicus** of foals in the first days of life. *S. zooepidemicus* is present in approximately 50% of cases of **cervicitis** and **endometritis** (*q.v.*) in the mare, in which it rapidly replaces *E. coli* that enters the reproductive tract devitalized by dystocia. Pneumovagina, retained placenta (*q.v.*) or an endocrine abnormality such as anestrus associated with pseudopregnancy (*q.v.*) are other abnormalities that predispose to invasion by *S. zooepidemicus*.

Although showing >97% DNA homology with the highly uniform (clonal) *S. equi*, *S. zooepidemicus* shows great variation in its SzP protein and in its colony morphology. In epizootics of nasal catarrh in young horses, isolates of the organism usually produce mucoid colonies with similar SzP proteins, suggesting that more virulent clones have been selected and become widespread.

Pathogenesis and clinical findings

S. equi enters the horse via the **nose and mouth** and attaches to cells in the crypt of the lingual and palatine tonsils. In a few hours it penetrates and is carried to one or more of the lymph nodes that drain the pharyngeal/tonsillar region. Multiplication occurs extracellularly in the lymph node resulting in the formation of long chains of the organism. Large numbers of neutrophils are drawn to the site by complement-derived chemotactic factors. Failure of phagocytosis and killing of the streptococcus appears to be due to a combination of the hyaluronic capsule, antiphagocytic SeM, and Se18.9 proteins.

The incubation period varies from 3 to 14 days after exposure, and clinical signs include sudden onset of fever (39.5–40°C) caused by the pyrogenic exotoxin SePE-I, loss of appetite, halitosis, difficulty in swallowing, intermittent cough, extension of the head and neck, swelling in the submandibular and/or supralaryngeal areas, nasal discharge and inflammation of the lymphoid nodules of the soft palate and tonsillar areas. During the following 3–7 days the swelling in the intermandibular or suprapharyngeal areas may increase because of lymphostasis and enlargement of the affected lymph node(s).

The occlusive effect of the **lymph node enlargement** is the source of the disease description "**strangles**", which in severe cases may result in suffocation unless emergency tracheotomy is performed. In most cases **abscesses** in affected lymph nodes rupture 7–14 days after the first clinical signs. Suprapharyngeal lymph node abscesses usually drain into the pharyngeal area resulting in a **copious nasal flow** of purulent material. This drainage may also occur into the **guttural pouch**, which may become distended and palpable posterior to the vertical ramus of the mandible.

Metastasis of purulent material may result in abscess formation in other locations such as the lungs, brain and thoracic or abdominal lymph nodes. This complication has a poor prognosis and is commonly termed "**bastard strangles**" (*q.v.*). Other complications during and after recovery from the typical disease include **purpura hemorrhagica** (*q.v.*), an immune complex-mediated vasculitis that occurs at 1–4 wk, paralysis of the left recurrent laryngeal nerve, anemia possibly associated with hepatic clearance of immune complexes bound to erythrocytes, and myopathy characterized by coagulative necrosis or chronic rhabdomyolysis and atrophy.

Outbreaks of strangles in horse populations with **pre-existing antibody** to *S. equi* may be present as an atypical or catarrhal form of the disease characterized by a slight purulent nasal discharge, cough, occasional slight fever of short duration and abscessation of lymph nodes in a few affected animals. Its progression in a group of horses is much slower than that of the typical disease. Older horses experiencing a secondary infection often exhibit the catarrhal form of strangles.

Approximately 70% of animals develop a solid, **enduring immunity** to the typical disease following recovery from strangles. This immunity is associated in part with mucosal IgG and IgA, and serum opsonic antibodies. Opsonic antibodies are slow to develop and do not attain adequate titers until 6–8 wk after clinical signs appear. Immunity is expressed in the tonsil and blocks further invasion. Nasal shedding of *S. equi* may continue for 3–4 wk following appearance of clinical signs and the organism may remain in the guttural pouch of some recovered animals for months thereafter.

S. zooepidemicus is a constant **secondary invader** of the upper respiratory mucosa as a sequel to influenza or herpes viruses. Many small purulent foci are produced in the lymphoid follicles of the mucosa and the resulting nasal discharge is mucopurulent. The draining lymph nodes often become **enlarged and hardened** and may become abscessed in some animals, but abscessation is much less frequent than in the case of strangles. Affected animals have nasal and ocular discharges, cough, may be slightly febrile and lose body condition. Secondary pneumonia due to *S. zooepidemicus* occurs in a portion of foal populations infected with influenza virus and is responsible for much of the morbidity and mortality in this age group. In **donkeys**, these secondary pneumonias are often fatal.

S. zooepidemicus is occasionally isolated from lesions of pleurisy or peritonitis. It is a common cause of **joint ill** (*q.v.*) in foals that may acquire infection in the birth canal. The organism enters the umbilicus and the ensuing bacteremia results in synovial infection, pyoarthritis and permanent damage to the joint(s).

In the mare, *S. zooepidemicus* infections of the cervix and uterus are transient and occur shortly after parturition. Dystocia or retention of the placenta (*q.v.*) may result in more persistent infections. However, most mares will recover from endometritis if they go through one or two estrous cycles free of new entry of bacteria into the uterus.

Prevention

The very contagious nature of strangles makes control of spread very difficult. Clinically affected animals as well as animals detected as infected by culture of nasal swabs or washes should be isolated immediately. The first clinical sign is sudden onset of fever to 39.5–41°C. Animals at this stage are not shedding *S. equi* and so may be isolated before transmission to others has occurred. Twice-daily temperature taking is therefore an invaluable aid in minimizing transmission and containing an outbreak.

All containers used for feed or water should be cleaned and disinfected. Surfaces of stalls contaminated with discharges should be similarly cleaned and disinfected. Effective disinfectants are povidone iodine, chlorhexidine gluconate, 0.6% sulfuric acid, glutaraldehyde and phenol (1:200).

Where possible, **fly infestations** should be reduced by use of screens, insecticides and electronic bug poppers. **Contaminated bedding** should be removed to a protected location and covered with a plastic sheet to compost. Cases held in isolation should be handled last and the **animal attendant** should be meticulous about hand and arm washing, removal of coveralls and boots, etc., before leaving the isolation area. **Pasture** upon which cases have grazed should be rested for at least a month before being grazed again by horses.

In large breeding enterprises, weanlings and yearlings should be located in small geographically separated groups remote from areas where mares and stallions are held. Incoming animals should be held in a designated isolation/holding area for 2 wk before release into a group on the farm. Ideally, these animals should be subjected to one or more **nasal swab cultures** during the 2 wk isolation period and rectal temperatures taken twice daily. This aspect of control cannot be overemphasized as the usual source of *S. equi* for uninfected premises is the recently **introduced infected animal**. Nurse mares frequently introduce infection in this way and should be isolated with their adopted foals.

Antibiotics such as a **long-acting penicillin** administered parenterally, e.g. benzathine penicillin (30 000 IU per kg IM q 2 days), or feed supplementation with low levels of tetracycline (60–80 ppm feed) are very effective in preventing or stopping an outbreak. However, **herd immunity will not develop during this time and animals will be highly susceptible to infection when the antimicrobial drug is withdrawn**. Use of low-level tetracycline also carries a slight risk of **antibiotic-induced clostridial enterocolitis** (*q.v.*) should the horse's environment be contaminated with toxigenic strains. Penicillin administration is most effective at the **onset of fever** before abscess development.

Vaccination with acid-extracted M protein or mutanolysin-extracted M protein commercial vaccines is effective in stimulating serum opsonic antibodies when administered in a course of two inoculations. However, these vaccines do not confer a high level of protection in the field against natural challenge. At best, the number of clinical cases is reduced by half and the disease is less severe in those cases that develop. Bacterin-type vaccines often elicit local and systemic reactions to peptidoglycan in bacterial cell walls; M protein extract vaccines contain less peptidoglycan and are better tolerated.

The incomplete protection stimulated by commercial vaccines is probably related to failure to stimulate mucosal IgG and IgA antibodies. Vaccination with live avirulent organisms is often effective in stimulating these antibodies and a high level of resistance to experimental challenge results. However, given that recovery from the naturally occurring disease provides solid protection in only 70% of horses, it is unlikely that vaccines based on live avirulent organisms will protect a much higher percentage than this. Live vaccines have the disadvantage that they may cause large painful abscesses if accidentally introduced into muscle at remote injection sites.

Vaccination of mares has been shown to increase colostral titers of IgG antibodies to SeM protein. Serum titers of these antibodies in suckling foals may thereby be increased.

The multiplicity of M-like (SzP) protein types involved suggests that vaccines developed against *S. zooepidemicus* or *S. equisimilis* must be multivalent or based on conserved epitopes or antigens.

Diagnosis

The clinical signs of classical strangles in which **lymphadenitis** is exhibited are easy to recognize. A pronounced leukocytosis with neutrophilia and fibrinogenemia accompanies the fever. However, **bacteriologic examination** is essential to confirm the diagnosis. Moist nasal swabs may be used to sample the medial nasal mucosa 10–15 cm in from the external meatus of each nostril and

plated on colistin–nalidixic acid (CNA blood agar). Nasal washes obtained by instilling warm physiologic saline (50 mL) into the retronares and collecting the washings that drain into a disposable cup for culture are more sensitive than swabs in detection of *S. equi* since a much larger area of the mucosa is sampled.

The **polymerase chain reaction (PCR)** using primers from the sequence of SeM is now widely used in presumptive detection of *S. equi* in clinical samples. The PCR test is approximately three times **more sensitive** than culture and is **highly specific**. However, in chronic cases of guttural pouch empyema, *S. equi* DNA may persist for days or weeks following bacteriologic cure.

Pus may also be aspirated aseptically from lymph nodes with a needle and syringe. Swabs or pus should be plated without delay. Beta-hemolytic colonies are identified after incubation overnight at 37°C by a combination of Lancefield grouping reaction and fermentation reactions in lactose, sorbitol and trehalose. Assay of convalescent antibody to *S. equi* by ELISA is available in specialized laboratories and is performed with recombinant SeM as antigen.

Serologic examination is helpful in detecting horses with internal abscesses and in confirming a diagnosis of *S. equi*-associated purpura hemorrhagica (*q.v.*). In both of these instances, very high levels of serum antibody are present.

Placentitis and metritis caused by either *S. zooepidemicus* or *S. equisimilis* may be diagnosed in the laboratory by culturing swabs or specimens on CNA agar. Uterine swabs, tampons or biopsies should be cultured, preferably between 10 and 14 days after ovulation. Tracheal aspirates cultured on CNA and stained by the Giemsa method are important in the laboratory confirmation of respiratory *S. zooepidemicus* infections of young horses.

Treatment

The equine group C streptococci are very sensitive to penicillin, ampicillin, erythromycin, chloramphenicol, cephalosporins and tetracyclines. Gentamicin resistance has been noted in *S. zooepidemicus* isolates from equine sources. Where appropriate, strangles is usually treated with IM doses of penicillin of up to 10 million units. Cases treated immediately at time of onset of fever will respond within hours and usually do not develop abscesses. However, since **most cases recover uneventfully and develop enduring immunity**, antibiotic administration is usually reserved for relief of life-threatening lesions that are intruding on the airway or for *S. zooepidemicus* infections in foals complicated by pneumonia.

Although penicillin is very effective for **prophylaxis** of in-contact animals and in treatment of respiratory tract disease caused by the equine group C streptococci, use of antibiotics requires **careful consideration** as they may delay maturation and draining of abscesses and ablate the protective immune response.

Abscesses should not be opened surgically until the capsule and fluid contents can be readily palpated beneath the skin. Insertion of a 16 or 18 gauge needle through surgically prepared skin into the abscess often establishes a tract along which the abscess capsule dissolves and speeds evacuation without the need for surgical incision.

Supportive therapy of strangles cases includes twice-daily cleansing of draining sites and nostrils, application of fly repellents and provision of a

high quality soft, moist feed. Guttural pouch infections (*q.v.*) may require irrigation with surgical antiseptic or penicillin solutions.

Streptococcal endometritis or placentitis may be treated with IM injections of penicillin (22 000 IU/kg BW/day) for 2 wk. Streptococcal placentitis must be treated at the first sign of vaginal discharge but with the caveat that the fetus already may have become septicemic by the time the discharge is noted. Treatment of chronic **streptococcal endometritis** (*q.v.*) is most effective during estrus when the non-specific natural antibacterial clearance mechanisms are most efficient.

Treatment of horses with purpura hemorrhagica includes corticosteroids to reduce polymorphonuclear leukocyte responses and antibiotics to protect against secondary bacterial infection. Blood transfusions (*q.v.*) may be indicated in cases with anemia or thrombocytopenia. Edematous legs should be bandaged.

CORYNEBACTERIUM PSEUDOTUBERCULOSIS

Etiology

Corynebacterium pseudotuberculosis produces a syndrome of ulcerative lymphangitis or abscess formation. Folliculitis and abortion have also been reported. The bacterium is a Gram-positive, non-motile facultative anaerobe that survives well in the environment and can infect other species, including man.

Epidemiology

The disease occurs worldwide in areas where horses are raised. However, there is a marked variation in clinical signs in geographic locations throughout the world. Pectoral, ventral midline, abdominal and inguinal abscesses are frequent presentations in areas of the western USA, whereas ulcerative lymphangitis is more typical elsewhere. The incidence of disease varies from year to year, and outbreaks can occur. Common names for the abscess form of the disease are "pigeon fever", "pigeon breast", "dry-land distemper" or "Colorado distemper".

Folliculitis (contagious pustular dermatitis, "contagious acne" or "**Canadian horsepox**") caused by *C. pseudotuberculosis* results in pustules that are often distributed in areas where tack or harness make contact with the skin. The disease may be transmitted by **contaminated grooming utensils**. Trauma to the skin, existing folliculitis or seborrhea may predispose the horse to infection. **Ulcerative lymphangitis** is a fairly uncommon disease that is usually associated with poor sanitation. Open draining tracts can be a source of environmental contamination.

Pathogenesis

The organism finds a portal of entry through abraded mucous membranes or compromised skin surfaces such as may be caused by **badly fitting tack**. **Biting insects** may also provide a portal of entry. This phenomenon may explain the seasonal incidence of the disease, particularly for the abscess form.

The infection may establish itself locally or spread via lymph or blood. Entry into the lymphatics of the limb is likely to be through local skin lesions and results in typical ulcerative lymphangitis.

The incubation period for the disease can be long and varies from weeks to months. Exotoxin production by the organism is thought to be significant in abscess formation.

Clinical findings

Typical **abscess formation** occurs most commonly in the pectoral region and occasionally in the abdomen along the ventral midline or in the inguinal region. Abscesses are often thick walled and can progress in size. Ventral or inguinal edema can be seen in association with abscesses. Depression, fever and anorexia may be present but are atypical. Axillary abscesses may result in gait abnormalities before abscesses are identified. Internal abscesses may produce signs of weight loss or abnormal pain.

The lower limb form of the disease may be initially identified as a nondescript swelling that can produce severe lameness. **Subcutaneous nodules** frequently develop, often in the area of the pastern, but they can spread to other sites. Nodules may range from a few mm to several cm in diameter. Ruptured nodules discharge creamy pus and generally result in an ulcer of the skin at the site of rupture. Lymphatics draining the area may become enlarged and firm. Nodules and ulcers can develop along these lymphatics. Recurrence of the disease may occur after resolution.

The papules and pustules of the skin form of the disease usually occur in groups. These are often associated with frequently abraded skin (from harness or tack) but can be more diffuse. Smaller papules may develop into pustules. The rupture of pustules leads to a crust formation. Lesions are usually not pruritic but may be painful.

Clinical pathology and necropsy

Elevations in white blood cell counts or fibrinogen may be identified early in the course of the disease. Chronically diseased animals may be hematologically normal. **Thick-walled abscesses** are a typical post mortem finding. Abscesses generally contain a tan-colored liquid exudate, whereas pustules may contain whitish-green pus. Abscesses are identified along lymphatics in peripheral limbs.

Diagnosis

Characteristic clinical signs such as large abscesses in the pectoral region, ulcerative lymphangitis or cellulitis with multiple small skin erosions of one or more limbs may suggest a *C. pseudotuberculosis* infection. A definitive diagnosis requires bacterial culture. Pure cultures can be obtained from the lesions. Abdominocentesis may identify abdominal abscesses, but normal peritoneal fluid does not rule out their presence. Ultrasonography can be useful in identifying deep abscesses in inguinal abdominal or axillary regions.

Treatment

Surgical incision into, and **open drainage** of abscesses is often required and aids resolution of infection. Pectoral and inguinal abscesses are often very

deep and may require deep incision or the use of large trocar drains. Ultrasonographic localization of abscesses can be beneficial. Daily flushing and local therapy may be required to maintain open drainage.

The efficacy of antibiotic therapy is controversial. The in vitro susceptibility of *C. pseudotuberculosis* is broad. Procaine benzylpenicillin (20 000 IU/kg IM b.i.d.), potassium penicillin (20 000–40 000 IU/kg IV q.i.d.) and sulfa-trimethoprim (5 mg/kg of the trimethoprim portion b.i.d.) are commonly used. The failure of antibiotic therapy may be a result of the intracellular nature of the organism or the inability of antibiotics to reach adequate levels in large, thick-walled abscesses. Rifampicin (5 mg/kg PO b.i.d.) and erythromycin (20–30 mg/kg PO q.i.d.) have also been recommended for treatment, as they reach good intracellular levels. The course of therapy, particularly when abscess drainage cannot be achieved, is protracted. Analgesics and anti-inflammatory drugs should be used when pain is present. Reduction of edema and inflammation may improve appetite and reduce the incidence of laminitis (*q.v.*) in the opposite limb.

Control

Improvement of **sanitation** and a reduction in constant **exposure to moisture** are imperative in reducing the incidence of the peripheral limb form of the disease. Preventing skin abrasions from tack or harness is useful. Quarantine or culling of infected horses reduces environmental contamination. *C. pseudotuberculosis* is susceptible to most disinfectants. Fly control and the use of screened stalls may reduce insect vector spread. Claims have been made for the successful application of autogenous bacterins, which have been used on a limited scale without serious adverse effects.

GLANDERS

Glanders is one of the most ancient of all diseases recognized. A scourge of solipeds, glanders was frequently seen in an acute form in the ass, in a subacute form in the mule and in a chronic (or even latent) form in the horse. Because the causal organism, *Burkholderia* (*Pseudomonas*) *mallei* (earlier known as *Bacillus*, *Pfeiferella*, *Loefflerella*, *Malleomyces*, *Actinobacillus* or *Pseudomonas mallei*), survives so poorly outside these hosts, the disease was always most prevalent in horses massed for military purposes or in horses in the growing cities and towns of the second half of the nineteenth century. In London, for example, there were at least 1000 clinical cases of the disease annually in horses in 1900 but some 25 years later there was none in the whole of the UK. The disease now appears to be confined to a few regions in Asia.

B. mallei can produce glanders in a wide range of species including humans and carnivores.

Etiology

B. mallei has few bacteriologic features in common with other members of the genus and its taxonomic position has always been problematic.

Epidemiology and pathogenesis

B. mallei is an obligate parasite that does not survive for more than about 6 wk outside its hosts. It is very sensitive to sunlight and drying even when partly

protected by the purulent exudate it produces in its host. Horses usually acquire the infection by **ingestion or inhalation**.

After penetrating the mucosae passively, the organism, like the tubercle bacillus, has a marked propensity to travel and deposit itself in **lymphatic tissues**. It also infects **pulmonary tissue** where it is associated at first with microscopic inflammatory foci. These foci enlarge to form macroscopic nodules and ultimately larger, **chronic granulomas**. A diffuse interstitial pneumonia can accompany this process. At any point during these events exudates containing the bacilli from the nodules can be discharged into the airways and so reach the upper respiratory tract where they produce nodules in the nasal cavity similar to those in the lungs. These nodules eventually rupture to produce the characteristic **punched-out ulcers** along the nasal septum. The ulcers discharge a gluey, purulent exudate. They can be seen in the congested and even hemorrhagic mucous membrane of the nasal cavity simply by everting the alar cartilage.

The bacilli may also infect the lymphatic tissues of the limbs where they give rise to **farcy**. Farcy comprises a chronic lymphangitis (the "farcy cords") and lymphadenitis (the "farcy buds"). As in the nasal cavity, these lesions rupture to discharge purulent exudate. The exudate contaminates stables, tack, harness and utensils with *B. mallei* and is thus a major source of infection for other animals and humans. The clinical and pathologic events that follow inhalation (or cutaneous inoculation) of *B. mallei* are similar to those that occur after its ingestion.

Although horses that have apparently recovered from the disease are resistant to further infection, they may suffer the occult form of the disease. In **occult (latent) glanders**, the pulmonary lesions are quiescent but can be provoked by **stress** into renewed development, leading to dissemination of the agent in the body and its release to the exterior. The reactivation of these quiescent lesions in the infected horse explains why in the past the severe strain of military operations was often associated with major outbreaks of the disease in the cavalry.

Although humans are much more resistant to *B. mallei* than Equidae, the organism can produce disease that chronically affects the skin and subcutaneous tissues and can generalize with fatal consequences.

Diagnosis

Clinical glanders is distinctive once the nasal and cutaneous lesions have formed and *B. mallei* is easily recognized in smears from such lesions. It is a Gram-negative, beaded rod approximately 1–5 μm long by 0.5 μm wide. *B. mallei* is easy to grow in the laboratory, but growth is slow even with media such as those containing glycerol which favor it and on which its colonies resemble drops of honey that gradually become brown. Affected horses can also be detected by serologic methods and the **complement fixation test** is generally regarded as the most reliable. However, **counterimmunoelectrophoresis** with appropriate antigen is fast and simple and is said to be as reliable as the technically more complicated CFT.

The **mallein test** can also be employed to detect infected horses. Mallein is a protein produced by *B. mallei* during growth. When it is inoculated

intradermally into the eyelid or instilled into the conjunctival sac, it gives rise to swelling of the eyelid and the formation of a purulent exudate in the eye of a glanderous animal within 24 h. This test, like the CFT, is a prescribed test for international trade and is indispensable in the control of glanders.

Treatment and control

The horse is essential to the persistence of *B. mallei*. Consequently **no convincing case can be made for treating a horse with the confirmed disease** or infection. The destruction of infected animals has eliminated the disease from the horse populations of many areas of the world.

HISTOPLASMA FARCIMINOSUM

Histoplasma farciminosum causes **epizootic lymphangitis**, a condition still encountered in parts of the African and Asian continents. In these enzootic areas new cases usually arise in autumn or winter. This fungal infection has superficial clinical similarities to glanders (as farcy) and ulcerative lymphangitis and for that reason can be considered briefly here. It is a notifiable disease in many countries.

The lesions of epizootic lymphangitis affect the lower limbs, and their distribution and other circumstantial evidence suggests that the infection is acquired from a mycelial phase in the **soil**. The fungus is present in its yeast phase in the thickened and suppurating vessels and aggregates of lymphoid tissue. In this form the agent is an ovoid cell approximately $4 \times 3\,\mu m$. It is irregular in outline due to buds of cytoplasm extruding from the thick cell wall. Infection is thought to be acquired through minor **abrasions or wounds** in the skin. After some weeks, the inflammatory process in the thickening lymphatic vessels leads to local ruptures. Deep ulcers in the skin exude thick pus in which yeast cells can be detected microscopically.

Without treatment the clinical course lasts about a year but affected animals eventually recover. A related organism, *H. capsulatum*, produces histoplasmosis in many areas of the world. Although many infections with *H. capsulatum* are clinically inapparent, frank disease is occasionally seen in the horse in the enzootic areas in the USA.

MELIOIDOSIS

Pseudomonas pseudomallei, the cause of melioidosis, has many more resemblances to *P. aeruginosa* than *Burkholderia mallei*, including a **relative insensitivity to antibiotics**. The organism is widespread in the soils and waters of tropical or subtropical regions of Asia, Australia and elsewhere, but the agent has been detected also in temperate soils.

Most instances of infection with *P. pseudomallei* are contracted from the environment and not from other affected animals, and do not give rise to a clinical condition.

When frank disease does result from infection with *P. pseudomallei*, which is an opportunistic pathogen, it strongly resembles, clinically and pathologically, acute, systemic glanders in most instances. The disease has been observed in a

wide variety of wild and domesticated animals, including, very occasionally, the horse. *P. pseudomallei*, a Gram-negative, bipolar-staining, pleomorphic bacillus may be cultured from abscesses, discharges or blood. It can be differentiated from *B. mallei* by its biochemical characteristics.

There are no vaccines available against melioidosis. Since *P. pseudomallei* is resistant in vitro to many antimicrobial drugs, treatment must be based on the results of sensitivity tests and empiricism. In humans, mild cases of melioidosis have responded to therapy with **tetracyclines**.

EHRLICHIOSIS

Among the bacteria there exists a taxonomic grouping of small coccoid organisms that are obligatory intracellular parasites. These organisms—the **rickettsias**—have the typical structure and most of the enzymes of other bacteria and are Gram-negative. Rickettsias will not grow in artificial media but can be propagated in the yolk sac of the chick embryo or in tissue cultures.

The rickettsiae are well-established **vector-borne pathogens**. They form a heterogeneous group that includes species capable of producing disease in domesticated animals. They are mostly **tick transmitted** and an intermediate host has been identified for several well-characterized rickettsias. Two species of rickettsial pathogens, *Anaplasma phagocytophila* and *Neorickettsia risticii*, produce disease in the horse in parts of North America and Europe.

Potomac horse fever (equine monocytic ehrlichiosis)

Etiology

Neorickettsia risticii (formerly *Ehrlichia risticii*), which has emerged as a pathogen of American horses in the early twenty-first century, is related antigenically to *N. helminthoeca*, the agent of salmon poisoning in dogs. *N. risticii* is a morphologically typical rickettsia and grows well in cultures of macrophages.

Epidemiology and pathogenesis

Serologic evidence indicates that infection with *N. risticii* is widespread in the USA but the disease itself only occurs sporadically and is often confined to an individual animal in a group. Younger animals appear to be less susceptible.

Potomac horse fever (PHF) (*q.v.*) occurs only in the summer and autumn and is most prevalent inland near rivers. The agent is associated with a **trematode vector**, which uses freshwater snails and aquatic insects as intermediate hosts, and insectivores (bats and birds) as definitive hosts. The natural route of infection is **oral** through the accidental ingestion of aquatic insects such as **caddis flies**. The disease is infectious but not contagious. An attack induces high levels of antibody and recovered cases are apparently immune to further clinical episodes and probably even infection.

Clinical and pathologic findings

The end of the incubation period of 9–15 days is marked by depression, anorexia and fever. Profuse or even projectile diarrhea follows quickly in about half of the cases; in other affected animals, the diarrhea is milder. Colic,

anasarca, abortion and laminitis also occur in about a third of the cases; the onset of laminitis is regarded as indicating a poor prognosis.

As the syndrome progresses the severest cases go into deep **hypovolemic shock** (*q.v.*). The clinical severity of the disease is variable, but the case fatality rate is approximately 30% in untreated animals.

At the onset of the condition a marked leukopenia is succeeded by a leukocytosis and the increasing packed cell volume (PCV) and plasma protein concentrations are a reflection of the severity of the **diarrhea**. This in turn reflects the extent of the erosive or **ulcerative lesions** seen principally in the cecum and colon but found throughout the gut. Aortic, cardiac and hepatic hemorrhages may be present. Vasculitis and thrombus formation may be seen microscopically.

Diagnosis

Clinically, the disease is difficult to distinguish from an acute attack of salmonellosis or clostridiosis (*q.v.*). However, clinical signs in the proven absence of other pathogens and the clinicopathologic changes (leukocytosis, increased PCV, plasma protein) may assist in diagnosis. *N. risticii* is rarely seen in monocytes in suitably stained blood smears and isolation of the organism in the laboratory is difficult. PHF is diagnosed by PCR on whole blood and or feces.

The serologic examination of **paired blood samples** collected at an appropriate interval assists in retrospective diagnosis. A rise in antibody titer against *N. risticii* can be determined by immunofluorescent antibody, ELISA or Western blot. The examination of a single sample is of questionable value. The antibody response induced by infection with *N. risticii* appears early in the course of clinical disease and persists for at least a year.

Treatment and control

As with other rickettsial diseases, the **tetracyclines** (8–10 mg/kg IV s.i.d. or b.i.d.) are favored for therapy. No instance of resistance of *N. risticii* to tetracyclines appears to have been recorded. Non-specific supportive therapy, especially to correct the dehydration induced by diarrhea, is also **mandatory** in severe cases. Killed bacteria are effective experimentally in protecting against challenge. In the field, vaccines have shown poor protection.

Equine ehrlichiosis (equine granulocytic ehrlichiosis)

Anaplasma phagocytophila (formerly *Ehrlichia equi*) produces disease in horses in some parts of the USA and Europe and is transmitted by *Ixodes* ticks. **Equine ehrlichiosis** is characterized principally by depression, fever, edema of the legs, ataxia and jaundice. Most of the clinical signs are a result of the **vasculitis** with hemorrhage that the agent produces. Recovered horses are immune and are not carriers.

When the disease is at its peak, the agent is readily observable in the granulocytes. Approximately half of the neutrophils in the circulation can contain the agent in the acute stage of the disease. The organism is usually present as morulae, i.e. loose clusters approximately 3 μm in diameter, of coccoid bacterial cells. Fluoresceinated antibody is also available for the diagnosis of

suspected cases. **Oxytetracycline** (8–10 mg/kg IV s.i.d. or b.i.d.) is effective in curing the disease. No vaccine is available and the disease can be prevented by good tick control.

LYME DISEASE (BORRELIOSIS)

Lyme disease was first described in humans in the northeastern USA in the early 1940s. It took the form of a fever, malaise and shifting arthritis extending over many weeks. Its occurrence correlated with the season of activity of **ticks** of the genus *Ixodes*. The condition has since been reported in other parts of North America, in Europe, including the UK, and Australia. Since its recognition in humans, similar cases have been detected in domesticated animals. The dog is most commonly affected but the horse is also susceptible.

Etiology

The cause of Lyme disease is *Borrelia burgdorferi*, a helically coiled organism some 20 μm long by 0.2 μm wide. The genus *Borrelia* is related to *Treponema* and *Leptospira* (*q.v.*), and with them forms part of a major group of bacteria, the **spirochetes**. These organisms differ significantly from other bacteria in their morphology. The cell is slender, flexuous and helically coiled. It is enclosed in an outer membrane or sheath. This sheath envelops the flagella (the axial filaments) that arise near each pole of the cell and overlap at the centre. The action of the flagella gives rise to the movements of flexion and rotation that are characteristic of the spirochetal cell.

Epidemiology and pathogenesis

Borrelias are **arthropod-borne** parasites of humans and many other species of mammals and birds. *B. burgdorferi* is maintained in, and transmitted by, nymph and adult ticks of the *Ixodes* complex. However, **in the absence of the vector**, *B. burgdorferi* can also be transferred among susceptible animals by blood, urine, synovial fluid or transplacentally. In the USA, *B. burgdorferi* circulates in mice and deer.

Clinical and pathologic findings

Lameness, lymphadenopathy and fever are the cardinal clinical signs and they are accompanied by malaise and inappetance. A characteristic **shifting polyarthritis** develops. In the horse, uveitis and encephalitis have also been recorded in conjunction with the arthritis. In the acute stage of the disease the affected joints are hot, swollen and painful and neutrophils are abundant in the synovial fluid. In general, the disease exhibits the features of an immune complex (type III) reaction and can become chronic.

Diagnosis

The history and clinical syndrome in animals that are or have been in known endemic areas is suggestive of Lyme disease. However, the joints may appear radiographically normal, as do various blood profiles. The agent can be isolated by culture of blood, urine or synovial fluid drawn from an acutely affected

joint. *B. burgdorferi* is difficult to grow in the laboratory and also grows slowly. However, in acute cases the organisms are usually **abundant in the affected joints**. The agent can be recognized by its distinctive morphology using dark-field microscopy or serologically with fluorescein- or peroxidase-labeled antibody. Humoral antibodies can also be measured.

Treatment and control

More is known of the benefit of antimicrobial agents in the treatment of this disease in humans and in the dog than in the horse. In humans, the tetracyclines, penicillins and cephalosporins have all been effective and even chronic cases have responded to IV penicillin. In the dog, antibiotic therapy has been curative when maintained for 21–28 days. **Tetracyclines**, for example doxycycline (10 mg/kg PO b.i.d.), are effective in horses. Serologically positive but clinically normal animals are also treated. A **killed vaccine** is available for use in dogs at risk from the disease in the USA. Annual revaccination is recommended.

Measures to control the **tick infestation** of individual animals, including daily inspection, are recommended (*q.v.*), although searching for the nymphal stage (approximately 1 mm long) is hardly practical.

PYODERMA AND SADDLE SORES OR GALLS

Pyogenic dermatitis in horses is usually associated with *Staphylococcus* spp. (chiefly *S. aureus*) although it may also be caused by other bacteria including *D. congolensis* and *C. pseudotuberculosis* (*q.v.*). The lesions, which vary from superficial and slight to deep and persistent, frequently arise after mechanical injury to the skin from chafing by harness or saddlery. If affected animals are neglected or abused, abscesses, furunculosis, or an indurated proliferative dermatitis may occur.

When the bacterial dermatitis is in its earlier stages, topical antiseptics (such as hexachlorophene or iodine preparations), emollients and shampoos (benzyl benzoate preparations) or antibiotics are helpful. The choice of antibiotics for topical or parenteral treatment should rest on isolation of the causal agent and determination of its sensitivity. *S. aureus* can be resistant to a wide range of antibiotics. **Autogenous vaccines** can be administered in extreme cases.

Historically, *S. aureus* was implicated in **botryomycosis** in the horse in which chronic granulomatous lesions develop in the spermatic cord after castration or in the stump of the tail after docking, usually as a consequence of poor aseptic techniques. The lesions, which can attain a remarkable size, exude pus containing hard coarse granules and abundant staphylococci.

FISTULOUS WITHERS AND POLL EVIL

Fistulous withers and poll evil reflect two features of the genus *Brucella* in horses, namely: (1) the propensity of the organisms to lodge in synovial structures, and (2) the ability of brucellae to infect domesticated species other than their principal host.

The horse is a **coincidental host** of *B. abortus* or *B. suis* and the prevalence of fistulous withers and poll evil in horses in a given region is an indirect

indication of the **respective prevalence** of brucellosis in the cattle or pigs of that region and the extent of contact between horses and the definitive hosts.

Although infection of the **bursae** is most usual, *B. abortus* can also infect other synovial structures such as the joints and tendon sheaths. Infection of the supra-atlantal and supraspinal bursae probably occurs after ingestion of brucellae. Bacterial localization in the synovial membrane causes a clear, thick exudative inflammation leading to swelling of the bursae. The thickening of the chronically inflamed bursal wall is insufficient to prevent its eventual rupture. When rupture does occur, infection with other bacteria, e.g. *Actinomyces bovis*-like anaerobes and other opportunists such as staphylococci, induces **suppurative changes** in the fistulae and the bursa. These chronically discharging lesions constitute a **source** of *B. abortus* to the horse and other animals, including, importantly, cattle.

A diagnosis of poll evil or fistulous withers can be confirmed by isolating *B. abortus* from fluid aspirated from the affected bursa. As these organisms cause brucellosis in man, the material for examination needs to be collected, transported and handled with special care and appropriate containment. Support for the diagnosis can also be achieved by determination of the titer of humoral antibody to *B. abortus* (or *suis*). Once the diagnosis has been confirmed, poll evil or fistulous withers are best treated by **surgical removal** of the bursa.

LEPTOSPIROSIS

Infection with leptospires occurs in all domesticated animals. In endemic areas the majority of infections are clinically inapparent. The horse and the cat are less susceptible to leptospirosis than other domesticated species.

Etiology

Leptospires are related taxonomically to treponemes and borrelias and are principally aquatic saprophytes, which are divided into two species, *Leptospira interrogans* and *L. biflexa*. The former species contains all the pathogenic varieties and it is divisible into groups of serovars on the basis of serologically distinct, superficial antigens. There are some 200 serovars that differ in their pathogenicity for different species of animals and in their geographic distribution throughout the world.

Epidemiology

Leptospires tend not to be highly host adapted and to have maintenance or **reservoir hosts** among small wild animals in the environment. However, in some instances certain serovars have become so well adapted to a particular species that the final host serves also as the maintenance host for the pathogen.

Leptospires are principally transmitted in **urine** and **water**. Serologic evidence of exposure to leptospires is most prevalent in the wetter, warmer parts of the world. Most equine infections are associated with serovars *hardjo*, *icterohaemorrhagiae*, *pomona* or *bratislava*.

Clinical signs

Infection with leptospires usually results in **subclinical disease** but if the infection is acute the horse is pyrexic, depressed, anorexic and jaundiced.

Hemoglobinuria may occur. Leptospirosis in the pregnant mare may result in abortion during, or some weeks after, a clinically vague febrile episode. Several serovars such as *pomona, hardjo, icterohaemorrhagiae* and *bratislava* have been isolated from aborted equine fetuses.

Months or even years after exposure to leptospires a horse may suffer **periodic ophthalmia** (*q.v.*). Affected horses have repeated attacks of hypopyon, keratitis, conjunctivitis and iridocyclitis that occur in one or both eyes. These lesions are of sufficient severity ultimately to produce blindness. The nature of the whole process is suggestive of a hypersensitivity reaction between the antibodies in the anterior chamber and antigen (probably in tiny amounts) reaching it from elsewhere in the body.

Diagnosis

Leptospires can be detected in specimens of blood or urine by culture or by injection of hamsters or guinea pigs. Leptospires are not exceptionally difficult to grow in the laboratory but their nutritional and cultural requirements are unusual in that they require a pH of 7.0–7.2, long-chain fatty acids, vitamins B_1 and B_{12}, protein (or ammonium salts) and aerobic incubation at 30°C. Appropriate media (usually liquid or semi-solid) for their isolation often contain 5-fluoracil to inhibit other agents that may be present in contaminated material. Growth in the laboratory may require **several weeks**.

When leptospires are present, either as part of an acute episode or as a consequence of **chronic nephritis** (*q.v.*), the organisms are also demonstrable in **urine**, especially if it has been concentrated by centrifugation. Lightly pelleted material when resuspended is examined **microscopically** by dark-field illumination or by UV illumination after the application of fluoresceinated antibody. The helically curved bacteria are up to 30 μm in length but slender in width (0.1 μm). **DNA probes** for the detection of elements of the leptospiral genome are also available.

An increased antibody titer in paired serum samples taken at appropriate intervals during the course of a suspicious episode also assists in diagnosis. Seroconversion can be demonstrated by simple microscopic agglutination tests. However, the availability of a wide choice of suitable antigens is often necessary and the ability to conduct diagnosis by serologic means tends to be restricted to specialized laboratories. In periodic ophthalmia, leptospires cannot be demonstrated in the afflicted eye but there are antibodies against leptospiral antigens in the circulation and especially high titers in the aqueous humor.

Treatment and control

Penicillin (20 000–40 000 IU/kg IV q.i.d.) or the **tetracyclines** (8–10 mg/kg s.i.d. or b.i.d.) are the antibiotics of choice for the treatment of acute leptospirosis and for eliminating the persistent or intermittent leptospiruria that occurs in the chronically affected animal or the carrier animal.

For **periodic ophthalmia** the parenteral administration of an appropriate antibiotic such as penicillin (20 000–40 000 IU/kg IV q.i.d.) or tetracycline (8–10 mg/kg s.i.d. or b.i.d.) should be coupled with the local administration of an anti-inflammatory steroid or non-steroidal agent. Immunization of horses against leptospirosis is not practiced.

CONTAGIOUS EQUINE METRITIS

Etiology

Contagious equine metritis (CEM) (*q.v.*) is a very highly contagious disease of mares that was first described some 15 years ago. It is caused by infection with *Taylorella equigenitalis*, a microaerophilic Gram-negative rod (approximately 1 μm long) that grows slowly (2.5 days) in the laboratory.

Epidemiology and pathogenesis

Spontaneous infection with *T. equigenitalis* in species other than the horse is not known. The organism is an obligate parasite of the surface of the **terminal urethra and its fossa** in the stallion and in the **clitoral sinuses and fossa** of the mare. *T. equigenitalis* has also been isolated from sexually immature animals, some of which might have acquired the infection at birth.

T. equigenitalis is transmitted to susceptible mares by an infected stallion during mating, although transmission by other means (instruments, procedures and attendants) is also possible. Infected stallions do not mount a humoral immune response or give any clinical sign of the infection. Their libido and fertility is unimpaired. The disease is **highly contagious**. A susceptible mare that has been covered by an infected stallion soon develops clinical signs of an acute infection in the reproductive tract.

Contracting infection with *T. equigenitalis* does not preclude a normal pregnancy in the mare although the organism can be isolated from the placenta. Occasionally, inapparent infections in barren or in-foal mares occur.

Clinical and pathologic findings

The clinical signs of the disease in the mare vary from mild to severe. In a typical case, an increasingly copious grayish exudate is discharged from the vulva 2–12 days after the service, soiling the tail and quarters. There is evidence of vaginitis, cervicitis, endometritis and salpingitis. The conception rate in acutely affected animals is low. Fertility is regained when the acute disease abates. After the acute attack ends, however, the mare sheds the organism continuously or intermittently for lengthy periods.

Pathologically, the acute disease is a simple **catarrhal infection** of a mucous membrane with the production of an exudate that is rich in neutrophils and accompanied by edema and infiltration of mononuclear cells into the lamina propria of the mucosa.

Diagnosis

The clinical signs in the acutely affected mare are highly suggestive. The agent (including those organisms phagocytosed by neutrophils) can be observed in simple, stained smears of the exudate that appears during the course of the acute disease. However, since the occurrence of the disease has serious implications for breeders, **isolation of the organism** is essential for a confirmatory diagnosis. For bacteriologic culture, specimens should be obtained by guarded swabbing of the uterus or cervix, the clitoral fossa and/or sinus as appropriate in barren, maiden, post parturient or served mares.

If the mare is pregnant, a swab of the clitoral sinus should be collected. In the stallion, swabs from the terminal urethra, its fossa, the prepuce and penis (including the pre-ejaculatory fluid) are required. To maximize the survival of *T. equigenitalis*, swabs should be held at 4°C in Amies medium (or Stewart's medium) until processed in the laboratory.

Bacteriologic examination can be supplemented by serologic investigation in acutely affected mares to detect humoral antibodies by immunosorbent assays, CFTs, passive hemagglutination tests or simple agglutination tests. These serologic procedures are not suitable for diagnosis of the infected stallion or the chronically infected mare.

Treatment and control

If an animal is infected it must not be mated until it has responded to appropriate treatment and been shown conclusively not to be a carrier. *T. equigenitalis* is sensitive to various antibiotics including those commonly available in veterinary practice. Topically applied nitrofurazone is the treatment of choice. As with other important venereal diseases, however, control best depends upon well-organized and **thorough checking** of the breeding animals before each breeding season with the aim of excluding the chronically infected animals.

There is a common **Code of Practice** (*q.v.*) for the control of CEM in France, Germany, Ireland, Italy and the UK. Stallions and mares should not be mated until it has been confirmed by a "designated" or "approved" laboratory that they are free from CEM. The procedures for the routine swabbing, certification and management of "low risk" mares, "high risk" mares, stallions and teasers and the action to be taken if CEM occurs are clearly documented in the Code.

OTHER BACTERIAL INFECTIONS OF THE REPRODUCTIVE TRACT AND MASTITIS

Pseudomonas

Pseudomonas aeruginosa is a ubiquitous, slender Gram-negative rod that produces a formidable array of virulence factors including proteases, elastases and toxin A, which inhibits protein synthesis.

P. aeruginosa can be found on normal skin and in the mucosa of the upper respiratory tract, alimentary tract and external areas of the reproductive tract in animals. It is also found in water and soil.

P. aeruginosa behaves principally as an opportunistic pathogen in domesticated animals. Its establishment and production of lesions, for example in the equine **cornea**, is usually preceded by some form of local or general **debilitation**, such as might be induced by natural or surgical trauma, burns, natural or induced states of immunosuppression or by prolonged administration of antimicrobial drugs.

Mares that have had difficulty at parturition are susceptible to infection with *P. aeruginosa*. The organism can also be transmitted to mares by an infected stallion at the time of covering. The frequent use of chlorhexidine as an antiseptic at the time of service can lead to a build-up of the numbers of *P. aeruginosa* present in the prepuce of the stallion. Venereal infection with certain serotypes of *P. aeruginosa*, for example the O3H3 group that predominate in the UK, is associated with **metritis** and even abortion (*q.v.*).

The bacteria are very easy to grow and recognize in the laboratory. Recognition is facilitated by the fact that the cells produce: (1) pigments (a greenish fluorescein and bluish-green pyocyanin) which diffuse into the agar and oxidize with time to yellow and brown, and (2) an aminoacetophenone, which smells like the ripe grape. Some strains giving a very mucoid growth on agar are commonly found in the pulmonary lesions in children with cystic fibrosis and have also been recorded in the damaged guttural pouch in a horse.

P. aeruginosa is resistant to many antimicrobial drugs. This resistance can be spontaneous or induced. The induced form can be provided by R factors or chromosomal changes. Antibiotics known to have some activity are gentamicin, tobramycin, amikacin, polymyxin B and colistin (*q.v.*).

Antibodies against the virulence factors of *P. aeruginosa* protect against the effects the organism can have. **Vaccines** are effective against the devastating disease which *P. aeruginosa* produces in young, farmed mink but in racehorses these vaccines diminish the severity and decrease the recovery time from associated corneal ulceration.

Klebsiella

Klebsiella pneumoniae produces disease in the reproductive tract of the mare. The bacterium is a markedly encapsulated, rather coccobacillary rod that can be grown easily in the laboratory. The capsule is easily recognizable in suitably stained smears and is composed of serologically distinct, heat-stable polysaccharides, the existence of which provides the basis for a typing scheme. Some 80 such serotypes are known, but of these very few (types 1, 5 and 7) appear to predominate in the diseased mare.

The bacterium is a member of the enterobacteria but is merely a minor constituent of the gut flora in normal animals. It also occurs in the general environment and can be detected in large numbers in damp wood products such as shavings or sawdust. Some mares harbor strains of *K. pneumoniae* on their urethra or clitoris. Although the stallion can therefore contract and transmit klebsiellae, the bacteria are not usually able to persist in the normal reproductive tract of mares. Hence the stallion is rarely a source of this infection. In mares an invasion of the reproductive tract leads to infertility, metritis and/or abortion (*q.v.*).

Mastitis

Acute mastitis in the lactating mare is observed most frequently when the animal is drying off. One or both glands can be affected. The infected gland is swollen, tender and painful. The infection can be sufficiently severe to produce systemic disturbance. When the changes in the gland are extreme they affect the posture and gait of the mare. The excretion is abnormal in consistency, content and cell numbers.

In the mare **prompt treatment** of mastitis is needed, otherwise there is a risk of chronicity or induration with permanent loss of secretory tissue. The cause of mastitis should be determined by bacteriologic examination of a sample of the affected milk. The specimen should be collected before any intramammary

infusion or parenteral injection of antibiotics is made. If treatment with intramammary infusions is selected, **both teat canals** in the gland should be infused.

The bacteria producing mastitis in the mare are mainly Gram-positive cocci, particularly of the genus *Streptococcus*, including *S. zooepidemicus, S. equisimilis* and *S. equi*, although a wide range of bacteria have been implicated.

MAJOR INTERNAL PARASITES OF HORSES

HELMINTH PARASITES

Introduction

Helminth (worm) parasites are ubiquitous in horses. Horse owners are generally aware of the fact that worms are transmitted via infective stages on pasture, and usually assume that regular worming is necessary and effective in controlling these parasites. As a result, veterinary involvement in providing advice on worm control is often not sought until obvious clinical problems arise. However, **anthelmintic resistance** in some of the most important helminth parasites of horses has become widespread. It is now crucial that veterinarians communicate to horse owners and managers of equine establishments that excellent worm control can be achieved by using knowledge of parasite life cycles and good pasture management coupled with strategic dosing only where necessary.

The major helminth parasites of horses are shown in Table 1.1. **All** grazing horses are likely to be infected with some or all of these worms. In general, low burdens are tolerated well, with the development of clinical disease or subclinical ill-thrift depending on the numbers and species of worm present, which in turn depends on various environmental and epidemiologic factors.

Table 1.1 Major internal parasites of horses

Type of parasite	Species involved	Predilection sites	
		Adults	*Larvae*
Cyathostomins	About 50 species known, 4 especially common	Large intestine	Intestinal wall
Roundworm	*Parascaris equorum*	Small intestine	Liver, lungs
Large strongyles	*Strongylus* spp., *Triodontophorus*		
Tapeworms	*Anoplocephala* spp.	Ileocecal junction	Invertebrate intermediate host (forage mites)
Lungworm	*Dictyocaulus arnfieldi*	Airways	Lung parenchyma
Roundworm	*Strongyloides* spp.	Small intestine	–
Pinworm	*Oxyuris equi*	Large intestine	Intestinal wall
Bots	*Gasterophilus* spp.	Female flies lay eggs on hairs	Stomach
Apicomplexa protozoa	Various, including *Sarcocystis, Neospora, Babesia*	Various tissues	N/A

Although **mixed infections are the rule**, a number of specific disease syndromes may emerge, for example strongyloidosis due to threadworm infection in young foals, parascariosis due to the roundworm *Parascaris equorum* in older foals and yearlings, and most important in animals of all ages, strongylosis and cyathostominosis due to infection with the large and small strongyles or redworms. A range of drugs are active against these parasites.

Three classes of anthelmintics are available for control and treatment of helminths in horses:

1. Avermectins/moxidectins
2. Pyrantel/morantel
3. Benzimidazoles.

With the rise in benzimidazole resistance (*q.v.*) among the cyathostomins, it is essential that development of further resistance be slowed through **strategic anthelmintic use** together with maximal use of complementary control methods such as **pasture management** and **dung removal**.

Generally, it is advisable to treat horses only when this is indicated by fecal egg counts, to leave a proportion of the population undosed where possible, and to rotate the drug family used annually or twice a year. In many cases anthelmintics are **overused** in horses, and the true potential of grazing management and dung removal for helminth control is not realized.

Strongylosis/cyathostominosis

The term **strongylosis** is used to describe disease caused by infection with the large strongyles (*Strongylus* spp., *Triodontophorus* spp.) and small strongyles (*Cyathostominae*). Equine strongylosis is usually due to a mixed infection with these parasites. Heavy infections, characterized by loss of condition and anemia, are common in horses of all ages, but especially in animals between 1 and 3 yr of age. There are special features associated with infection with the larval stages of small strongyles or cyathostominae, (larval cyathostominosis) and of *Strongylus vulgaris*.

Life cycles—pathogenesis

Equine strongyles comprise the **large strongyles** (three *Strongylus* spp., including *S. vulgaris*), several *Triodontophorus* spp. and over 51 species of the subfamily cyathostominae, also called "small strongyles". All of these helminths have direct life cycles, all produce typical strongyle eggs, and all develop in a similar way on pasture: eggs hatch to release the first larval stage (L1) which then molts to the second larval stage (L2) and then the infective stage (L3) on pasture. The time taken for development through to the infective stage is dependent on ambient temperature.

In temperate climates, some eggs and larvae **survive over the winter**, serving as an initial source of infection for susceptible animals on pasture in springtime. As temperatures increase over the summer, the time taken for development to infectivity decreases, thus leading to a peak in pasture infectivity in mid-summer. In continental climates, cold temperatures during winter prevent carry-over of infectivity on pastures, and very hot, dry weather in summer may also limit the build-up of infectivity.

The parasitic phase of the life cycle, together with the pathogenesis of infection, differs between the different groups of strongyle parasites. These are dealt with separately here. The same general principles apply to the control of all of these parasites.

The **cyathostomes** or **small strongyles** are now considered to be the most common helminth parasites of horses and the cause of the most **intractable** disease problems. Although over 50 species of the subfamily (in four genera) are recognized as occurring in the horse, perhaps a dozen are commonly found, usually as mixed infections. The adult worms are found in the lumen of the cecum and colon where they feed on plugs of mucosa, leaving small **erosions and hemorrhages** at each feeding site. Adult cyathostomes contribute to the general syndrome of **ill-thrift**, anemia, and the "wormy horse" along with *Strongylus* and *Triodontophorus* spp.

Before reaching the large intestine, ingested infective larvae first burrow into the mucosa, where they may undergo a period of **hypobiosis** (arrested development) for several months or even longer before molting to L4 and L5, and emerging to mature in the lumen. The triggers for larval hypobiosis and for resumption of larval development are not well understood. However, post mortem examination has revealed that most horses have high burdens of hypobiotic larvae in the mucosa of the large intestine.

The synchronous reactivation and re-emergence of larvae into the lumen is important in the pathogenesis of larval cyathostominosis (LC). Cases of LC typically occur sporadically, in late winter or early spring, in yearlings or other young horses after a season at grass. Synchronous larval re-emergence is associated with **intense intestinal inflammatory stimuli**, rapid weight loss, sometimes diarrhea, and a poor prognosis.

The pathogenesis, still incompletely understood in terms of the inflammatory pathways and mediators responsible, is in many ways analogous to ostertagiosis in cattle occurring due to re-emergence of hypobiotic larvae ("type-2 ostertagiosis"), and is therefore also termed a "type-2" disease. Some of the triggers for re-emergence of cyathostomin larvae may include **recent anthelmintic administration**, removing the adult population of worms from the intestine, immunologic or nutritional factors.

Apart from LC occurring during larval re-emergence, the potential of large burdens of hypobiotic larvae in the lumen to interfere with neuromuscular control of intestinal motility, and to predispose to **colic**, is now widely recognized.

Strongylus *spp. and* Triodontophorus *spp.*

The three *Strongylus* species (*S. vulgaris*, *S. equinus* and *S. edentatus*) have migratory life cycles, with the larvae spending extended periods of time in various predilection sites before returning to mature in the large intestine. This results in relatively long prepatent periods of infection. In addition, the migratory stages of *S. vulgaris* are associated with damage to the **cranial mesenteric artery**, the resting site of predilection for larval stages, or sometimes other visceral arteries.

Larval presence in arteries results in **thrombosis** (*q.v.*), sometimes embolism, and ensuing disruption of the blood supply to the intestine and colic. Unusual but dramatic sequelae can result from long-standing damage due to repeated infections, with **aneurysm** and **fatal internal hemorrhage**.

Adult worms of these three species contribute, through plug feeding, to ill-thrift, anemia and other low-grade signs of helminth infection.

There are several *Triodontophorus* spp. that commonly occur as part of mixed strongyle infections. These worms do not undergo migration within the host, so the pathogenic mechanisms associated with infection are attributable to adult stages only, and are similar to those described above for *Strongylus* spp. One particular species, *Triodontophorus tenuicollis*, tends to feed in groups, thus leaving larger erosions on the mucosa than is the case with other strongyle worms, and may be associated with slightly more severe clinical signs.

A marked trend over recent years has been the decline in prevalence of infection with large strongyles and an increase in the incidence of disease due to the cyathostominae. This can be attributed to the greater ability of the latter to evade the action of modern anthelmintic drugs by hypobiosis and/or acquisition of drug resistance.

Epidemiology

All horses, but particularly those reared on permanent horse pastures, are susceptible to ill-thrift and anemia as a result of large burdens of adult strongyles, but horses under about 3 years of age, together with those of advanced age, more often show obvious clinical signs of infection. Signs may occur at any time of year, although pasture burdens peak in mid to late summer.

Acute cases of **larval cyathostominosis** most often occur in late winter or early spring following a grazing season in which large parasite burdens have been acquired. One animal, or sometimes a group of animals, may be affected. A common factor in many of these cases is a recent history of anthelmintic treatment. As **hypobiotic larvae are not susceptible to anthelmintics**, anthelmintic treatment has the effect of clearing out the adult worm burden, which may in turn remove signals responsible for preventing resumption of larval development. Other predisposing factors may include genetic predisposition, previous infection history and degree of acquired immunity. Individual animals experiencing the most severe clinical signs are those developing the most intense inflammatory and immunologic responses to the stimulus of larval re-emergence.

Clinical pathology

In individual cases of strongylosis, strongyle fecal egg counts are difficult to interpret since the level of egg output gives little indication of the number, species and stage of development of the worms present, either as immature adults in the gut lumen, or as hypobiotic larvae in the mucosa. However, egg counts from a group of animals sharing the same pasture are a very useful tool as a measure of potential pasture contamination, in designing and implementing worm control programs and in monitoring the success of control programs.

Although not specific, most cases of strongylosis and larval cyathostominosis will show evidence of anemia, eosinophilia and neutrophilia on hematologic examination, and serum albumin levels will be low. A hyperglobulinemia involving beta-globulins has been associated with larval infections of both the cyathostomins and *S. vulgaris*, however this is not pathognomonic of recent infection with these parasites.

Post mortem findings

At post mortem there is evidence of anemia and poor body condition associated with the presence of large numbers of different species of strongyles in the lumen of the cecum and colon and in the large intestinal mucosa. Lesions include **hemorrhagic spots or ulcers** caused by the feeding of adult parasites, with inflammation and edema of the mucosa and enlargement of associated lymph nodes.

Very large numbers of coiled, developing cyathostomin larvae may be seen on close inspection of the **mucosa** and there may be numerous **necrotic nodules** resulting from recent larval emergence; these nodules involve extensive areas of the large intestinal mucosa in cases of larval cyathostominosis.

S. vulgaris larvae may be found in association with thrombosis, inflammation and thickening of the **cranial mesenteric artery** and its main branches; infarction and necrosis of parts of the small and large intestine have been seen within a few weeks after experimental infection due to arteritis and thrombosis of small arteries close to the intestinal wall. Patches of subserosal hemorrhage may be seen as a result of the migration of *S. edentatus* larvae in the flanks.

Diagnosis

Strongylosis should always be considered in young horses that have lost condition, particularly if they are **anemic**.

The detection of strongyle eggs in the feces is of limited value in diagnosis as substantial worm burdens may be associated with fecal egg counts of only a few hundred eggs per gram due either to **low egg output** by adult worms or to the presence of many immature parasites. For example, in cases of larval cyathostominosis, fecal egg counts may be **negative** but many bright red larvae may be passed in diarrheic feces or seen on the glove used for rectal examination. In such cases there is also a history of rapid marked weight loss, and a neutrophilia and hypoalbuminemia are generally found on examination of a blood sample.

Treatment

Anthelmintics for use in horses are usually marketed for oral administration either in the feed, for example as a powder or granules, or for direct administration as a paste, gel or suspension. See also Table 10.2, page 593.

Of the three chemical groups of anthelmintics licensed for use in horses, the **pyrantel/morantel** drugs have the advantage of being effective also against tapeworms (*q.v.*) and the **avermectins** have residual activity and associated long egg reappearance times. **Benzimidazoles** have been very widely used in horses over the past 30 years, and resistance to this group is now widespread among the strongyles of horses.

In order to slow down the development of further **drug resistance** within the strongyles, anthelmintics should be used as **infrequently** as possible in horses as is compatible with health. When clinical cases of ill-thrift, anemia or diarrhea occur in individuals or groups of horses, either pyrantel or an avermectin type dose should be given, taking care to calculate the dose rate correctly. Steps should also be taken, by appropriate pasture management and strategic dosing if necessary, to prevent the conditions leading to clinical disease recurring in the future.

Cases of **acute larval cyathostominosis** carry a guarded prognosis. Some success has been achieved by administering daily doses of **fenbendazole** at 7.5 mg/kg BW for several days until the clinical signs have abated. This drug may be effective in killing larvae that are on the point of emerging into the mucosa, hence the necessity of administering daily doses.

It is clear that the clinical signs of this condition are due to an **exaggerated host inflammatory response** to emerging larvae, although much remains to be done to describe the exact mechanisms involved. Although there are few studies on the use of anti-inflammatory drugs in the management of clinical cases, logic suggests that appropriate anti-inflammatory therapy, along with anthelmintics, has a role to play.

Control

Although control programs at different equine establishments will vary according to conditions such as management and availability of grazing, the following measures will dramatically reduce the level of infection:

1. **Collect feces** frequently (up to twice weekly) during the summer and less frequently (every couple of months) in cold weather. Depending on circumstances, this can be done manually or by using specialized "pasture-sweeping" machines. Fecal collection before parasite larvae have migrated out from the fecal pat is extremely effective in reducing pasture contamination and is the **single most important measure** that can be taken to prevent problems from equine strongylosis. It is also cost effective when the reduced anthelmintic dosing requirements are taken into consideration.

2. Implement a **strategic helminth control program** involving representative fecal sampling to assess the need for strategic use of anthelmintics. Generally, helminth burdens are overdispersed, such that most of the worm burden occurs in a minority of the population. This group represents the animals most at risk of clinical disease. Ideally, only this vulnerable group should be treated. Leaving some animals undosed dilutes the selection pressure of anthelmintic use, as some larvae contaminating pastures will not have been exposed to this selection. The intervals between dosing depend on the residual period of the drug used, and the stringency of fecal collection. The chemical group of drug used (see p. 96) should be rotated **annually or biannually**, again to minimize the effect of selection on acquisition of drug resistance by helminth populations.

3. Stress the importance of additional **management factors** such as good stable hygiene and paddock rotation and/or mixed grazing, reserving the least contaminated pastures for nursing mares and their foals. At the end of the grazing season, if the animals are housed, treatment with a compound active against small strongyle larvae in the intestinal mucosa should prevent outbreaks of larval cyathostominosis during late winter or the following spring. A **5-day treatment with fenbendazole** (7.5 mg/kg BW) is one recommended regimen for this purpose. It is also good practice to dose all animals arriving from other establishments, and to isolate them for 72 h, to prevent introduction of anthelmintic resistance.

Parascariasis

Heavy infections with the roundworm *Parascaris equorum* are extremely common in foals and yearlings, the prevalence of infection decreasing with age. The main clinical sign is **unthriftiness** with rare reports of death due to impaction or rupture of the small intestine (*q.v.*).

Life cycle and epidemiology

The large adult parasites (up to 40 cm long) live in the small intestine and produce circular, sticky, typical ascarid eggs that are passed in the feces. These develop to the infective stage, which is the egg containing the L2, in a minimum of 10–14 days, and foals are infected by ingesting these eggs. *P. equorum* larvae migrate through the liver and lungs to their final site in the **small intestine** and the prepatent period is approximately 3 mo.

The important factors in the epidemiology of *P. equorum* are the high egg output of the adult worms and the ability of these eggs to survive for several years in the environment. The sticky outer coat enables the egg to **adhere to stable floors** and fittings and facilitates passive spread of the eggs.

Pathogenesis

Migration of larvae through the liver and lungs results in small, focal hemorrhagic lesions, which in the case of the liver are followed by grossly visible white areas of fibrosis. The major pathogenic effect of these parasites, however, is caused by large numbers of adults in the small intestine, which, although not responsible for gross lesions, compete with the young host for nutrients and cause marked **weight loss** or failure to thrive.

It has been shown experimentally that foals infected with *P. equorum* have **reduced gut motility**, an increase in the ratio of body water to body solids and decreased body pools of albumin.

Clinical findings

In experimental studies in young foals, **coughing** and a white/gray nasal discharge have been observed during the third and fourth week after infection when larvae are making their way, via the trachea, back to the small intestine.

Foals with large numbers of worms in the intestine often eat well and remain alert but, in spite of this, they show marked **unthriftiness** with weight loss, leading in some cases to emaciation. In foals and yearlings fatal cases due to intestinal rupture with subsequent peritonitis have been reported.

Clinical pathology

Parascaris eggs, which are circular with thick shells, are usually present in large numbers in the feces of clinically affected animals and the majority of infected animals also have low serum albumin levels.

Post mortem findings

Apart from the finding of large numbers of worms in the small intestine, which may be associated with some reddening of the mucosa, there may be

few gross lesions. The carcass will probably be emaciated and edematous and there may be small white lesions in the liver as a result of previous larval migration. In the lungs, small subpleural grayish-green lymphocytic nodules that have developed around dead or disintegrating larvae may be seen.

Diagnosis

Parascariasis is a common cause of **unthriftiness** in foals and yearlings. Infection may be confirmed by the finding of typical brown, thick-shelled, spherical eggs in feces, although fecal egg counts may vary from day to day. Anthelmintic treatment of unthrifty young foals in which fecal examination has proved negative may result in the expulsion of large numbers of well-developed but sexually immature parasites.

Treatment

Piperazine and all modern broad-spectrum anthelmintics at the usual recommended dosages are effective against *P. equorum* in the small intestine.

Control

Since it is extremely difficult to remove infective eggs already present on pasture, control measures should be aimed at preventing further contamination. This is achieved by scrupulous anthelmintic dosing of foals. Treatment should begin at **1–2 mo of age** to remove parasites before they start laying eggs, which would otherwise become available to infect foals of the same or succeeding generations. Where possible, mares and foals should avoid **for several years** pastures previously grazed by young animals.

Strongyloidosis

Infection with the threadworm *Strongyloides westeri* is common in foals aged 2 wk to 4 mo but seldom persists in animals >6 mo of age.

Life cycle and epidemiology

Foals are commonly infected by the larvae in their **dams' milk** but infection may also occur by ingestion or from **penetration of the skin** by infective larvae. The prepatent period of *S. westeri* is 8–14 days and eggs can be found in foals' feces before 2 wk of age.

Although animals may be infected from larvae in the environment, the main source of infection for **sucking foals** appears to be the reservoir of larvae in the tissues of the mare. How these larvae are acquired, stored and migrate to the mammary gland is not well understood, but it is possible that in immune animals infective larvae penetrating the skin may be inhibited in development until triggered to migrate to the mammary gland in late pregnancy/early lactation. Successive foals from certain mares appear to suffer heavy infections.

Heavy, clinically significant infections are most likely to be found in animals housed in **unhygienic conditions** or in foals with an underlying immunodeficiency (*q.v.*).

Pathogenesis
Heavy infections may cause enteritis and diarrhea associated with inflammation of the anterior third of the small intestine, with atrophy of the villi and increased numbers of lymphocytes in the lamina propria.

Clinical findings
In severe infections, diarrhea may occur up to 4–6 wk of age. Older foals may have high fecal egg counts without any clinical signs.

Clinical pathology
Although thin-shelled larvated eggs may be found on examination of diarrheic feces from infected foals, the presence of these eggs in some cases may be incidental.

Diagnosis
Diagnosis is based on the occurrence and persistence of yellowish diarrhea in very young foals associated with the presence of large numbers of typical eggs in the feces. Diagnosis may be confirmed retrospectively by a rapid response to suitable anthelmintic treatment.

Treatment
Benzimidazoles or avermectins are recommended for the treatment of clinical infections, at manufacturers' recommended dose rates.

Control
Attempts to treat mares to prevent infection of foals have been largely unsuccessful, daily treatments being required to prevent larvae being passed in the milk.

Where strongyloidosis is a **recurring problem** on a stud, routine anthelmintic treatment of 1–2-wk-old foals with avermectins or pyrantel has been reported to be beneficial. Attention should also be paid to improving environmental conditions.

Lungworm infection

Although larvae of the equine lungworm *Dictyocaulus arnfieldi* are frequently found in fecal samples from **donkeys**, infection is **rarely** associated with signs of respiratory disease in this host.

In horses, on the other hand, lungworm infection is often incriminated as a cause of **chronic coughing**. The true prevalence of infection in the horse is not known since larvae are rarely found in the feces (except in foals and occasionally in pregnant mares).

Life cycle and epidemiology
Infection occurs by ingestion of infective third-stage larvae (L3) on pasture. These larvae then travel from the intestine via the lymphatics and blood to the

lungs where they develop to the adult stage in the **bronchial tree**. Adult females produce larvated eggs, which are passed in the feces, but these hatch almost immediately to first-stage larvae. The prepatent period is a minimum of 2 mo.

The epidemiology of lungworm infection in horses is poorly understood but in the majority of confirmed cases there is a history of previous contact with **donkeys**. In the donkey, patent infections usually establish during the first season at grass and, in the absence of anthelmintic therapy, the majority of animals subsequently remain infected throughout their lives.

Pathogenesis

The presence of worms in the lungs produces valve-type lesions that lead to discrete, 3–5 cm areas of overinflation. Although infection is well tolerated in donkeys, the presence of lungworms in the horse can lead to chronic coughing.

Clinical signs

Despite the prevalence of *D. arnfieldi* in donkeys, clinical signs directly attributable to lungworm infection are rarely seen. In the horse it has been shown that infection of young foals is associated with the development of patent infections in the absence of clinical signs. Infection of horses and ponies >1 yr of age does not usually result in the establishment of patent infections but may be associated with marked clinical signs including coughing, increased respiratory rate and adventitious lung sounds. It is also possible to detect **lungworm larvae** in feces samples from a very small proportion of apparently healthy horses (most often foals and pregnant mares).

Clinical pathology

Laboratory tests are of little value in the diagnosis of lungworm infection in the horse. In very few cases, chronic coughing may be associated with a patent infection with first-stage larvae being found in feces. In contrast, in donkeys, larvae are frequently found in the feces of apparently normal animals.

Post mortem findings

Grossly raised circumscribed areas of **overinflation** are visible if the lungs are examined soon after death but these can gradually disappear and may not be obvious if post mortem examination is delayed.

Microscopically, there is hyperplasia of the bronchial epithelium, an increase in the size and number of goblet cells and infiltration of lymphoid cells around the airways. Often only a few parasites are present coiled up in the lower bronchi and these are difficult to recover.

Diagnosis

Diagnosis is based on history, clinical signs and examination of feces for *D. arnfieldi* larvae, although in the horse patent infections are not common. A modified Baermann technique is used to examine fecal samples for lungworm larvae. It is important to use fresh feces taken from the rectum, otherwise free-living and first-stage strongyle larvae may be present in fairly large numbers and make examination for first-stage *D. arnfieldi* larvae difficult.

Treatment

Clinical trials have indicated that **fenbendazole** at a dose rate of 15–30 mg/kg is successful in the treatment of horses while in a controlled trial in donkeys treatment with **mebendazole paste** at a dose rate of 15–20 mg/kg daily for 5 days was shown to have 75–100% efficiency against parasites in the lungs. However, **avermectins** at manufacturers' recommended dose rates are probably the treatment of choice.

Control

To reduce the risk of infection in horses, contact with **untreated donkeys** should be avoided. To reduce the overall level of infection in donkeys, regular treatment (every 8 wk) with ivermectin is recommended: fecal samples collected at the time of treatment should be examined to monitor the effectiveness of such a treatment regimen.

Oxyuris equi infection

Infection with the horse pinworm *Oxyuris equi* is relatively common, especially in young animals. The female worms lay eggs around the anus, which causes a **perineal pruritus**. Broken hairs and occasional bare patches on the tail are caused by rubbing in response to the pruritus and on lifting the tail the egg masses are seen as grayish/yellow streaks on the perineum.

Oxyuris is susceptible to all of the modern broad-spectrum anthelmintics (see p. 96) and should be adequately controlled by routine parasite control measures.

TAPEWORM INFECTIONS

Anoplocephala perfoliata is the common tapeworm of horses.

Epidemiology and pathogenesis

Infection is by ingestion of **forage mites** containing the intermediate cysticercoid stage. Occasionally specimens 4–5 cm long and resembling large flukes are found in feces.

A. perfoliata occurs in the small intestine and cecum near the ileocecal valve, and is often seen in association with **erosive changes** in the mucosa. The occurrence of several *A. perfoliata* worms at their predilection site around the ileocecal junction is associated with interference with passage of ingesta through this "bottleneck", and with some cases of spasmodic colic (*q.v.*). Whereas this parasite was formerly regarded as a minor, occasional pathogen, there is now sufficient evidence of its involvement in colic to warrant specific control measures being taken.

Diagnosis

McMaster examination (*q.v.*) or fecal flotation may reveal typical *A. perfoliata* eggs which are distinctive with an internal "**pyriform apparatus**". However, low numbers of eggs may be missed using this method. An ELISA is available for serologic diagnosis and not only detects infected horses but can also estimate the extent of the parasite burden.

Treatment and control

A double dose of pyrantel (13.2 mg/kg BW) is recommended for eliminating *Anoplocephala* burdens. This should be administered **in addition** to other anthelmintic treatment in years in which other chemical groups are used for roundworm control.

BOTS

Infection with horse bots is common, as evidenced by the frequent finding of bot fly (*Gasterophilus* spp.) larvae in the stomach at post mortem examination, and the presence of fly eggs on the hairs of many horses during the later summer and autumn.

In temperate areas bot flies have only one generation per year. The flies are active during July to September and during this period eggs are laid. After hatching, the larvae migrate and develop in the stomach for 9–10 mo. When they mature the following June they are passed out in feces to pupate and develop to the adult stage. In tropical and subtropical areas bot flies can survive throughout the year and infection cycles are continuous.

The pathogenic significance of bot larvae in the stomach is not well understood but the **adult flies** may cause a great deal of annoyance when approaching horses to lay their eggs.

From the life cycle it is obvious that removal of the bots after they have accumulated in the stomach during the late autumn and winter will effectively break the life cycle. Drugs with a high activity against developing bot larvae in the stomach are **ivermectin, dichlorvos and metrifonate**.

OTHER INTERNAL PARASITES OF HORSES

Several less common or less important helminth parasites that may infect horses are the stomach worms *Trichostrongylus axei* and *Habronema* spp., and the liver fluke *Fasciola hepatica*. Horses also harbor the intermediate hydatid cyst stages of the tapeworm *Echinococcus granulosus*.

TRICHOSTRONGYLOSIS

Trichostrongylus axei, a common parasite of ruminants, can infect horses but burdens are usually low. The life cycle is direct, infection occurring by ingestion of L3 from pasture. Following ingestion, larvae invade the gastric mucosa and lesions develop as circular thickened areas several centimeters in diameter. Experimentally infected animals have shown diminished appetite and progressive weight loss but infection is usually asymptomatic. Treatment is rarely called for but *T. axei* is susceptible to most broad-spectrum anthelmintics.

HABRONEMIASIS

Although *Habronema* spp. infections are common they are rarely considered important and are usually discovered only at post mortem examination, sometimes in association with a mild chronic, catarrhal gastritis. One species,

H. (*Draschia*) *megastoma*, provokes the formation of **large fibrous nodules** in the stomach, but even these are well tolerated unless they occur close to the pylorus. Treatment against adult worms is rarely called for.

The chief importance of *Habronema* spp. is as a cause of **cutaneous habronemiasis** (*q.v.*) or "summer sores" in warmer climates. **Ivermectin** is the drug of choice for the treatment of skin lesions but several doses may be required depending on the response. Control is almost impossible due to the ubiquity of the fly intermediate hosts but treatment of skin wounds with fly repellents may reduce the incidence of "summer sores".

FASCIOLIASIS

Most mammals may be infected with *Fasciola hepatica* but infection of horses is perceived as relatively uncommon. However, in spite of infrequent ante mortem diagnosis, **liver flukes** are quite a common **incidental finding** at post mortem examination.

Although eggs of this parasite may be found in the feces of horses and donkeys grazing in known "fluke" areas, clinical signs of infection such as loss of weight, poor performance and anemia are rare. Successful treatment has been reported with rafoxanide, oxyclozanide and triclabendazole. The advent of reliable serologic diagnostic tests will provide a useful tool for investigating the true prevalence and clinical significance of this parasite in horses.

HYDATIDOSIS

Hydatid cysts are often seen at post mortem examination, situated mainly in the liver but occasionally in other organs. They may occur as a few large spherical cysts projecting from the surface, or as many small cysts scattered throughout the parenchyma. Infection appears to be completely tolerated.

Equine hydatidosis is not a public health problem since the subspecies involved, *Echinococcus granulosus equinus*, has an exclusively dog-fox/horse cycle and has never been found in other animals. *E. multilocularis* has occasionally been reported in horses.

ALIMENTARY PROTOZOA

A number of enteric protozoan parasites such as *Cryptosporidium, Eimeria* (*Globidium*) *leuckarti, Giardia* and *Tritrichomonas* spp. have been reported occasionally as causes of **clinical enteritis** in the horse.

Although *Cryptosporidium* has been incriminated as a cause of diarrhea in immunocompromised foals and in young animals with concurrent viral infections, the true pathogenic significance of this parasite in the horse is poorly understood. At present there are no therapeutic agents with known efficacy against *Cryptosporidium*.

In the case of *Giardia, Tritrichomonas* spp. and coccidiosis due to *E. leuckarti*, there are some reports of infection associated with diarrheic syndromes of varying severity. These are generally considered to be of fairly minor pathogenic significance.

BLOOD PROTOZOA

Several blood protozoa may be responsible for serious infections in horses, especially in the tropics and subtropics, for example tick-transmitted *Babesia* and some *Trypanosoma* species.

Piroplasmosis (babesiosis)

Equine piroplasmosis caused by *Babesia caballi* and *B. equi* (syn. *Theileria equi*) occurs in many parts of the world including Europe, Asia, Africa and the Americas and there are endemic foci of *B. caballi* infection in the southern USA.

These organisms are transmitted by **ticks** of the genera *Dermacentor, Hyalomma* and *Rhipicephalus*. The pathogenic effects of different strains of equine *Babesia* are variable and clinical signs include anorexia, fever and anemia; jaundice and hemoglobinuria may accompany *B. equi* infection. Horses raised in endemic areas are often **asymptomatic carriers** due to premunity (*q.v.*) and may only show clinical signs when **stressed**.

Diagnosis is based on clinical signs and the demonstration of parasites in the **red blood cells** in acute cases. A CFT may be used to detect parasite antibodies within 5 days of infection and a negative CFT is required for all horses entering the USA from endemic areas. Molecular tests are now also available.

A number of drugs, including imidocarb, diminazene and buparvaquone, are recommended for the treatment of equine piroplasmosis but for all drugs the manufacturers' doses and instructions should be carefully observed.

Trypanosomosis

Equine trypanosomosis may result from infection with *Trypanosoma congolense, T. vivax, T. brucei* and *T. evansi*, which are transmitted by tsetse flies and other biting flies. Horses may also suffer from a chronic wasting disease, **dourine**, caused by a venereally transmitted species, *T. equiperdum*. A summary of some of the main features of the diseases caused by trypanosome infection in horses is given in Table 1.2.

Table 1.2 Equine trypanosomosis

Disease (distribution)	Trypanosome species involved	Method of transmission	Major clinical signs
Nagana (Africa; also South America—*T. vivax*)	*T. congolense* *T. brucei* *T. vivax*	Tsetse transmission. Also mechanical, by biting flies in *T. vivax*	Acute-chronic disease. Intermittent fever, anemia, weight loss, edema of limbs and genitalia
Surra, mal de caderas (Africa, South America)	*T. evansi* *T. equinum*	Mechanical. Biting flies and vampire bats	Often acute. Similar to nagana with progressive paralysis of hindquarters in chronic cases
Dourine (Africa, Asia, South America)	*T. equiperdum*	Coitus	Genital and ventral edema, progressive emaciation, ascending motor paralysis, in some cases fatal

Diagnosis in most cases depends on clinical signs and the demonstration of **trypanosomes in the blood**. A CFT is necessary in the case of *T. equiperdum* infection. A number of trypanocidal drugs can be used in the horse including **quinapyramine, ethidium and suramin.**

TISSUE PROTOZOA

A number of protozoan parasites occur in the tissues of horses, for example species of the genus *Sarcocystis* in the muscles and *Klossiella equi* in the kidneys. With a couple of notable exceptions, these are of minor pathogenic significance, being incidental findings on routine histopathology.

Equine protozoal myeloencephalitis

Equine protozoal myeloencephalitis (EPM), identified in North America, is characterized by various degrees of gait abnormalities, ataxia, paresis, weakness and asymmetrical hypermetria.

Etiology and life cycle

The organism responsible for most cases of EPM is *Sarcocystis neurona*, which like other members of the Sarcocystidae has an indirect life cycle, using the **opossum** as definitive host and various species of mammals (terrestrial and marine) and birds as intermediate hosts.

The life cycle is typical of the genus *Sarcocystis*, with oocysts or free sporocysts in the feces of the definitive host infecting intermediate hosts by the oral route.

Horses are not as permissive of the intermediate stages of life cycle as other intermediate hosts. Parasite stages in the **brain and spinal cord**, and the host response to them, are responsible for eliciting clinical signs in some animals, although many animals are infected with no apparent clinical consequences.

Epidemiology

Horses may become infected if they graze areas contaminated by **opossum feces.** Other species capable of acting as intermediate hosts and maintaining an infection reservoir include cats and raccoons, as well as some species of birds.

Serologic evidence indicates that up to 50% of horses in the USA have been exposed to the causative agent. Most clinical cases have been described in North America but there are also cases documented in horses imported into various countries from the USA. Recently, cases similar to EPM have been described in horses in France that had never been overseas. The epidemiology and precise etiology of these cases have not yet been established. Recently, Neospora spp., in particular *Neospora hughesi*, was implicated in some cases of protozoal encephalitis in horses.

Pathogenesis and clinical signs

Clinical signs are variable depending on the site of the **multifocal necrotic lesions**, which may occur in any part of the **CNS**, but most cases show

weakness, ataxia and muscle wasting, often with a history of a **long-standing vague lameness**.

The fact that many horses are infected without showing clinical signs points to involvement of host immunologic factors in the development of disease. Without treatment, most cases show **progressive deterioration**.

Diagnosis

A major problem in making a specific diagnosis in any disease caused by a *Sarcocystis* spp. is that of specificity. This is because various species of the genus commonly infect most mammals with few or no clinical implications. These share considerable serologic cross-reactivity with those few species that are clinically relevant.

Western blotting, using CSF samples reacted with separated antigens of *S. neurona*, is regarded as a reliable diagnostic test for EPM. The Western blot test is highly sensitive, but not very highly specific. As a result, a negative result can be regarded as ruling out EPM but a positive result may be false. In doubtful cases, examination of paired CSF samples may be necessary. At post mortem examination, immunocytochemical and PCR detection of parasites is also useful in confirming a diagnosis.

Treatment and control

Many cases, especially if diagnosed relatively early, respond well to treatment. Based on clinical experience, **pyrimethamine** combined with **sulfonamides** given over a prolonged period (150–180 days) gives good results, especially with the inclusion of anti-inflammatory drugs such as flunixin meglumine (at 1.1 mg/kg BW). Other effective compounds include **ponazuril** (5 mg/kg BW PO s.i.d. for 28 days) and related drugs.

Preventing opossums, feral cats and wildlife from accessing land grazed by horses is a commonsense control measure.

Neosporosis

Neospora caninum first came to attention as a pathogen of domestic animals in 1988 when it was recorded as being responsible for some cases of neuromuscular signs and ataxia in dogs previously attributed to *Toxoplasma gondii*. In the years since then, the parasite has become recognized as a very important cause of bovine abortion, as well as congenital and other disease in dogs. In 1998, it was established that the dog is the definitive host of *N. caninum*, although an inefficient one, producing only very low oocyst numbers following experimental infection. The existence of another definitive host, such as a wild canid, is still suspected. Infection in cattle may occur via exposure to a point source of infection, such as the feces of infected dogs, but vertical transmission is more important in maintaining infection in herds. Bovine infection is often subclinical, except during pregnancy, when an acute infection or reactivation of a chronic infection can occur, sometimes leading to fetal resorption, abortion, or birth of weak calves. The pathogenic mechanisms involved probably include a combination of direct fetal infection and immunopathology. *Neospora* infection is now recognized as being common in other species including horses.

Epidemiology and pathogenesis

Recent molecular studies have indicated that a *Neospora* parasite distinct from that found in cattle infects horses. This has provisionally been classified as a separate species, *Neospora hughesi*.

There have as yet been only a limited number of studies of *Neospora* infection in horses. At present it is safe to say that it is potentially a cause of **reproductive failure** as well as neonatal problems and neurologic disease, and should be considered as a differential diagnosis in such cases.

Diagnosis

There are several serologic assays available for neosporosis including an indirect fluorescent antibody test (IFAT), direct agglutination and ELISA.

Treatment and control

In dogs, clindamycin is effective in alleviating clinical signs in the early stages of disease. By extension from the situation with toxoplasmosis in sheep, in-feed medication with **monensin** may be effective in preventing maternal infection during pregnancy. However, there are no reliable data to support treatment regimens for neosporosis in horses. The recommendations for the treatment of EPM (*q.v.*) may be followed.

Chapter 2

The immune system

M. J. B. F. Flaminio (Consultant Editor)

Chapter contents

EQUINE IMMUNOLOGY

INTRODUCTION

Advances in immunology and technology have contributed significantly to the understanding of fundamental concepts of disease, to the identification of preventive methods and to the evaluation of treatment responses. Nevertheless, many areas in the field of equine immunology await reagents and technical

capabilities to expand our knowledge of the mechanisms involved in many infectious and non-infectious processes.

The development and characterization of **monoclonal antibodies** for equine molecules and the **decoding of the horse genome** are dependent on a cooperative effort among investigators concerned about the well being of the horse. When available, however, traditional and state of the art techniques can be used to reveal the role of immune cells in the pathogenesis and regulation of diseases. This chapter reviews the major conditions of the horse that directly involve the immune system and indicates the available diagnostic resources for the identification and monitoring of these processes.

A glossary of principal **immunologic terminology** is given in Box 2.1.

Box 2.1 A glossary of immunologic terms

Adjuvant: a substance that enhances the immune response to antigens.
Allele: any one of a number of alternative forms of the same gene occupying a given locus (position) on a chromosome.
Allergen: an antigen that induces IgE-mediated hypersensitivity reactions.
Alloantibody: antibody produced against a protein of an allele from another member of the same species and which can function as an antigen.
Anaphylatoxin: activated complement components (C3a, C5a) that induce mast cell degranulation.
Antibody: protein with specific binding properties produced by plasma cells in response to antigenic exposure.
Antigen: foreign molecule that can induce an immune response.
Antigen-presenting cell (APC): specialized type of cell (dendritic cells, macrophages) that can process and present antigens to lymphocytes.
Antigen processing: breakdown of molecules into peptides that can be presented to lymphocytes via major histocompatibility molecules.
Antigen receptor: the specific antigen-binding receptor on T (T cell receptor) or B (B cell receptor) lymphocytes.
B lymphocyte (B cell): lymphocytes that develop in the bone marrow, finish their maturation and differentiation in the periphery, and become antibody-secreting cells.
Blocking antibody: antibody molecule capable of blocking the interaction of antigen with other molecules.
Cell-mediated immunity: immune response mediated by T cells, often CD8+ T cell cytotoxic response.
Chemotaxis: directional migration of cells toward a concentration gradient of an attractant (chemotactic substance).
Classical pathway: the mechanism of complement activation initiated by antigen—antibody aggregates that induces the activation of C1, C4 and C2 components.
Cluster of differentiation (CD): cell surface molecules (markers) of leukocytes that can be identified by monoclonal antibodies to differentiate cell populations.
Complement: group of serum proteins involved in inflammation, phagocyte activity and lysis of cell membranes; the complement cascade is triggered classically by the interaction of antibody with specific antigen.
Complement receptor: a structure that binds C3 fragments found on phagocytes (neutrophils, monocytes and macrophages) and lymphocytes (B cells).
Coombs test: a test used to detect antibodies or complement on red blood cells using anti-immunoglobulin antibodies.
Cytokines: soluble substances secreted by cells, which have a variety of effects on other cells.
Cytotoxic T cell: lymphocyte (CD8+ T cell) that kills infected cells expressing processed antigen peptides via major histocompatibility class I.
Dendritic cells: cells present in tissues that capture and process antigens, migrate to regional lymph nodes and present processed antigen peptides to T lymphocytes.
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Box 2.1 A glossary of immunologic terms [continued]

Enzyme-linked immunosorbent assay (ELISA): assay that measures quantitatively the amount of a substance using enzyme-conjugated antibodies and a substrate that produces a colored end-product upon binding of the enzyme.
Epitope: part of the antigen that contacts the antibody or T cell receptor.
Fc receptor: receptor on a cell surface with specific binding affinity for the Fc portion of an antibody molecule.
Flow cytometry: analysis of cell populations in solutions according to their size, granularity and fluorescence of cell markers detected by fluorescent monoclonal antibodies.
Fluorescent antibody: antibody conjugated with fluorescent dye often used in flow cytometric analysis and immunofluorescent assays.
Germinal centers: distinct areas in secondary lymphoid tissues (spleen, lymph node) in which B cells aggregate and go through differentiation and antibody class switching.
Helper T (Th) cells: class of T cells (CD4+ T cells) that help B cells to produce antibody and generate cytotoxic CD8 T cells; helper T cells recognize processed antigen peptide presented via major histocompatibility class II.
Humoral response: immune response mediated by antigen-specific antibodies present in serum and tissues.
Hypersensitivity: state of reactivity to an antigen that is far greater than the antigenic challenge presented.
Idiotype: the combined antigenic determinants (idiotopes) found in the variable region of antibodies.
Immune complex: antigen bound to antibody that may or may not contain complement components.
Immunoglobulins: proteins (antibodies) produced by plasma cells. There are five main types of antibodies: IgA, IgD, IgE, IgG and IgM.
Immunomodulators: substances that enhance or decrease non-specifically the immune response.
Immunosuppression: a mechanism (treatment) for producing a specific state of immunologic unresponsiveness.
Interferons: proteins with antiviral activity, which are involved in signaling between cells.
Interleukins: glycoproteins secreted by a variety of leukocytes, which are involved in signaling between cells.
Isotypes: classes of antibody that differ in the constant region of their heavy chain (Fc portion).
Isotype switching: the shift of a B cell from the secretion of antibody of one isotype (e.g. IgM) to a different isotype (different heavy-chain, e.g. IgG).
Leukotrienes: metabolites of arachidonic acid involved in inflammation.
Lymphokine-activated killer cells: cytotoxic cells generated ex vivo by stimulation with IL-2.
Major histocompatibility complex (MHC): cluster of genes encoding cell surface molecules that are polymorphic (multiple alleles at a particular genetic locus); this polymorphism codes for antigenic differences that can lead to graft rejection between members of a single species; the molecule is also involved in processed antigen peptide presentation to CD8+ T cells (MHC class I) and CD4+ T cells (MHC class II).
Mitogen: substance that stimulates the proliferation of many different clones of lymphocytes (e.g. phytohemagglutinin, PHA; concanavalin A, ConA; pokeweed mitogen, PWM; lipopolysaccharide, LPS).
Monoclonal antibody: antibody that is produced from a single A clone is the progeny of a single cell. In immunology, monoclonal generally describes a preparation of antibody that is monogenous, or cells of a single specificity.
Opsonin: antibody or complement component that coats a foreign particle (opsonization) to enhance phagocytosis by phagocytic cells.
Oxidative (respiratory) burst: increased oxidative metabolism within phagocytic cells stimulated by the phagocytosis of organisms; the reactive oxidative products that originate from this metabolism have killing properties.
Passive immunity: preformed antibody solution (e.g. colostrum, plasma) transferred to an individual.
Phagocytosis: the engulfment of a particle or a microorganism by phagocytes (neutrophils, macrophages); phagocytosis is facilitated by the binding of immunoglobulin- or complement-coated particles to the Fc receptors on the cell surface.
Primary immune response: cellular and humoral response to the first encounter with antigen; in general, this response has a long induction phase.
Protein A: component of the cell wall of certain staphylococci that binds the Fc portion of most IgG antibodies.
Glossary continues on page 116

Box 2.1 A glossary of immunologic terms [continued]

Reticuloendothelial system: network of phagocytes present in the liver and spleen, which remove abnormal circulating cells (e.g. antibody-bound erythrocytes).
Secondary response: cellular and humoral immune response that follows a subsequent encounter with a known antigen; often this response is faster and more specific than the primary response.
T cell: lymphocyte originating in the bone marrow that goes through differentiation and selection in the thymus.
Toxoid: nontoxic derivative of a toxin used as an antigen for the induction of antibodies.

VACCINATION

Vaccination is an important component of disease prevention programs and it is a relevant example of **modulation of the immune system**. The development of an effective vaccine requires detailed knowledge of the organism, the host's natural immune response to it, and risk factors of disease. Therefore, microbiologists, immunologists and epidemiologists work together in the design of vaccination programs. Great effort is dedicated to discovering vaccine elements that stimulate, similar to natural infection, a long-lived protective immunity with humoral and cellular components at the systemic and mucosal levels.

Serious **side effects** to vaccines, including anaphylactic or anaphylactoid reactions, swellings and abscesses at the injection site, laminitis and death, are rare. **Fever and malaise** are however expected, and they are **indicators of response** to the vaccine. In general, the small risk of vaccine side effects is greatly outweighed by the benefits.

All vaccine products must go through safety tests before commercialization. The same requirement is not always true for tests that evaluate **efficacy**. Rarely, there is scientific evidence of efficacy from experimental challenge trials, and the estimation of protection is often taken from clinical and epidemiologic observations. In addition, almost no data are available on the efficacy of multivalent vaccines. Although immunization with different antigens is practical, differences in the risk of exposure (e.g. time of the year, age and group of risk), the duration of immune protection to each antigen, and the quality of the desired immune response may require dissimilar frequencies of vaccine administration.

Types of vaccines

There are two main categories of vaccines:

1. **Dead or inactivated vaccines:** these vaccines contain the whole inactive pathogen or selective antigenic elements of the pathogen; they induce mainly humoral immunity, however DNA vaccines may induce both humoral and cell-mediated immunity.
   (a) Chemically inactivated whole pathogen vaccines—immunogenic and easy to prepare vaccines that require adjuvants and regular boosters
   (b) Protein vaccines—naturally produced protein of organisms that are used as antigens; also require adjuvants

(c) **Recombinant subunits vaccines**—synthetic production of antigenic peptides using expression systems to retain immunogenicity of the native protein; require the knowledge of a pathogen antigen that is important for immunity and adjuvants

(d) **DNA vaccines**—the objective is to mimic natural immune response by the in vivo synthesis of antigenic proteins with both MHC class I and MHC class II antigen presentation, hence both cytotoxic and antibody responses.

2. **Live vaccines:** the attenuated organism is able to invade a cell and use its replication machinery. Therefore, the organism is processed by the endogenous pathway for MHC class I presentation to generate cytotoxic T cells (CTLs), and MHC class II presentation to generate long-lasting humoral responses.

   (a) **Modified live vaccines (MLV)** are modified organisms that have attenuated pathogenicity but still replicate in the vaccinated animal; the organism may be attenuated in cell culture by growing it in abnormal conditions, by the creation of temperature-sensitive mutants (random mutants that may reacquire virulence), by using recombinant DNA technology for predicted deletion mutation that cannot be reversed, or by using variant forms of the organism that affect other species.

   (b) **Recombinant vector vaccines (RVV)** are engineered bacteria or viruses (vaccinia virus) that become carriers (vectors) of selected antigenic peptides from other pathogens. The bacteria or virus infect cells in the host and carry a target peptide that is known to induce a protective response against the organism. A variant of this type of vaccine is a multivalent vaccine in which one modified-live virus of interest carries another virus peptide.

Vaccination programs

A **vaccination program** should be tailored according to the degree of exposure to pathogen, number of animals in the herd, age groups involved, type of activity, horse transit, degree of stress, geographic location, management and hygiene and ventilation of the facilities housing the horses.

Primary and secondary vaccinations should be timed to precede the period of greatest exposure to the organisms. In addition, **all the animals of the herd should be vaccinated at the same time** to minimize replication of the infectious organisms and increase the protection of those animals that respond poorly to the vaccine.

It is possible that **maternally derived antibodies may interfere with antigenic response** and endogenous antibody production in foals. Ideally, vaccination of the foals should be performed after antigen-specific serum maternal antibody levels decline. In general, colostral IgG half-life is 28–35 days; however, specific antibodies may be transferred to the foal in different concentrations, and their catabolism may depend on environmental challenge.

The protocol for the immunization of foals has been revised because of a better understanding of the foal's immune response to distinct vaccines in early life. Nevertheless, vaccination of foals is initiated around 3–6 mo of age,

followed by one to two boosters 3–4 wk apart. In addition, vaccination of mares in **late gestation** against agents that are responsible for disease in early life is recommended in order to confer passive transfer of organism-specific immunoglobulins, e.g. rotavirus (*q.v.*) and *Clostridium botulinum* (*q.v.*).

HYPERSENSITIVITY REACTIONS

Hypersensitivity reactions are **immune responses to previously encountered antigens** with subsequent detrimental effect to the host. The classification of hypersensitivity reactions is based on the type of cells and the immune mediators that promote tissue injury:

TYPES OF REACTION

1. **Type I hypersensitivity reactions** are mediated by antigen-specific IgE, mast cells, basophils and their mediators. Examples are urticaria (*q.v.*), insect-bite hypersensitivity (*q.v.*) and food allergy.
2. **Type II hypersensitivity reactions** involve autoantibodies IgM or IgG against specific (often self) cell surface or extracellular matrix antigens. Subsequently, there is opsonization and phagocytosis of these cells and complement- and/or Fc receptor-mediated cell destruction. Examples include autoimmune hemolytic anemia (*q.v.*), thrombocytopenia (*q.v.*), incompatible blood transfusions, pemphigus foliaceus (*q.v.*) and drug hypersensitivity (*q.v.*).
3. **Type III hypersensitivity reactions** are promoted by the random deposition of immunocomplexes of circulating antigens (self or foreign) and IgM or IgG antibodies in blood vessels, with subsequent complement- and Fc receptor-mediated recruitment and activation of leukocytes and vasculitis. Examples include serum sickness (antisera passive immunization) (*q.v.*), glomerulonephritis (*q.v.*) and purpura hemorrhagica (*q.v.*).
4. **Type IV hypersensitivity reactions** do not involve antibodies and are mediated by sensitized CD4+ T cells (Th1 response) and CD8+ T cells (direct cytotoxic effect), which induce infiltration of macrophages and inflammation mediated by cytokines. An example is contact dermatitis (*q.v.*).

Homeostasis is widely dependent on a protective and balanced response of the immune system, which involves complex and redundant regulatory mechanisms. Occasionally, the immune system responds to a non-self structure or a danger signal with extreme properties that may lead to disease. In these conditions, selective activation or suppression of specific responses without affecting peripheral immune function becomes necessary.

ANAPHYLAXIS AND ANAPHYLACTOID REACTIONS

Anaphylaxis is a severe form of immediate hypersensitivity that manifests within minutes following exposure to an allergen (e.g. insect bite/sting, drugs

or vaccines, food). The hypersensitivity reaction involves a primary exposure to an antigen, CD4+ T cell cytokine-mediated activation of B cells for the production of IgE, and the binding of IgE to receptors on mast cells and basophils. Upon a successive exposure to the sensitizing antigen, its cross-linking with IgE triggers the release of mediators in cytoplasmic granules. These mediators (histamine, tryptase, leukotriene [LT] C_4, prostaglandin [PG] D_2, tissue necrosis factor [TNF]) **cause early effects** of vascular permeability and dilatation, and **late effects** of inflammation that last approximately 24 h.

The more rapid the onset of clinical signs, the more severe is the event. The release of allergic mediators may lead to mild effects including nasal swelling, urticaria, erythema and pruritus. However, anaphylactic responses may be moderate to severe and lead to **vasculogenic shock** characterized by hypotension (vasodilation, increased vascular permeability, reduced venous return, cardiac arrhythmias, myocardial ischemia), **difficulty in breathing** (increased bronchial smooth muscle tone, increased mucosal secretion, laryngeal edema, pulmonary edema), and **death**. In addition, there may be **gastrointestinal clinical signs** including colic and diarrhea.

Anaphylactoid reactions are anaphylactic-like reactions that do not involve IgE. The degranulation of mast cells and basophils is directly induced by the agent (e.g. drug) and activation of complement cascade components C3a and C5a. Therefore, this type of reaction may happen at the **first time of exposure** to the molecule. Nevertheless, the vasogenic effects, clinical signs and treatment do not differ from the anaphylactic reaction.

Confirmation of anaphylactic and anaphylactoid reactions may be pursued by measuring **serum or plasma tryptase** (peak concentration in 1 h of exposure) or **methyl histamine** in the urine (collect the second urine sample after exposure to antigen).

Anaphylaxis is an **emergency** condition that requires immediate diagnosis and treatment. **Epinephrine** (adrenaline) (0.01 mL/kg BW of a 1 mg/mL solution, IM) should be given by injection without delay. Epinephrine has positive inotropic and chronotropic effects, increases cardiac output, and promotes peripheral vasoconstriction and bronchodilation. **IV fluid therapy** may assist in fighting hypotension but should be used cautiously in the event of pulmonary edema; hence, **colloids** should be considered. **Airway patency** should be assessed and endotracheal intubation or tracheotomy considered in cases of severe angioedema.

After lifesaving measures and epinephrine administration, **antihistamines** (both H_1 and H_2 blockers) and **corticosteroids** (methylprednisolone 20–30 mg/kg BW IV slowly) may be given to further reduce clinical signs. **Bronchodilators** (β_2 adrenergics such as albuterol, clenbuterol, salmeterol) (*q.v.*) and oxygen therapy may also be used in severe cases.

Anaphylactic reactions can be uniphasic, biphasic or protracted. In the **uniphasic reaction**, clinical signs resolve within hours. In the **biphasic reaction**, there is a recurrence of the anaphylactic signs any time between 1 and 30 h after the initial remission. In some cases, the severity of the biphasic reaction is comparable to and often involves the same clinical signs and body systems as the initial reaction. In human patients, delay in the administration of epinephrine is associated with an increase in biphasic reactions and anaphylactic death. It is not clear in human medicine whether steroid therapy

prevents biphasic reactions although its anti-inflammatory properties could counter the delayed inflammatory response of anaphylaxis.

In the **protracted reaction**, profound hypotension may last beyond 24 h despite treatment. It is important to remember that, although rarely used in equine medicine, beta-blockers (e.g. propranolol) and angiotensin converting enzyme (ACE) inhibitors (e.g. enalapril) may **increase the severity** of anaphylaxis by decreasing blood pressure, promoting bronchoconstriction, and **antagonizing the response to epinephrine**. Therefore, in patients with refractory reactions, the dose of epinephrine may have to be repeated IM q 10–20 min, or epinephrine may be given IV (0.01 mL/kg BW of a 0.1 mg/mL solution). Other **beta-adrenergic drugs** (e.g. dopamine 10 μg/kg BW/min IV, isoproterenol 0.05–0.2 μg/kg BW/min IV) may also be used in non-responsive cases.

ALLERGY OR ATOPY

Allergy or atopy is an immediate hypersensitivity response of skin and mucosal membranes mediated by IgE, mast cells and basophils in **genetically susceptible individuals**.

A primary exposure to the allergen is required, in which CD4+ T helper cells and Th2 cytokines induce B cell class switching and the production of high concentrations of allergen-specific IgE. Subsequently, the IgE binds to high-affinity Fc receptors specific for the ε heavy chain on mast cells present in tissues or circulating basophils. Upon **successive exposure**, the allergen binds to the cell-associated IgE, and the cross-linking with other IgE molecules and Fc receptors **triggers the release of mediators** present in the cytoplasmic granules.

In addition to IgE-mediated allergy, the release of cytoplasmic granules by mast cells and basophils can be mediated by complement components C3a, C4a or C5a, which are known as **anaphylatoxins**. Elements that may trigger this hypersensitivity response include **exercise, opiates, cyclo-oxygenase inhibitors and IV contrast materials.**

Hypersensitivity diseases in horses may result from exposure to allergens via ingestion (food allergy), inhalation (heaves), injection (drug, insect bite) or percutaneous absorption (contact dermatitis). A familial or hereditary component seems to be involved, and it may be associated with major histocompatibility class I haplotype.

In **urticaria** (*q.v.*), cutaneous wheals of various sizes and shapes, pitting edema and pruritus develop within minutes to hours after exposure to the antigen. Urticaria may not involve an IgE-mediated hypersensitivity response, and **angioedema** secondary to systemic diseases, physical (dermatographism in areas of pressure), temperature-sensitive, cholinergic, and exercise-induced urticarias are possible. A complete history, physical examination and dermatologic testing may help identify the primary cause of the disease. Histopathologic findings in urticaria may include vascular dilation in the superficial and middle dermis and infiltration of inflammatory cells (mononuclear cells, neutrophils, mast cells and eosinophils) in the perivascular regions.

Sweet itch or **insect-bite hypersensitivity** (*q.v.*) is a **seasonally recurrent** hypersensitivity skin reaction to antigens in the saliva of *Culicoides* species characterized by widely distributed pruritic crusting dermatitis. Following antigen

exposure, eosinophils are recruited to the affected skin in response to histamine, platelet-activating factor (PAF) and eotaxin. Eosinophils may contribute to the disease with the release of proteases and inflammatory mediators.

To date, clinical studies have indicated that allergic tests still lack levels of sensitivity and specificity when horses affected by sweet itch are compared to normal horses. Therefore, allergic testing alone should not be used to diagnose this hypersensitivity reaction, and results should be evaluated in combination with the history and clinical manifestation of the disease. **Serologic testing** (ELISA for IgE or radioactive [RAST] or fluorescent allergosorbent [FAST] tests) may be used to aid in the design of a treatment plan. A positive reaction indicates the presence of antigen-specific IgE but alone it does not indicate whether that specific antigen is the cause of the disease. **Intradermal allergy testing** is probably more clinically significant than serology because it tests not only the presence of antigen-specific IgE but also the level of sensitization upon exposure to the allergen.

Acute idiopathic hypersensitivity reactions may be responsive to antihistamines (e.g. **hydroxyzine hydrochloride** 0.5–1 mg/kg BW t.i.d. PO) and corticosteroids (**dexamethasone** 0.05–0.1 mg/kg BW s.i.d. IV or PO; **prednisolone** 1 mg/kg BW s.i.d. or b.i.d. PO).

Management of chronic allergic reactions is based on **minimizing or removing exposure to the allergen**, which is often not possible. Treatment of recurrent allergies may be frustrating and prevent horses from competing due to regulatory drug withdrawals.

Hyposensitization with a vaccine formulated with antigens selected on the basis of history and results of intradermal testing seems to be a long-term treatment option, and response rates vary from 50% to 85%. The chronic administration of low doses of allergen (1 mL of a 20 000 protein nitrogen unit [PNU] of allergen per milliliter of water SC or IM q 21 days) may stimulate the Th1 type response and/or production of IgG "blocking antibody" that anticipates the binding of IgE to the antigen. In addition, hyposensitization may decrease the number of B cells expressing IgE receptor and restore antigen-stimulated IL-4 production to the levels of non-affected individuals.

AUTOIMMUNITY

Autoimmune diseases

Autoimmunity is an immune response against self-molecules. The presence of autoimmunity is common to all individuals and may or may not have an adverse effect on the body. **Autoimmune diseases** are clinical manifestations that involve B lymphocytes (antibodies) or T lymphocytes (CD4+ helper or CD8+ cytotoxic cells) reactive to self-antigens. Auto-reactive B and T cells are controlled by mechanisms of central and peripheral tolerance. However, immune dysfunction involving antigen presentation and co-stimulation, genetic defects (often familial) and environmental factors may lead to failure of autoimmunity control and, consequently, to autoimmune disease.

The failure of the anti-idiotype control mechanism of antibody production may allow the production of **autoantibodies**. In addition, **molecular mimicry of microbes** and self-epitopes may result in immune responses that overcome

immunologic tolerance and lead to tissue injury. Exposure of auto-antigens present in systems that are **not normally visited by lymphocytes** (e.g. a breakdown of the blood–brain barrier in the central nervous system) or the development of new epitopes on normal proteins may stimulate an immune response.

Viruses, particularly those that infect lymphoid tissues, may be capable of interfering with immunologic control mechanisms. **Exotoxins produced by bacteria** (e.g. *Clostridium* spp.) may promote damage of red cell membranes and the development of antigenic epitopes for the production of autoantibodies. **Penicillin-induced immune-mediated hemolytic anemia** is caused by the strong binding of the drug hapten to the surface of red cells. The complex induces the production and subsequent binding of antibodies. In some cases, autoimmunity is associated with the **aging process** and immune system malfunction, or the effect of **sexual hormones**. The mechanisms that induce tissue injury are those described in hypersensitivity reactions (*q.v.*).

Immune-mediated thrombocytopenia

Thrombocytopenia is a rare condition in horses, and most cases are of unknown cause. In addition to disseminated intravascular coagulopathy and decreased megakaryopoiesis, thrombocytopenia may be associated with autoimmunity. In the latter, it may occur in patients with infectious agents such as equine infectious anemia (*q.v.*) or *Clostridium* spp. (*q.v.*), after administration of drugs (e.g. penicillin, heparin, quinidine, thiazides, digoxin, sulfonamides, erythromycin) or in neoplasia (lymphosarcoma).

Clinical signs include **hemorrhagic diathesis** characterized by **epistaxis**, prolonged bleeding from injection sites, mucosal petechiae, hematomas, occult blood in urine and feces, melena, hemoarthritis, and/or hyphema. These findings may be differentiated from vasculitis by the **absence of heat, pain and swelling**. In general, clinical signs are not detectable until platelet counts are $<40\,000/\mu L$, and spontaneous bleeding may occur when counts are $<20\,000$–$10\,000/\mu L$.

A **coagulation profile** (*q.v.*) often reveals prolonged bleeding time, abnormal clot retraction, slightly prolonged activated coagulation, elevated fibrinogen degradation products (FDP), normal prothrombin time (PT) and normal activated partial thromboplastin time (APTT). Megakaryocytic hyperplasia is an expected response to the platelet destruction in the periphery and, when absent, may indicate immune-mediated destruction of megakaryocytes or myelophthisic disease.

Immune-mediated thrombocytopenia results either from the production and binding of immunoglobulins to platelets or megakaryocyte antigen surface (**primary** or **idiopathic thrombocytopenia**), or from the binding of immunocomplexes (antibodies against microorganisms, or a drug hapten) to the Fc receptors on platelets (**secondary thrombocytopenia**). In addition, platelet-bound IgM may fix complement. The antibody- or antibody–complement-coated platelets are non-specifically removed from the circulation by the reticuloendothelial system (macrophages in the spleen and liver that phagocytose the platelets via their Fc and complement receptors). The mechanism for autoantibody production may involve auto-reactive B cell clones that are stimulated during an immune response to infectious organisms,

dysfunction in CD4+ T cell regulation of B cell response, antigenic mimicry and altered anti-idiotypic regulation of antibody production.

Thrombocytopenia should be confirmed by performing an automated platelet count (*q.v.*) using a blood sample preserved in citrate anticoagulant, and/or a platelet hand count to rule out pseudothrombocytopenia. **Flow cytometric analysis** of IgG and IgM coated platelets may confirm the diagnosis of an immune-mediated process. The immuno-injury assay that measures antiplatelet activity in plasma of affected horses often renders false negative results. The presence of young platelets in the circulation as an indicator of bone marrow response to thrombocytopenia can be assessed by the staining of blood platelets with thiazole orange and flow cytometric analysis. Physical examination and ancillary diagnostics should be used in an attempt to identify the presence of **bacterial or viral infections and tumors**. A **Coggins test** should be used to diagnose equine infectious anemia (*q.v.*). In confirmed cases, intermittent hemolysis occurs concomitantly with viremic states.

If **drug-induced thrombocytopenia** is suspected, discontinuation of the medication is imperative for remission of the autoimmune response.

Platelet-enriched plasma transfusion may partially replace the loss of platelets to levels that prevent spontaneous bleeding or diathesis. Platelet-enriched plasma is prepared by centrifugation at 200 *g* for 10 min at room temperature of **aseptically collected blood** in plastic bags containing 2.5% sodium citrate. This therapy may be more effective in horses of small size (foals). The shelf life of platelet-enriched plasma is just a few hours before platelet function inactivation.

Immunosuppressive therapy may be attempted with the use of **corticosteroids** (**dexamethasone** 0.1–0.2 mg/kg BW s.i.d. IV), which suppress phagocytic function and antibody production. After 4–5 days, an increase in platelet counts may allow progressive reduction of the dexamethasone dose (20% daily) and, potentially, its substitution with **prednisolone** (starting at 1 mg/kg BW b.i.d. PO, with subsequent reduction in dose). Low dose corticosteroid treatment or early discontinuation of therapy may result in persistence or recurrence of disease. Therefore, in many patients, immunosuppressive therapy may last for 30 days.

The use of other **immunosuppressive therapy** (**vincristine sulfate** 0.01 mg/kg BW IV one or two doses a week apart, in combination with dexamethasone; or **azathioprine** 3 mg/kg BW s.i.d. PO, and subsequent decreasing doses) is an option in cases refractory to corticosteroid therapy. Immunoglobulin transfer using IV plasma transfusion may assist by interfering with macrophage Fc-receptor clearance of immunoglobulin-coated platelets.

Immune-mediated hemolytic anemia

Immune-mediated hemolytic anemia has been reported in horses **secondary** to neoplasia (lymphosarcoma), bacterial infection (*Clostridium* spp.) or viral (equine infectious anemia) infections, chronic inflammatory diseases and exposure to certain drugs.

Clinical signs are determined by the severity of red cell destruction and include mild depression, icterus, tachycardia and tachypnea. Blood analysis

reveals **progressive anemia** and **indirect hyperbilirubinemia**. Frequently, red cells coated with autoimmune IgG go through extravascular destruction by the reticuloendothelial system in the spleen via Fc receptors. Auto-reactive IgM-coated red cells facilitate complement fixation and red cell removal by the hepatic macrophages via complement receptors. When antibody and complement fixation activity increases, **severe intravascular hemolysis** may result with discoloration of serum and, occasionally, urine. Bone marrow cytology reveals regenerative erythropoiesis.

Diagnosis is confirmed by the detection of red cell auto-agglutination after 1:4 dilution of blood with saline. The presence of antibody on red cells can be evaluated by **Coombs test** (rabbit antiserum against equine IgG and IgM) or direct detection of IgG and IgM antibodies on the cell surface by flow cytometry. Physical examination and ancillary diagnostics should be used in an attempt to identify the presence of bacterial or viral infections and tumors. A **Coggins test** should be used to diagnose equine infectious anemia (*q.v.*). In confirmed cases, intermittent hemolysis occurs concomitantly with viremic states.

Treatment should include the discontinuation of any current therapeutic drug and investigation of potential causes of immune-mediated disease. The overall treatment goal is to **remove the primary cause of disease**. In life-threatening anemia, rapid hemolysis can cause somnolence and dyspnea, packed cell volume (PCV) <12% and low venous pO_2 (PvO_2). In these cases, **blood transfusions** are necessary to stabilize the patient. On the other hand, when red cell lysis is slow, PCV remains >12–15%, and the patient is stable, blood transfusion should be avoided so as not to cause suppression of bone marrow erythropoiesis. In the latter case, frequent monitoring of the patient's condition and PCV will indicate whether blood transfusion has become necessary.

Slow whole blood transfusion (4 mL/kg BW/h) should be performed after blood cross-match between donor and patient, and under close supervision for anaphylactic and anaphylactoid reactions. A horse blood donor can donate up to 20% of total body blood volume (body weight [kg] × 8%). For adult horses (500 kg), 6–8 L of blood may be collected and transfused; proportional doses can be calculated for ponies and foals. Whole blood should be collected using aseptic technique and blood collection sets with anticoagulant (e.g. 2.5% sodium citrate). Blood transfusion should be given by blood administration sets (with filter), which should be replaced every 3–4 L. During transfusion, the patient should be monitored for adverse reactions, which are expressed by tachypnea, restlessness, piloerection and muscle fasciculation. If these clinical signs develop, the blood transfusion should be stopped immediately and anti-anaphylactic treatment considered (epinephrine 0.01 mL/kg BW of a 1 mg/mL solution, IM).

Alternatively, **polymerized bovine hemoglobin** solution (e.g. Oxyglobin, Biopure Corporation, Cambridge, MA) can be used as an emergency treatment to improve hemodynamics and oxygen transport.

Immunosuppressive therapy should be considered in patients with rapid red cell hemolysis. In general, immune-mediated hemolytic anemia in horses is responsive to dexamethasone (0.1–0.2 mg/kg BW s.i.d. IV). The **corticosteroid therapy** should be aggressive until PCV value is >20%. In this case,

the dexamethasone dose can be gradually decreased (20% per day) and slowly substituted by prednisolone (1 mg/kg BW s.i.d. or b.i.d. for a week PO). In refractory cases and when the underlying disease cannot be treated, the use of immunosuppressive therapy is prolonged and tailored to the patient's needs.

Vasculitis

In horses, **vasculitis of the small vessels** is often associated with autoimmunity. Although the skin and mucous membranes are mostly affected, the gastrointestinal, respiratory, renal and muscular systems may also be involved. This immune-mediated condition may be **primary** (type II hypersensitivity) or **secondary** (type III hypersensitivity) to infections caused by *Streptococcus equi, Streptococcus zooepidemicus*, equine viral arteritis, equine influenza virus, equine infectious anemia virus, equine herpesvirus 1 and *Anaplasma phagocytophila* (formerly *Ehrlichia equi*). In addition, tumors and drugs may supply antigens for the hypersensitivity response.

Clinical signs include diffuse or localized edema of skin, subcutaneous tissues and/or mucosa, exudation, petechiations and necrosis. The purplish discoloration of the skin and mucous membranes produced by the breakage of small vessels describes the condition known as **purpura hemorrhagica**. In the horse, purpura hemorrhagica is associated with high levels of circulating C3 complement component, immune complexes of IgA and *S. equi* M protein, and low levels of IgG specific for *S. equi* during the acute phase. In the initial phase, edema, heat and pain to the touch are observed in the distal extremities. In severe cases, fibrinoid necrosis of blood vessels may lead to respiratory (dyspnea) and gastrointestinal (colic) lesions. The presence of fever has been associated with poor prognosis.

Diagnosis is based on history, clinical signs and **histopathology of skin biopsies**. In the latter, neutrophilic infiltration of vessels of the skin and subcutaneous tissues is often seen. The presence of immune complexes or antibodies against endothelial cells may be observed by direct fluorescent tests in the initial phase of the lesions. In the case of infection, serology of paired samples and tests for *S. equi* M protein levels may indicate the organism implicated in the disease process.

Treatment should aim at the **removal of the antigenic stimulus** by treating the primary disease (antimicrobials) if possible. The inability to identify or eliminate the antigenic stimulus may lead to systemic vasculitis, debilitation (synovitis, thrombophlebitis, skin necrosis/sloughing) and death. When there is concern about drug-induced vasculitis, it is imperative to **stop the administration of all medications** and to change those that are indispensable. Immunosuppressive therapy can be used to decrease immune and inflammatory responses, although some cases of vasculitis have spontaneous remission. **Corticosteroids** (dexamethasone 0.1–0.2 mg/kg BW s.i.d. IV; prednisolone 1 mg/kg BW s.i.d. or b.i.d. PO) should be used in higher doses in the initial phase of the disease, and the dose decreased or discontinued according to the individual response. Prolonged immunosuppressive therapy is often needed, and premature discontinuation of therapy may result in recurrence of disease.

Heaves or recurrent airway obstruction

Heaves (*q.v.*) is an allergic respiratory disease of horses characterized by **bronchoconstriction** and **mucus production**, leading to exercise intolerance, nasal discharge, chronic cough, respiratory distress at rest, depression and weight loss. Affected horses often present **expiratory effort**, which is noticeable by a prolonged expiratory phase and the formation of a **"heave" line** along the abdominal muscles. At auscultation, expiratory wheezes and tracheal rattles are easily identified. The age of onset is between 9 and 13 yr of age, and horses that are stabled and bedded on **straw** and fed **hay** are at risk.

The hypersensitivity reaction seems to be in response to **inhaled dust** present in hay and straw. In addition, there is evidence for the implication of specific antigens: candidates are molds and endotoxin lipopolysaccharides. Horses pastured in hot, humid climates may present hypersensitivity to molds on grasses and develop a similar syndrome known as **summer-pasture associated heaves**.

When exposed to the triggering factors in the environment, susceptible horses may develop **pulmonary dysfunction** within hours and demonstrate diffuse bronchospasm, low tidal volume, high lung volumes, increased maximal transpulmonary pressures, reduced dynamic compliance, increased pulmonary resistance, and hypoxemia. **Bronchoalveolar lavage fluid** cytology reveals **neutrophilic inflammation** (neutrophil percentage 50–70%) with concomitant reduction in the lymphocyte and macrophage populations. There is an increase in the CD4+/CD8+ T cell ratio. These changes are often proportional to the clinical parameters. Airway obstruction and neutrophilic inflammation may be reversed within a week after removal from exposure to the insulting factor.

The immuno-pathophysiology of heaves has not been completely determined. In addition, it is not known whether heaves and summer-pasture associated heaves share the same mechanisms of disease. Diffuse bronchospasm seems to be caused by the direct effect of inflammatory mediators and an indirect vagal stimulus on smooth muscle. Nitric oxide (NO) deficiency, histamine and cyclo-oxygenase derived prostaglandins do not seem to play a role in this process because NO levels are increased in horses with heaves, and the use of **anti-histamines and non-steroidal anti-inflammatories does not relieve bronchoconstriction**. Bronchiolitis is characterized by smooth muscle hypertrophy, peribronchial lymphocytic infiltration and IgA-secreting lymphocytes. **Thoracic radiographs** may be useful to rule out other causes of pulmonary disease; in the case of heaves, they reveal peribronchial inflammation, mild interstitial opacity and flattening of the diaphragm (pulmonary overinflation).

Treatment of heaves primarily involves **management changes** to minimize exposure to dust particles, i.e. strict pasture and pelleted feed management. During acute episodes, **corticosteroid therapy** is the most effective treatment to decrease peribronchial smooth muscle contraction and production of mucus, and improve pulmonary function. This effect is mediated by glucocorticoid receptors and affects cytokine and inflammatory mediator transcription. Dexamethasone (0.1 mg/kg BW s.i.d. IV) is indicated for horses with severe respiratory distress. After 3–4 days, maintenance may be accomplished

with prednisolone (1 mg/kg BW PO s.i.d. or b.i.d.). Alternatively, mild cases of heaves may be treated with **aerosolized corticosteroid therapy** (fluticasone propionate, beclometasone dipropionate).

Metered-dose inhaler therapy using a mask or nostril delivery system allows direct delivery of the drug to the lower respiratory tract, which reduces total therapeutic dose and minimizes the exposure of other systems to the drug. Nevertheless, severe respiratory distress may not allow adequate drug delivery due to the strong expiratory phase of respiration and bronchoconstriction. In these cases, the use of parenteral corticosteroids or bronchodilators is recommended before the administration of inhalatory corticosteroids. Important adverse side effects of corticosteroid therapy, including the inhalatory form, are **adrenal suppression and susceptibility to infection**.

Bronchodilators are an important component of the treatment of heaves because they provide immediate improvement of bronchoconstriction and pulmonary function. An inhaled β_2-adrenergic agonist (short-acting **albuterol** or long-acting **salmeterol**) and anticholinergic bronchodilators (**ipratropium bromide**) may be used individually or in combination depending on the severity of disease and tolerance of the drug. In addition, **clenbuterol**, another β_2-adrenergic agonist, may be administered PO to manage mild cases.

Pemphigus foliaceus

Pemphigus complex is a group of autoimmune skin disorders characterized by the production of **autoantibodies** directed against the **intercellular cement in the skin**. The inflammatory response disrupts adhesion between cells to cause bulla or pustule formation. The classification of the lesions is based on their distribution: pemphigus vulgaris (persistent thin blisters at mucocutaneous junctions), pemphigus vegetans (thick blisters or pustules in intertriginous areas or folds of skin), **pemphigus foliaceus** (superficial lesions on the face, ears, muzzle and limbs), and pemphigus erythematosus (milder lesions than pemphigus foliaceus with features of lupus erythematosus). **Bullous pemphigoid** has a similar presentation to pemphigus and the lesions involve skin and mucocutaneous junctions. In the horse, pemphigus foliaceus is the most common autoimmune skin disease, and it likely involves the destruction of desmosomes by autoantibodies against a desmosomal glycoprotein.

The **diagnosis** is confirmed by histopathology (acantholysis of keratinocytes, intraepidermal and subcorneal vesicles, non-degenerative neutrophils) and direct immunofluorescence of immunoglobulins deposited in the intercellular cement. Because the lesions are very superficial, fresh blisters should be sampled using excisional biopsy. **Treatment** can be instituted with corticosteroids (dexamethasone 0.1–0.2 mg/kg BW s.i.d. IV) in combination with azathioprine (3 mg/kg BW s.i.d. PO) or gold salts (aurothioglucose 1 mg/kg BW once a week decreasing to once a month IM). **Corticosteroid therapy** should be aggressive until the clinical signs have resolved. The dexamethasone dose can then be gradually decreased (20% per day) and slowly substituted by prednisolone (1 mg/kg BW s.i.d. or b.i.d. for a week PO). In refractory cases, immunosuppressive therapy is prolonged and tailored to the patient's needs.

NEONATAL ISOERYTHROLYSIS

Neonatal isoerythrolysis (NI) is a hemolytic disease that develops within hours to a few days of life and involves the **maternal alloantibodies** absorbed from the colostrum. The alloantibodies are directed against the incompatible antigens on the red cell of the foal. The binding of the antibodies causes extravascular hemolysis, red cell agglutination and complement-mediated intravascular hemolysis.

Clinical signs include depression, weakness, lethargy, tachycardia, tachypnea, icteric or pale mucous membranes, moderate to severe anemia, normal total protein, metabolic acidosis due to poor tissue oxygenation, hyperbilirubinemia, hemoglobulinemia and hemoglobinuria. In severe cases, pigmentary nephropathy, azotemia, tissue inflammation due to hypoxia (central nervous system, gastrointestinal tract, liver), fever and seizures may occur. In addition, kernicterus or bilirubin encephalopathy may lead to severe depression, opisthotonus, rigidity, convulsions and death due to the deposition of unconjugated bilirubin and necrosis of cerebral gray matter.

The **alloantibodies are produced by the dam during gestation** under specific conditions:

1. The foal must have inherited antigenic blood factors from the sire that are not common to those of the dam.
2. If the mare becomes exposed to fetal blood close to parturition, she produces antibodies against these factors.
3. Because peak antibody production is only achieved approximately 9 days after foaling, these antibodies do not reach the colostrum in time to be absorbed by that foal; however, in the **following pregnancy**, the mare will transfer to the colostrum high levels of antibodies against that blood factor.
4. If the foal expresses the incompatible blood factors, the absorbed maternal antibodies will cause **red cell lysis**.

An exception to this sequence of events, and one that leads to the possibility of neonatal isoerythrolysis in the **first pregnancy**, is that the mare had received a blood transfusion from an incompatible blood type that is the same as that of the foal.

There are numerous **blood types** in horses but the most important blood groups associated with neonatal isoerythrolysis are A and Q. The antigens Aa and Qa are responsible for more than 90% of cases; other less important antigens include Ab, Qrs, Qc, Dc, Da, Ka, Pa and Ua. All breeds can be affected with different levels of incidence of disease.

Neonatal isoerythrolysis can be predicted and avoided using appropriate testing, which includes blood factor assays, hemolytic assays, cross-matching and the jaundice foal agglutination test. **Blood factor assays** test for the presence or absence of factors Aa and Qa on the red cells of the dam and sire at any time before breeding. If the dam does not have factor Aa or Qa, she is at risk of producing NI-causing antibodies and needs to be tested for antibodies before foaling.

If the dam is positive for one of the blood groups, there is no risk for that specific blood group. If the sire is negative for both blood groups, there is no

risk for the disease. In addition, the mare's serum can be cross-matched with the sire's red cells: a negative reaction indicates no risk for the foal; a positive reaction indicates a 50% risk of NI, and a cross-matching test should be done at foaling or colostrum withheld.

Hemolytic assays test for antibodies against the blood factors in the mare's serum within 30 days of foaling. Different dilutions of the serum from the mare are mixed with red cells expressing Aa or Qa or Ca (other factors—D, K, P, U and T—may be tested in some laboratories). If antibodies are present in the mare's serum they bind to the red cells (antigen–antibody complex) and, after adding rabbit complement, lysis of red cells is induced. Cell lysis intensity is determined from 0 to 4, and the last dilution of serum that promoted cell lysis is identified. Serum dilutions above 1:16 for Aa and Qa that cause hemolysis in vitro may produce NI; therefore, **withholding colostrum is recommended**. Antibodies to Aa and Qa factors detected at 1:2 serum dilutions require retest before foaling. If antibodies are found against other factors, withholding colostrum is recommended because of the uncertainty of the interpretation of the results. Antibodies against Ca factor do not cause NI but can cause false positive reactions.

Cross-matching at the time of foaling tests for the presence of absorbed colostral antibodies against the blood factors in the foal's serum, or for antibodies in the dam's serum (minor cross-match).

Jaundice foal agglutination tests for NI-causing antibodies in the colostrum against the foal's red cells. In this test, serial dilutions of the dam's colostrum with saline (1 mL of 1:2, 1:4, 1:8, 1:16 and 1:32 dilutions) are mixed with one drop of the foal's whole blood. A 1 mL saline sample is used as a negative control. The mare's blood may be tested under the same conditions as a negative control. The presence of agglutination in the red cells may be observed after centrifugation for 2–3 min at a medium speed and inversion of the tubes. A positive **Coombs' test** is not specific for NI.

Prevention of NI can be accomplished by milking out and discarding the colostrum from the dam for 36 h after birth. The foal should be fed with a safe source of **good quality colostrum or IV plasma**. Meanwhile, the foal should be muzzled and fed milk replacer or another mare's milk using a bottle or nasogastric intubation. To ensure adequate levels of antibodies, the foal's serum should be tested for immunoglobulin G levels.

Treatment decisions should be based on the patient's condition (depression, dyspnea) and blood analysis (PCV <12%, low venous pO_2), wherein abnormalities are often proportional to the amount of alloantibody absorbed and its affinity to the red cell antigen. **Transfusion of whole blood** from a cross-matched donor (Aa and Qa negative) or washed red cells from the dam can be used. If a cross-match is not available, whole blood from a gelding with no history of previous blood transfusions may be used. Another option until cross-matching or whole blood for transfusion becomes available is the administration of **polymerized bovine hemoglobin** (Oxyglobin, Biopure Corporation, Cambridge, MA). Whole blood transfusion may be necessary in addition to polymerized hemoglobin because its half-life in the circulatory system is short (18–43 h). Rare anaphylactoid reactions to this product have been reported in horses. Calculated fluid therapy may be needed to maintain renal function and to prevent renal disease due to the hemolysis.

The prophylactic or therapeutic value of **Sn-mesoporphyrin**, a heme oxygenase inhibitor that decreases bilirubin production, is still to be determined for its protection against kernicterus in the horse. Immunosuppressive therapy to decrease removal of antibody-coated red cells by the reticuloendothelial system is not indicated for the treatment of NI because of the short presence of maternally derived antibodies against red cells, and the side effects of general immunosuppression in foals.

NEONATAL ALLOIMMUNE THROMBOCYTOPENIA

Neonatal alloimmune thrombocytopenia (NAIT) may occur in **neonate foals** and mules that ingested colostrum containing alloantibodies against **platelet cell surface antigens**.

Similar to NI, the dam produces antibodies against paternally inherited, incompatible surface molecules on the foal platelets. Megakaryocytic hyperplasia is an expected response to the platelet destruction in the periphery and, when absent, may indicate immune-mediated destruction of megakaryocytes or myelophthisic disease.

Thrombocytopenia develops despite platelet production because the binding of maternally derived antibodies to platelets decreases platelet survival time to a few hours. Antibody-bound platelets are efficiently removed from the circulation by the reticuloendothelial system. Fortunately, this same process favors the clearance of reactive antibodies and shortens their negative effect.

The most common **clinical signs** include petechiation, extensive bleeding from injection sites, hematomas, hemarthrosis and hyphema. The coagulation profile often reveals prolonged bleeding time, abnormal clot retraction, slightly prolonged activated coagulation, elevated fibrinolytic degradation products (FDP), normal prothrombin time (PT) and normal activated partial thromboplastin time (APTT).

Diagnosis is based on the history, clinical signs and presence of antibody-bound platelets in the foal, which can be tested using a direct flow cytometric assay (fluorescent antibodies against horse immunoglobulin [Ig] G, M or A). In addition, confirmation of the diagnosis can be attempted by platelet aggregation and an **immunoradiometric assay** using staphylococcal protein A (SPA) to test for platelet-bindable antibody. In this assay, isolated platelets are incubated with radiolabeled SPA, excess radiolabeled SPA is washed out, and platelet-bound radioactivity is measured in a gamma counter. These techniques may confirm the diagnosis by testing the absence of antibodies on the maternal platelets, circulating antibodies in the foal plasma that bind foal and sire platelets, allotypic differences between dam and foal platelets, and/or the presence of antibodies in the dam's serum and colostrum against the foal and sire platelets.

Differential diagnoses include autoimmune or drug-induced thrombocytopenia (*q.v.*), sepsis, disseminated intravascular hemolysis (*q.v.*), equine infectious anemia (*q.v.*) and myelophthisic disease.

Treatment is based on transfusion of platelet-rich plasma (*q.v.*) from a donor, or washed maternal platelets. For the same reasons described for

neonatal isoerythrolysis (*q.v.*), immunosuppressive therapy is not indicated for the treatment of NAIT.

EQUINE PERINATAL IMMUNOLOGY

EQUINE FETAL IMMUNOLOGY

A significant portion of the development of the equine immune system happens during **fetal life**. Thymic corticomedullary organization of lymphocytes is present as early as 80 days of gestation, and these cells are responsive to mitogenic and allogenic stimulation by 100 days of gestation. Fetal spleen lymphocyte distribution in periarteriolar sheaths and germinal centers, and response to stimulation are present by 200 days of gestation. Peripheral lymph nodes are also populated and responsive to stimulation by this age. The mesenteric lymph nodes and intestinal lamina propria become populated by lymphocytes by 13 wk of gestation. Peripheral blood lymphocytes are detected by 120 days of gestation, and they are responsive to mitogens by 140 days. B lymphocytes are functional during normal gestation despite negligible exposure to organisms. Serum IgM concentration of 4–10 mg/dL may be identified in fetuses older than 185 days of gestation, and values >16 mg/dL in presuckle foals. Serum IgG concentration of 5 mg/dL can be detected at 180 days of gestation, and presuckle foals may show a variable amount of serum IgG. Specific antibody response following in utero vaccination has been detected in equine fetuses as early as 200 days of gestation.

PASSIVE TRANSFER OF MATERNAL IMMUNOGLOBULINS

The **epitheliochorial placentation** of horses does not allow in utero transfer of maternal immunoglobulins to the fetus. Because of lack of immunogenic stimulation in utero, the presuckle foal is essentially **agammaglobulinemic**, although low levels of IgM and IgG can be detected. Immunoglobulins are transferred from the blood to the mammary secretions through selective Fcγ receptors on the surface of epithelial cells. This immunoglobulin transfer to colostrum is intense 2–3 wk before parturition and decreases throughout lactation. The correlation between IgG and IgM concentrations and mare's serum and colostrum, or between immunoglobulin concentrations in the foal's serum and in the mare's colostrum is largely dependent on the time of colostrum and serum sampling.

The rate of mammary secretion of **colostrum** is approximately 300 mL/h in mares, and total colostral volume is 3–7 L. Colostrum contains mainly IgG and IgG(T), intermediate levels of IgM, and less IgA, lactoferrin and complement. It is replaced by milk with low levels of IgG and high levels of IgA **within 12 h** from the time the mammary gland is first suckled by the foal. After parturition, the colostral IgG concentration is 6500–30 000 mg/dL, and decreases significantly beyond 8 h. At foaling, the colostral IgM concentration ranges from 12 to 240 mg/dL, and decreases significantly beyond 6 h. Approximately 20% of total colostral IgG and 14% of total IgM contents are found in the initial 500 mL of colostrum.

Specialized epithelial cells in the small intestine absorb the colostral immunoglobulins via non-selective pinocytosis. The absorbed immunoglobulin reaches the lymph system and later the blood system through the thoracic duct. **Immunoglobulin uptake** peaks within 8 h of parturition and declines with time, regardless of the time of oral intake of macromolecules. The specialized epithelial cells are replaced within 24–36 h by mature cells. If the foal nurses within 2 h of birth, serum IgG levels become detectable at 6 h and peak at 18 h.

Although newborn foals are **immunocompetent at birth**, the primary immune response requires at least 2–3 wk to be established and this window favors bacterial invasion and spreading. Therefore, transfer of maternal antibodies plays an important role in controlling infection during this period. The **persistence of maternal antibody** in the foal is proportional to the amount of immunoglobulin absorbed in the colostrum. Serum IgG concentrations in foals may vary from 500 to 6000 mg/dL after ingestion of colostrum.

Foals suckling colostrum from dams vaccinated within the last month of pregnancy have higher, prolonged serum IgG concentrations compared with foals from non-vaccinated mares. The significance of high immunoglobulin concentration in enhanced protection against environmental pathogens is not known. However, the amount of maternal immunoglobulin absorbed by foals may influence maternal immunoglobulin catabolism and delay the synthesis of neonatal endogenous antibody. The half-lives of colostral IgG and IgM are 26–32 and 5–10 days, respectively. Typically, maternal IgG concentrations decrease and foal endogenous serum IgG concentrations increase around the fourth to sixth week of life. During this transitional period, the total immunoglobulin concentration is often low.

FAILURE IN THE TRANSFER OF MATERNAL IMMUNOGLOBULINS

Failure in the transfer of maternal immunoglobulins is characterized by serum immunoglobulin levels <800 mg/dL in the foal 18–24 h after ingestion of colostrum, and values between 400 and 800 mg/dL are considered partial failure.

There are a few methods available for the **measurement of serum immunoglobulins**, which vary in their sensitivity and specificity; they include glutaraldehyde coagulation, the modified zinc sulfate turbidity test, the latex agglutination test, and the SNAP ELISA test (Idexx Laboratories), which is extensively used in practice with moderate sensitivity and high specificity in comparison to radioimmunodiffusion tests (RID).

The **incidence** of total or partial failure of passive transfer in well-managed practices wherein foals are ensured to nurse within 3 h of life is 3–17%. Failure of transfer of maternal antibodies may involve one or more of the following factors:

1. Colostrum with low immunoglobulin concentration
2. Prepartum colostrum loss
3. Ingestion of an inadequate amount of colostrum
4. Delayed ingestion of colostrum
5. Inappropriate immunoglobulin absorption related to prematurity and poor development of the intestinal epithelium.

Of importance is the absence of antibodies in the colostrum against specific pathogens in the environment, which occurs with **mares in transit** to a new environment in the period close to foaling.

Despite the fact that approximately 78% of foals with failure of passive transfer become ill with infectious organisms, a small percentage of such foals do not become sick. It is possible that the innate immune system, along with partial transfer of maternal antibody, is capable of providing immune protection on well-managed farms.

IV plasma transfusion is an efficient means of transferring adequate levels of immunoglobulin to the foal after the absorptive period is gone. In general, 1 L of plasma suffices to provide final serum immunoglobulin levels >800 mg/dL and increase opsonization capacity. Nonetheless, foals with septicemia may require additional doses. Plasma transfusion should be administered using a blood transfusion set at a **slow rate in the initial 15 min** to evaluate for adverse anaphylactoid reactions (piloerection, tachycardia, muscle tremors).

INNATE IMMUNE SYSTEM

Both the innate and adaptive arms of the immune system are complementary in the defense against organisms: they are both involved in the recognition and elimination of pathogens. The **innate immune system** may play an important role in response to pathogen challenge in foals until antigen-specific immunity responses are produced. For example, 2–4-month-old specific-pathogen free (SPF) foals inoculated intranasally with equine herpesvirus 1 developed clinical signs of disease (depression, fever, intermittent cough, nasal discharge) on the second day of inoculation. However, the foals were able to recover from disease before specific immunity was developed. Interferon activity was measured in nasal aspirates and was increased by the second day of the primary viral inoculation. This non-specific response was followed by detection of antigen-specific IgM in serum 6 days post inoculation and virus neutralizing antibody 14 days post inoculation. Interferon levels were very low or absent following secondary inoculation, a time when the humoral specific immune response was developed.

Phagocytic activity is facilitated by the presence of opsonins, which may function via C3 receptors (for complement) or Fcγ receptors (for IgG) on phagocytes. Complement activity in presuckle foals has been reported to be 13% of that in the adult, increasing to 64% by 1 mo of age, and 85% by 5 mo of age. **Complement activity** increases more rapidly during neonatal life compared to fetal life. In addition, foals deprived of colostrum have greater complement activity than foals that absorb adequate amounts of immunoglobulin from colostrum. Immunoglobulins and complement reveal synergistic interaction in phagocytosis and oxidative burst activity. This effect is evident by the benefits of plasma therapy in neonates, which significantly increases the opsonic capacity of foals' serum. The absence of antibodies and complement significantly decreases the ability of neutrophils to phagocytose and kill organisms.

Foal phagocytic function is dependent on the maturation of humoral chemotactic and opsonic factors rather than on the maturity of neutrophil function. For this reason, foals may have decreased neutrophil activity up to

4 mo of age in vivo, characterized by decreased migration, phagocytic and oxidative burst activity compared to adult horses. However, there is comparable or superior efficiency in the in vitro phagocytic capacity of foal and adult neutrophils when pooled-adult sera are used for opsonization, indicating that neonatal foal phagocytes are competent.

When foal phagocytes are opsonized with autologous serum, phagocytosis is much reduced up to 5 mo of age compared with adult serum opsonization. In spite of that, the CD18 receptor expression for complement-opsonized material on phagocytes is higher in neonates when compared with adult horses, which may explain the greater in vitro phagocytic activity of neonate phagocytes compared to adult horses.

ADAPTIVE IMMUNE SYSTEM

Despite the intense development of the immune system during fetal life, the horse's **immune system is naïve** to environmental organisms at birth. The intense **expansion of lymphocyte population** in early life may be a consequence of exposure to environmental antigens. In addition, T cell proliferation may respond to mechanisms of immune development that are independent of antigen contact. Along with the increase in the number of circulating cells, there is an increase in lymph node weight and cell output. Also, there is an increase in the circulation of cells through the gut and the appearance of gut-homing T cells, which are likely driven by antigen. Therefore, postnatal development is accompanied by the increase in size of the total lymphocyte compartment and appearance of primed cells.

Studies in foals indicate an **age-dependent distribution of peripheral lymphocyte subsets**. Foals are born with comparable lymphocyte counts to those of the adult horse. These counts increase 2.5–3 times by the third month of age, and CD8+ cells seem to be the major contributors to the increase in lymphocyte counts. Foals are born with B lymphocyte counts lower than adult values, and total and percent peripheral blood B cells increase from the fourth week to the third month of age. This period coincides with the increase in serum IgM and IgG concentrations and indicates activation of the humoral immune response.

Non-specific mitogens (phytohemagglutinin, PHA and concanavalin A, ConA) are known to induce cell signaling and promote **T cell proliferation**, and are extensively used to evaluate lymphocyte function. Phytohemagglutinin stimulation promotes a substantial response in peripheral blood lymphocytes shortly after birth. In addition, foal lymphocytes respond intensively to mitogens from 3 wk to 4 mo of age, a time that coincides with natural lymphocyte proliferation and activation. Foals also present competent **lymphokine-activated killing** (LAK) cell activity of peripheral blood lymphocytes at birth and early life.

Neonatal foals have fewer cells expressing **major histocompatibility complex** (MHC) class II antigen on T lymphocytes in the first month of life, and the number of cells expressing this activation molecule equates to that of adult horses by 4 mo of age. The age-dependent increase in the numbers of T cells expressing MHC class II molecules in the circulation suggests maturation of this cell population.

MUCOSAL IMMUNITY

Colostral and lactogenic passive mucosal protection in monogastric animals is associated primarily with **secretory IgA** against enteric organisms. Immunoglobulin A on the mucosal surface impairs bacterial binding to enterocytes, and neutralizes bacterial enterotoxins and enterotropic viruses. The participation of passively transferred leukocytes (lymphocytes and phagocytes) in defense against viruses and bacteria has not been described in the horse.

There is an apparent **age-related maturation** of the immune system of the respiratory tract of the equine neonate. At birth, foals do not present organized **lymphoid tissue** in the lungs, and T lymphocytes and plasma cells are virtually absent in the first week of life. Developed bronchus-associated lymphoid tissue is observed by 12 wk of age. Total bronchoalveolar lavage (BAL) leukocyte counts in foals <3 wk of age are half those found in adult horses. Although B cells in BAL fluid are almost undetectable in the first 4 wk of life, B cell values become comparable to those of adult horses by the second month of age. **Immunoglobulin** A, IgG and IgM plasma cells are present in the lower respiratory tract around 8 wk of age. The reduced number of pulmonary lymphocytes in the early neonatal period compared with values in weanling foals indicates dependence of mucosal immune defense on the expansion of the lymphocyte population. Temporal development of a competent mucosal immune defense is also a possibility. **Alveolar macrophages** have impaired chemotactic function up to 2 mo of age. In addition, these cells have lower phagocytic and killing capability compared to peripheral blood neutrophils from the same animal.

IMMUNODEFICIENCIES

Immunodeficiency is a rare disorder of the immune system that results in failure to build protection against pathogens and, consequently, in predisposition to recurrent infections and death. Immunodeficiencies may be primary or secondary. The etiologies of primary and secondary immunodeficiencies are diverse, and the characteristics and clinical manifestations may vary depending on the cells of the immune system that are affected (Table 2.1).

Table 2.1 Immunodeficiencies described in the horse

Immunodeficiency	Immunologic findings	Genetic defect	Breed and age
Failure of transfer of maternal immunoglobulins	IgG < 800 mg/dL at 24 h after birth	None (poor absorption of colostral Ig)	All breeds Neonates
Severe combined immunodeficiency (SCID)	Agammaglobulinemia, no serum IgM after 1 mo[1] T cell lymphopenia, absent B cells Hypoplasia of spleen, thymus and lymph nodes Susceptibility to adenovirus, *P. carinii*, *R. equi*, *Cryptosporidium*	Autosomal recessive trait DNA-dependent protein kinase (DNA-PK) gene VetGen test for carriers and affected animals (see p. 143)	Arab and cross-Arab Birth up to 3 mo

(*Continued*)

Table 2.1 (*Continued*)

Immunodeficiency	Immunologic findings	Genetic defect	Breed and age
Fell Pony immunodeficiency syndrome	Normal/ hypogammaglobulinemia[1] B cell lymphopenia, lack plasma cells <5% MHC class II on lymphocytes Lack secondary lymphoid follicles Normal CD4+ and CD8+ T cell counts and function Severe anemia with erythroid hypoplasia Neuronal chromatolysis in peripheral ganglia Susceptibility to adenovirus and *Cryptosporidium*	Autosomal recessive trait (?) Unknown	Fell Pony Birth up to 3 mo
X-linked agammaglobulinemia	Agammaglobulinemia[1] Lack of B and plasma cells Normal T lymphocyte response to mitogens	X-linked trait(?) Bruton's tyrosine kinase (*btk*) gene(?)	TB, SB, QH Only young males affected
Transient hypo-gammaglobulinemia	Transient pan-hypogammaglobulinemia[1] Normal B and T lymphocyte counts	Unknown	Arab, TB Young age
Selective IgM deficiency	Serum IgM deficiency 2× STDV below normal mean Normal IgG, IgA and IgG(T) Normal lymphocyte counts Normal T cell response to mitogens	Unknown Primary or secondary to lymphoma	All breeds Young or >2 yr
Common variable immunodeficiency (CVID)	Pan-hypo- or agammaglobulinemia No B cells or B cell lymphopenia	Unknown	TB, Arab, QH Adult first or second decade of life
Transient T cell deficiency	CD4+ T cell lymphopenia (CD8+ T cells may also be decreased) Susceptibility to *P. carinii*	Unknown	Paint Birth to 6 mo

[1] *Serum immunoglobulin levels are variable until maternally derived antibodies are circulating (up to 2–3 mo of age); because IgM is associated with primary immune response, IgM hypo- or agammaglobulinemia after 1 mo of age suggests humoral deficiency.*

CD, cluster of differentiation; Ig, immunoglobulin; MHC, major histocompatibility complex; QH, Quarter Horse; SB, Standardbred; STDV, standard deviation; TB, Thoroughbred; (?), not confirmed in the horse.

Clinical conditions that may indicate an immunodeficiency include:

1. Two or more episodes of pneumonia within 1 yr
2. Two or more episodes of sinus infection within 1 yr
3. Multiple sites of infection (pneumonia + sinusitis)
4. Recurrent pyodermatitis, deep skin or organ abscesses
5. A single episode of meningitis or osteomyelitis
6. Two or more mo on antibiotics with little or no effect
7. Failure to gain weight or grow normally
8. History of primary immunodeficiency in the family.

The most common clinical indication of immunodeficiency is **recurrent infections** with frequent treatment failures. In many cases, the horse does well while on antibiotic therapy. However, when antibiotic therapy is discontinued or bacterial resistance to antibiotic develops, the clinical signs of infection reappear. In addition, autoimmunity and neoplasia may be associated with an immunodeficient state.

CLASSIFICATION OF IMMUNODEFICIENCIES

Primary immunodeficiencies are congenital processes associated with a genetic hereditary defect. Therefore, the manifestation of these disorders is more frequently observed in young than in adult horses but it does not exclude the latter. Inheritance patterns should be evaluated when investigating an immunodeficiency. Importantly, many disorders have X-linked inheritance and manifest in male horses. Single recessive genes may result in autosomal recessive inheritance. Other disorders may not have a clear pattern of inheritance but may be found in several individuals in a family.

Secondary immunodeficiencies may occur at any time in life. These are acquired disruptions in immune function that, similar to primary immunodeficiencies, reduce the ability of the system to fight against opportunistic and/or pathogenic organisms. Conditions that may predispose to secondary immunodeficiencies include immunosuppressive treatment, infectious diseases, infiltrative diseases, metabolic/endocrine diseases, age and malnutrition.

Immunodeficiencies are grouped according to the components of the immune system affected (Box 2.2).

Box 2.2 Groups of immunodeficiencies

1. Antibody immunodeficiency disorders (B cell deficiency)
2. Cytotoxic and helper cell deficiencies (T cell deficiency)
3. Combined B and T cell deficiencies
4. Phagocytic deficiency
5. Complement deficiency

HUMORAL IMMUNODEFICIENCIES

Antibody deficiency is the most commonly diagnosed immunodeficiency in mammals. It is characterized by full or partial **failure of B cell development** and differentiation into plasma cells to produce different immunoglobulin isotypes. As a consequence, all or only selected isotypes of immunoglobulins are decreased or absent. **Recurrent, severe infections** caused by **opportunistic or encapsulated microorganisms** are the clinical manifestations in humoral immunodeficiencies.

Clinical signs include pneumonia, meningitis, osteomyelitis, sinusitis, lymphadenopathy, hepato- or splenomegaly, dermatitis, oral candidiasis and failure to grow. Some of the diseases associated with humoral disorders described in the horse include transient hypogammaglobulinemia of the young, X-linked agammaglobulinemia, common variable immunodeficiency, Fell Pony immunodeficiency syndrome (*q.v.*) and selective IgM deficiency.

Horses with humoral deficiencies may be temporarily managed with **plasma transfusions** (*q.v.*) when serum IgG is <500 mg/dL. Some horses may be managed with continuous **antibiotic therapy** alone. The addition of antifungal drugs (fluconazole 4 mg/kg BW s.i.d. PO) may be necessary in the presence of candidiasis (*q.v.*). These horses should be routinely evaluated for the development of infection, more commonly in the respiratory tract. In addition, vaccination of these horses with modified-live or live vaccines is **contraindicated**.

Agammaglobulinemia

A lack of mature B cells and plasma cells, but normal T cell counts and function has been reported in **young male horses** of different breeds. Horses with this syndrome develop bacterial infections of respiratory, gastrointestinal and tegument systems that are temporarily responsive to antibiotic and plasma therapies.

Agammaglobulinemia in male horses presents many features of the X-linked agammaglobulinemia (XLA) described in male human patients and xid-mutant mice. These patients carry a mutation of the *btk* gene on the X chromosome that encodes the Bruton tyrosine kinase. The absence of this protein affects sustained signaling in response to B cell receptor engagement, leading to defects in B cell differentiation and proliferation. Typically, XLA patients present with **recurrent bacterial respiratory infections**, absence of B cells and plasma cells, and hypo- or agammaglobulinemia early in life. Female carriers are healthy, although they may display non-random X chromosome inactivation in their B cells.

Transient hypogammaglobulinemia

Transient hypogammaglobulinemia has been described in foals with delayed production of endogenous antibodies. These foals present **recurrent bacterial and viral infection** when circulating maternally derived antibody levels decrease at around 2 mo of age. Peripheral blood B and T lymphocyte counts and distribution are normal. The T cell response to phytohemagglutinin is

normal in vivo and in vitro. Serum IgG and IgG(T) concentrations are low, and IgM and IgA levels may be normal or decreased. A weak response to immunization may be detected in these horses. Appropriate antibiotic therapy and plasma transfusion often protect foals during the period of abnormal immunoglobulin production.

Selective IgM deficiency

Selective IgM deficiency is a presentation of immunoglobulin abnormality reported in horses of both genders and different breeds. It may occur as a **primary** (young) or a **secondary** (adult) immune disorder, and in both cases this condition may be permanent or transient. In these horses, serum IgM concentrations are more than two standard deviations below the mean normal value of age-matched controls (<60 mg/dL). Serum concentrations for IgG, IgG(T) and IgA are normal, as are peripheral blood lymphocyte counts and responses to mitogens. A genetic basis has not been described, and transient conditions may be secondary to lymphosarcoma, immunosuppressive therapy or stress.

Common variable immunodeficiency

Common variable immunodeficiency (CVID) is a symptomatic antibody deficiency syndrome marked by **recurrent bacterial infection** and **impaired humoral response to vaccination** in **adult horses**. In the horse, this condition has been characterized by chronic respiratory disease, hypo- or agammaglobulinemia, progressive septicemia, and absence of B cells in the bone marrow, lymph node and spleen. The T cell percentage and distribution can be normal to slightly increased, and the T cell response to mitogens may be normal or decreased. Immunohistochemical analysis of tissue sections may support peripheral blood findings with absence or marked paucity of B cells in bone marrow, spleen and lymph nodes. Both sexes and different breeds (Quarter Horse, Thoroughbred, Arab) are affected, and clinical signs are often observed in the second decade of life.

Classification of CVID has been complex due its variable immunologic and clinical phenotypes. The initial diagnosis is usually made by exclusion of other primary causes of immunodeficiency. A method for classification of this heterogeneous disorder on the basis of in vitro immunologic responses of purified B cells to Sepharose-bound antibodies against surface IgM and interleukin-2 has been developed for human patients.

Different groups of disease can be identified based on the presence or absence of B cells, and B cell responses. In CVID, B cells are usually present in low numbers in the system, and a defect in antibody production may be associated with intrinsic abnormalities in differentiation into plasma cells and isotype switching, or impaired T cell co-stimulation of B cells. Other **unclassified immunodeficiencies** involving B cell lymphopenia or hyporesponsiveness have been reported in horses. In one case, a 10-month-old Arabian filly presenting with recurrent gastrointestinal disease and synovitis was diagnosed with non-detectable serum concentrations of IgM, IgA and IgG(T), but normal concentrations of IgG, decreased response of B cells to lipopolysaccharide stimulation, and normal T cell response to concanavalin A. Another case

involved a 3-month-old Thoroughbred colt with recurrent respiratory disease, normal T and B cell peripheral blood counts, decreased B cell response to lipopolysaccharide, and IgM deficiency. In addition, a 3-year-old Quarter Horse colt with chronic diarrhea has been reported to have hypogammaglobulinemia for IgG, IgA and IgM, B cell lymphopenia, and T cell hyporesponsiveness to mitogen stimulation.

Fell Pony Syndrome

An immunodeficiency condition has been described in Fell Pony foals <3 mo of age. Both genders are affected and clinical signs include **severe anemia**, diarrhea, pneumonia, neutrophilia, lymphopenia and death. In addition, repeated chewing and failure to suckle may result from an ulcerative, pseudomembranous coating of the tongue. This syndrome may be caused by an autosomal recessive gene anomaly, of which two thirds of the population is estimated to be carriers.

Immunologic testing using flow cytometric leukocyte phenotyping reveals a **B cell lymphopenia** and decreased cell surface expression of major histocompatibility complex class II on lymphocytes. The CD4+ and CD8+ T cell distribution in peripheral blood is normal, and these cells are responsive to mitogens phytohemagglutinin and concanavalin A, although the response to pokeweed mitogen may be decreased. Serum immunoglobulin levels are similar to those of healthy foals, yet Igm levels may be decreased. Nevertheless, serum immunoglobulin may reflect maternally derived antibodies at this age. Phagocytosis and oxidative burst activity are intact, and opsonization capacity is proportional to the levels of maternally derived immunoglobulins.

On histopathology, the thymus presents atrophy with no demarcation between cortex and medulla. There is a general **paucity of lymphocytes** and absence of germinal centers in the lymph nodes, spleen and gut-associated lymphoid tissues. In contrast, numerous macrophages and neutrophils are present in the primary and secondary lymphoid tissues. The intestine does not contain plasma cells and may be infected with *Cryptosporidium* spp. (*q.v.*) and/or adenovirus (*q.v.*) organisms. The bone marrow reveals severe red cell hypoplasia and abundant hemosiderophages, megakaryocytes and myeloid precursors. In addition, **peripheral ganglionopathy** is also present in these foals, characterized by neuronal chromatolysis with nuclear pyknosis in the trigeminal, cranial mesenteric and dorsal root ganglia.

SEVERE COMBINED IMMUNODEFICIENCIES

Severe combined immunodeficiency (SCID) is a condition in which both the acquired B (humoral) and T (cellular) cell functions are deficient.

This immunodeficiency occurs in **Arabian horses** that lack activity of the **enzyme DNA-dependent protein kinase** (DNA-PK) that is required for gene rearrangement of the antigen receptor on the B and T lymphocyte cell surface. The DNA-PK enzyme defect results from a deletion mutation of the gene encoding the catalytic subunit. The mode of inheritance of the genetic defect is as an **autosomal recessive trait**. Although foals appear normal at birth, this

condition is fatal unless the immune system can be reconstituted by transplants of immunocompetent tissue. Affected foals are susceptible to bacterial, fungal, viral and protozoal organisms by the time maternally derived antibodies wane.

Clinical signs primarily involve the respiratory and gastrointestinal systems, and infections with adenovirus, *Pneumocystis carinii*, *Rhodococcus equi* and/or *Cryptosporidium parvum* are common. The relevant findings that contribute to the diagnosis of SCID include **lymphopenia** (<1000 cells/μL), **marked serum IgM deficiency**, and **hypoplasia of secondary lymphoid tissues**. Ante mortem diagnosis can be determined by the characterization of the defective gene by a polymerase chain reaction (PCR) test (VetGen, Ann Arbor, MI, USA), which is very useful in identifying normal and heterozygous horses for the DNA-PK (catalytic subunit) gene. This valuable information should be acquired **before** making breeding decisions.

CELLULAR IMMUNODEFICIENCIES

In the horse, cellular immunodeficiency is difficult to diagnose unless the number and subpopulation distribution of T cells in the peripheral blood is abnormal. T cell disorders may affect directly the cytotoxic function, or indirectly the B cell function due to the lack of T helper cell signals. Autoimmune or tumoral diseases may be accompanied by T cell immunodeficiencies. Cellular immune disorders may be associated with **intracellular pathogens** (viruses, fungi, protozoa and mycobacteria). Recurrent pyogenic infections are common, and clinical signs are similar to those of humoral immunodeficiencies (*q.v.*). In the horse, a transient CD4+ and CD8+ T cell deficiency has been described in a 3-month-old Paint filly with ***P. carinii*** **pneumonia**.

Other cellular immunodeficiencies that are not recognized in the horse but are described in human patients include defects in the expression or function of cell surface activation molecules and their cell signaling components. As is the case in humorally immunodeficient horses, modified-live or live vaccines should not be used.

PHAGOCYTIC IMMUNODEFICIENCIES

Inherited forms of neutrophil dysfunction have not been described in the horse but should be suspected in cases of **recurrent infection** with *Staphylococcus*, *Pseudomonas*, *Serratia*, *Klebsiella* and fungi (*Aspergillus, Candida*). Affected patients often present with dermatitis, cutaneous abscesses, cellulitis, periodontal diseases and/or organomegaly. Some of the diseases associated with phagocytic disorders described in other species include leukocyte adhesion deficiency, cyclic neutrophil hematopoiesis, Chediak–Higashi syndrome, Pelger–Huët anomaly and chronic granulomatous disease.

COMPLEMENT COMPONENT IMMUNODEFICIENCIES

Primary diseases of the complement components are rare and have not been described in the horse. Deficiencies of complement components have been

described in human patients and other domestic species. Some of the diseases associated with complement component disorders include:

1. Deficiencies of early components of complement C1q, C1r, C1s, C4 and C2 (systemic lupus erythematosus-like signs, glomerulonephritis)
2. Deficiencies of late components of complement C5, C6, C7, C8 and C9 (recurrent disseminated *Neisseria* spp. infections)
3. Deficiencies of C3 component, factors D, I and H (pyogenic infections)
4. Deficiencies of C1 inhibitor (hereditary angioedema or lymphoproliferative disorders)
5. Properdin deficiency (meningococcemia).

DIAGNOSIS OF IMMUNODEFICIENCIES

A full **history** may assist in building a list of potential etiologies:

1. **Young animals** may present inadequate serum immunoglobulin levels due to failure of transfer of maternal immunoglobulins, or inadequate production of immunoglobulins (SCID, Fell Pony syndrome) (*q.v.*), whereas common variable immunodeficiency may affect adult horses in the second decade of life.
2. The **gender** of the horse may indicate hereditary traits: consider X-linked agammaglobulinemia in young males (*q.v.*).
3. Certain **intracellular or opportunistic pathogens** have been associated with disorders in immunodeficient horses: *Pneumocystis carinii* (T cell deficiency), *Candida albicans* (SCID, neutrophil deficiency), *Serratia* spp. (neutrophil deficiency) (*q.v.*).
4. **Immunization history** may suggest cellular immunodeficiency (infection after modified-live or live virus vaccine).
5. **Family history** may indicate an immunodeficiency condition (high incidence of young animal death in one family or autoimmunity).

On **physical examination**, poor growth due to chronic infection is a condition often associated with immunodeficiency. Other findings that may suggest impairment of the immune system include paucity of lymphoid tissues (SCID, Fell Pony syndrome), hepato- or splenomegaly (common variable immunodeficiency), chronic dermatitis and periodontitis (neutrophil dysfunction) (*q.v.*).

Laboratory assays and in vivo diagnostic experiments are useful in confirming and characterizing immunodeficiency conditions. For all tests, the use of **age-matched controls** is advised.

1. **Complete blood cell count** may indicate abnormal production, destruction or dysfunction of a distinct cell population: neutropenia, neutrophilia, lymphopenia, lymphocytosis, anemia and thrombocytopenia.
2. **Peripheral blood and bone marrow cytology** may suggest the presence of abnormal cells (lymphoblasts, large granular neutrophils) and hypoplastic cell deficiencies (myeloid–erythroid ratio, cell morphology and maturation).
3. **Humoral function** may be assessed by serum immunoglobulin isotype levels (radial immunodiffusion, ELISA), in vivo antibody response tests

(immunization with tetanus toxoid), and number of circulating B cells (lymphocyte phenotyping using flow cytometry).

4. **Cellular function** may be evaluated by the distribution of CD4+ and CD8+ T cells (lymphocyte phenotyping using flow cytometry), antigen skin tests (phytohemagglutinin, tetanus toxoid), in vitro response to mitogens (lymphocyte proliferation assays) and cytotoxic function (chromium release assays).
5. **Phagocytic function** and recruitment may be tested by flow cytometric assays for phagocytosis and oxidative burst activity, the expression of cell surface CD18 molecule, and chemotaxis assays.
6. **Complement component levels and function** may be measured by complement component radial immunodiffusion tests, hemolytic complement assays and flow cytometric opsonization assays.
7. **A genetic test** to identify the SCID carrier state or affected state is commercially available (VetGen, Ann Arbor, MI, USA).

IMMUNOMODULATORS

An immunomodulator or biologic response modifier is a substance that enhances or suppresses immune responses. **Immunostimulants** promote a non-specific activation of the immune system and may amplify different areas of immune defense: phagocytosis and intracellular killing of organisms, antigen presentation, cytotoxic and antiviral activity, cytokine release and antibody production. Once the immunotherapeutic agent is processed by antigen-presenting cells, **endogenous cytokines** become the mediators of the immune response that will resist infections or neoplastic conditions.

Common **side effects** following immunotherapy include reaction at the injection site, fever, lethargy and decreased appetite, probably related to induced endogenous cytokine release. For this reason, it is essential that immunostimulants mediate short-term responses; stimulation of the immune response without harmful inflammation and tissue damage is imperative. The **selection** and use of immunomodulators is still challenged by insufficient information on mechanisms of action in vitro and in vivo, deleterious and unknown side effects, lack of response by some individuals, and extra-label use with over-expectations of efficacy.

PROPIONIBACTERIUM ACNES

Inactivated *Propionibacterium acnes* (Eqstim, Immunovet, Neogen Co., Lansing, MI) has been indicated as prophylactic therapy to **reduce the incidence of transport stress-induced respiratory disease** and as an adjunctive therapy in the treatment of primary and secondary viral and bacterial infections of the respiratory tract of the horse. The recommended dose is 1 mL per 114 kg BW IV, 2–3 doses q 48 or 72 h, 1–2 days **before stress is induced** or as an adjunct to conventional therapy. *P. acnes* is known to induce macrophage activation, to enhance natural killer cell activity and CD8+ T lymphocyte cytotoxic activity, to inhibit tumor growth and to induce non-specific resistance to pathogenic challenge in mice, human patients and domestic animals.

In the horse, a series of three doses 24 h apart, IV, increased the CD4+ T lymphocyte population, non-opsonized phagocytosis and lymphocyte-activated killer (LAK) cell activity in peripheral blood and bronchoalveolar lavage fluid. In the latter, total leukocyte counts decreased and the proportion of macrophages increased.

MYCOBACTERIUM CELL WALL EXTRACT

Mycobacterium extracts are one of the most potent stimulants of macrophage function, resulting in subsequent release of inflammatory cytokines and lymphocyte activation. Equimmune I.V. (Vetrepharm Research Inc., Athens, GA) is an oil-in-water emulsion of purified *Mycobacterium* spp. cell wall extract for the treatment of equine respiratory disease complex (ERDC) (*q.v.*) resulting from viruses and/or bacteria.

In a clinical trial, horses receiving one IV dose of purified *Mycobacterium* spp. cell wall extract recovered from respiratory clinical signs in a shorter period of time compared with the placebo group. The recommended dose is 1.5 mL per animal, IV. It has been approved for use in pregnant mares. Hypersensitivity reactions characterized by formation of multifocal granulomas have been reported with the use of *Mycobacterium* spp. cell wall extract in horses and attenuated bacillus Calmette–Guérin (BCG) in humans.

PARAPOXVIRUS OVIS

Baypamun HK (Bayer AG, Leverkusen, Germany) is the commercially available form of purified and chemically inactivated parapoxvirus ovis strain D 1701 for use in horses and other domestic species. It is indicated for the prophylaxis of **stress-induced respiratory diseases** caused by **transportation, hospitalization and weaning**, for the metaphylaxis and therapy of infectious diseases, and to enhance immunization response. The general recommended dose is 2 mL per animal, IM, 2 or 3 doses 48 h apart, 1–2 days **before the stress** (weaning, transportation and commingling) is induced, immediately after birth or with conventional treatment for respiratory disease. Some limited swelling at the injection site may occur.

The mechanism of action of parapoxviruses in the immune system has been studied in humans and animal models for its activation of natural killer cells, phagocytic activity and release of interferon-α and interleukin-2 (IL-2). To this date, there are very limited in vitro data describing the effects of this immunomodulator in horse cells.

CAPRINE SERUM FRACTION

Caprine Serum Fraction Immunomodulator (Centaur Inc., Overland Park, KS) is a sterile, filtered, purified and standardized fraction goat serum preserved in phenol and thiomersal. The label recommendation is 2 mL IM injections, two applications, 7–10 days apart. Potential side effects are swelling and heat at the site of injection for 48–72 h. This immunomodulator is indicated for adjunctive treatment of **lower respiratory tract disease** in horses. In a clinical trial involving

horses with unspecified lower respiratory tract disease, administration of two IM injections of the Caprine Serum Fraction Immunomodulator promoted a reduction of monocyte and CD8+ T lymphocyte counts in peripheral blood, and total cell counts in bronchoalveolar lavage (BAL) fluid.

INTERFERON (IFN)-α

Type I interferons are produced by the innate immune system in response to the presence of viral organisms. Their antiviral effect is characterized by inhibition of viral protein synthesis, activation of cytolytic activity, increase in MHC class I expression of virus-infected cells, enhanced IFN-γ expression by lymphocytes, macrophage activation and dendritic cell maturation. Oral administration of low doses of IFN-α acts directly on oropharyngeal-associated lymphoid tissues, and has therapeutic benefit in horses with **inflammatory airway disease** and **active training**. In a clinical trial, natural, human IFN-α (50 U PO for 5 consecutive days) reduced airway inflammation, pharyngeal lymphoid hyperplasia, nasal discharge and cough compared with horses receiving placebo. Horses that received oral IFN-α recovered their BAL fluid to a non-inflammatory cytologic profile.

The use of commercially available recombinant IFN-α-2a (Roche Laboratories Inc., Nutley, NJ), which contains only one subtype of IFN-α in contrast to the natural form, failed to reduce virus shedding and respiratory disease in experimental herpesvirus 1 infection in horses. It is not known whether the less protective effect of the immunotherapy regimen used was due to inappropriate dosage or differences in the response to the recombinant form. High doses of IFN-α are more likely to cause side effects due to induced self-destructive inflammatory responses and immunosuppression.

LEVAMISOLE PHOSPHATE

Levamisole phosphate is a synthetic anthelmintic with immunomodulatory properties poorly characterized in vitro and in vivo. However, cell-mediated response and phagocytic activity may improve in immunocompromised individuals after immunotherapy. Extra-label use of levamisole, 2 mg/kg BW q 48 h, PO, in horses as an adjunct for the treatment of **respiratory disease** is based on clinical reports of prevention and treatment of chronic respiratory infections in children and neonate animals.

LEUKOPROLIFERATIVE DISEASES

LYMPHOMAS AND LYMPHOSARCOMAS

Lymphomas and lymphosarcomas are the most common malignant neoplasms of the horse. **Primary** (thymus and bone marrow) or **secondary lymphoid tissues** (lymph node, spleen, gut- associated lymphoid tissue and bronchus-associated lymphoid tissue) may be the origin of the tumoral cells. In contrast to other species, no viral etiology has been associated with the development of lymphoma (*q.v.*) or lymphosarcoma (*q.v.*) in horses. One clone

of lymphocytes may become **malignant**, and the type of cells belonging to this clone (B, T, plasma cells) characterizes the type of tumor and effects in the immune system. Horses of a **young age** may develop the disease, both sexes and all breeds may be affected, and clinical signs vary according to the system affected and stage of disease.

Classification of lymphomas and lymphosarcomas in the horse still relates to their anatomic distribution: generalized, intestinal, mediastinal or cutaneous. More importantly, the classification of **malignant lymphomas** should expand from the knowledge of architectural and cytologic characteristics of neoplastic elements to the investigation of multiple parameters, including morphology, immunophenotype, molecular genetics and clinical features. Therefore, as laboratory reagents for lymphoid lineage and cellular differentiation become available for the equine species, immune profiles for the primary diagnosis, classification, staging and immunotherapy of lymphoid neoplasms may develop. In addition, identification of oncogene and tumor suppressor gene products may aid in the understanding of pathogenic mechanisms of lymphomagenesis. Altogether, this information should improve efficiency in the application of novel treatment options based on the targeting of critical mechanisms of cell proliferation and activation.

Generalized or multicentric lymphomas constitute the most common form. It may be characterized by tumor growth in **several tissues**, including the secondary lymphoid tissues, or by the **systemic infiltration** of tumoral cells. Although neoplastic cells originating from metastasizing tumors can be identified in the blood, development of leukemia is rare. **Peripheral lymphadenopathy** is a common but not exclusive finding because abdominal or thoracic lymph nodes may be affected. In addition to lymphoid organs, tumors and infiltration of tumoral cells have been reported in the eye, lung, nasopharynx, liver, kidney, urinary bladder, liver, heart, brain, spinal cord, ovary and uterus. General clinical signs may include depression, emaciation, fever, anemia, hypoproteinemia, and edema due to impaired lymphatic drainage.

The **intestinal or alimentary** form involves the gastrointestinal tract, more frequently the **small intestine**. Metastases to the mesenteric lymph nodes, liver and spleen have been reported. This type of tumor is more common in horses <5 yr. Therefore, malabsorption of nutrients, weight loss, diarrhea, colic, protein-losing enteropathy, hypoalbuminemia and dependent edema may be the clinical signs suggestive of intestinal lymphoma. In advanced cases, necrotic tumoral masses may develop.

The **mediastinal** form of lymphoma is a primary neoplasm of the **thymus**. This type of tumor is more common in adult horses and often metastasizes to other systems. Clinical signs are consequent to the space-occupying lesion and compression of vessels and lymphatics and can include pleural effusion, edema of the ventral thorax and forelimbs, distended jugular veins, muffled heart sounds, tachycardia, tachypnea, dyspnea, cough, inappetence and weight loss. In addition, dysphagia can be induced by lymphadenopathy in the thoracic and retropharyngeal areas.

The **cutaneous** form of lymphoma may involve the dermis and/or subdermis of young adult horses. The **cutaneous sarcomatous** lesions are multiple, firm and not painful, from 1 to 20 cm in diameter, with a tendency to be distributed in the ventral aspect of the neck, chest, abdomen and perineum.

The lesions may develop slowly or rapidly, remain static or even regress in size. Most of the lesions do not show hair loss, although very large lesions may loose the hair and skin integrity due to trauma or necrosis. This type of tumor is usually of B cell origin, lymphadenopathy is present in half of the cases and metastasis to other systems is rare.

Mycosis fungoides is another form of **cutaneous lymphoma** in which there is **diffuse infiltration** of tumoral T helper lymphocytes in the dermis and subdermis. A variant of this type of tumor includes cutaneous and leukemic Sézary cells, which are malignant cells with a cerebriform appearance. Phenotypic and structural heterogeneity of cutaneous lymphomas is possible. In the horse, there is one report of B cell cutaneous lymphoma with Sézary cells and monoclonal gammopathy.

LEUKEMIAS

Leukemias are rare conditions in the horse and may be of **lymphoid** or **myeloid** (granulocytic, myelomonocytic, monocytic and eosinophilic) cell origin. In horses, myeloid leukemias are rare and the lymphoid leukemias characterized in the literature include the phenotypes B cell/IgM positive, B cell/IgM negative, CD5 positive T cell positive, and CD3 negative/CD4 positive T cell.

In **primary leukemia**, a neoplastic hematopoietic cell line develops in the bone marrow and leukemic cells may invade vascularized organs without forming masses. In **secondary leukemia**, tumoral cells metastasize to the bone marrow. When the bone marrow is diffusely infiltrated by neoplastic cells, the production of the non-tumoral cells may become compromised (myelophthisis).

In addition, leukemias can be classified into **leukemic, subleukemic** and **aleukemic** according to the presence and number of circulating tumoral cells. In plasma cell myeloma, there is a malignant proliferation and monoclonal expansion of a single plasma cell lineage in the bone marrow. When diffuse, the cell proliferation promotes bone marrow destruction, osteolysis, myelophthisis and lameness. The monoclonal gammopathy can be diagnosed by serum and/or urine protein electrophoresis, and it is often of IgG isotype. Secondary infections due to lack of diversity in immunoglobulin isotype production may occur.

DIAGNOSIS OF LEUKOPROLIFERATIVE DISEASES

The diagnosis of lymphomas and leukemias is based on the history, physical examination, and characterization of the tumoral cells. **A complete blood cell count** may indicate anemia due to chronic inflammation, myelophthisis, immune-mediated hemolytic processes (Coombs test positive) or, rarely, blood loss (secondary to immune-mediated or myelophthisic thrombocytopenia and tissue damage). Eosinophilia or diffuse eosinophilic infiltration of tissues is rarely seen as a response to paraneoplastic cytokine interleukin-5 (IL-5) and granulocyte–monocyte colony-stimulating factor (GM-CSF) production by certain lymphoma cells. **Hypoalbuminemia** is observed in infiltrative tumors of the gastrointestinal tract that cause malabsorption and/or protein-losing enteropathy.

Diagnosis of **malabsorption** may be made by testing the absorption of D-glucose or D-xylose. The horse should be fasted for 18 h. A 10% solution of D-glucose (1 g/kg BW) or D-xylose (0.5 g/kg BW) is administered via nasogastric tube. Heparinized blood samples are collected before and at 30 min intervals up to 3 h after administration. Plasma glucose or xylose values peak approximately 60–90 min after administration in normal horses. **Hyperglobulinemia** caused by high levels of alpha and beta globulins is associated with inflammation (along with neutrophilia, hyperfibrinogenemia and fever) whereas the presence of monoclonal gamma globulin may indicate plasma myeloma or B cell leukemias.

Blood chemistry may be useful to identify inflammation in organs that may harbor tumoral cells or masses. **Hypercalcemia** is not a consistent finding in lymphomas, yet it can be secondary to the production of parathyroid hormone-like protein by some neoplasms. Tumoral masses and/or infiltrative tumoral cells may not be readily recognized and require thorough testing (radiographs, ultrasound and exploratory surgery). **Cytology** of blood smears, bone marrow, pleural fluid and peritoneal fluid, or histologic examination of biopsies of enlarged lymph nodes or skin may reveal neoplastic cells.

Immunologic testing

To date, **immunologic testing** has been used only occasionally in horses with lymphoma and lymphocytic leukemias due to the limited number of laboratories performing these types of tests. Clinically, patients with cancer should be monitored for **immunodeficiency** because of the direct effect of tumoral cells on the immune system (inhibition of lymphocyte activation/function or antibody production) or because of the effect of immunosuppressive therapy. **Protein electrophoresis** and **serum immunoglobulin quantification** by radial immunodiffusion may characterize hypogammaglobulinemias or monoclonal gammopathies (IgG, IgA or IgM). Suppression of T lymphocyte function by tumors may be evaluated by **lymphocyte proliferation** response to mitogens in vitro.

Phenotyping of the tumoral cells may be accomplished by flow cytometry using a panel of monoclonal antibodies that characterize cell lineages (CD4+ T cell, CD8+ T cell, B cell and other cell surface molecules) in fluid or tissue aspirates.

Additional information about the tumoral cells can be obtained by flow cytometric analysis of **DNA content** to evaluate their ploidy status, and polymerase chain reaction (PCR) to identify clonal expansion of T or B cells by detecting single T cell (TCR) or B cell (BCR) receptor patterns.

Immunohistochemistry and **immunocytochemistry** may also be used for the phenotyping and distribution of tumoral cells in tissues (**biopsy or necropsy** samples) and cell suspensions (tissue or fluid aspirates). Most antibodies available for this type of assay do not work in fixed or paraffin-embedded tissues, therefore it is important to save snap-frozen tissues without preservatives (placed on dry ice or in liquid nitrogen vapor for freezing and maintained at −20ºC) and unfixed cytologic smears (dry impress smears preserved at room temperature).

These tests add to the histopathologic and morphologic information about the type of cell involved in the neoplasm. The classification of **myeloid**

leukemias may be difficult, especially if neoplastic cells are poorly differentiated. Therefore, cytochemistry using stains for chemical moieties and cellular products, along with cell morphology and cell counts, forms the basis for the **French–American–British (FAB) classification** of non-lymphoid leukemias. Due to variability in the cell phenotype and activation status of tumoral lymphocytes, this type of information may become fundamental in the development of treatment strategies based on the characteristics of the tumoral cells rather than their anatomic distribution.

TREATMENT OF LEUKOPROLIFERATIVE DISEASES

The treatment of lymphomas and lymphocytic leukemias in horses is often **unrewarding**. Some of the reasons for the failure of treatment are the advanced stage of tumoral development by the time it is perceived clinically, the lack of understanding of the phenotype and activation status of the tumoral cells, and the lack of clinical treatment trials that would support the use of a certain treatment regimen. In addition to supportive therapy, **immunosuppressive therapy** may be attempted with **corticosteroids** (dexamethasone 0.2 mg/kg BW s.i.d. IV or PO for 5 days), followed by maintenance with prednisolone (1–2 mg/kg BW s.i.d. PO).

In some cases, the combination of **chemotherapeutic agents** has been suggested with cytosine arabinoside (200–300 mg/m^2 q 1–2 wk SC or IM) plus chlorambucil (20 mg/m^2 q 2 wk PO) or cyclophosphamide (200 mg/m^2 q 2–3 wk IV) plus prednisolone (1–2 mg/kg BW s.i.d. PO). Remission of the tumor may be observed in 2–4 wk, and the protocol should be used for 2–3 mo, when the treatment interval is increased by a week in each cycle of therapy, to a total of 6–8 mo. Other treatment options include L-asparaginase (10 000–40 000 IU/m^2 q 2–3 wk) in combination or not with cyclophosphamide and/or prednisolone. In cases of **multiple myeloma**, melphalan (7 mg/m^2 s.i.d. PO for 5 days, then every 3 wk) has been used.

Chapter 3

Equine nutrition and metabolic diseases

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Chapter contents

INTRODUCTION

Nutrition can be defined as the process of feeding and the subsequent digestion and assimilation of food. It is, therefore, of fundamental importance to the well-being of any animal. However, good nutrition will only help a horse to be able to perform optimally; it cannot improve the intrinsic ability of the animal (nor the horse and rider combination). Poor nutrition, on the other hand, may impose limits on an animal's ability to perform. In most instances it is only when an adult horse is asked to exert itself that the result of imbalanced or inadequate nutrition becomes apparent.

Many of the nutrients we now take for granted were only recognized a relatively short time ago. Although in the early nineteenth century it was appreciated that calcium and phosphorus were needed for "hard bone", vitamin B_{12}, for example, was not seen as an essential nutrient until the 1940s and selenium not until the 1950s. The original research into the feeding of horses came mainly from army veterinarians and others involved with cavalry, working and pack horses. Mechanization and the replacement of the horse as a means of transport and a power source resulted in a decrease in equine research. The first **National Research Council (NRC)** report on equine nutrition was published in 1949. The second, in 1961, stated that little new information had been obtained since 1949 and contained many estimates based on extrapolations from ruminants. The next in 1966 was similar. The last one, carried out in 1989, is well overdue for revision. Since then increasing numbers of equine nutrition studies have been carried out, as the popularity of the horse for recreational purposes has increased.

However, many of the equine nutritional practices currently employed have not changed significantly from those followed hundreds of years ago,

although the nature and composition of the basic feedstuffs has changed in some instances. The most significant change in the twentieth century was probably the introduction of **pelleted feeds** around 1920. These became popular in the 1960s when competition, increased knowledge, more ethical companies and government regulations resulted in the evolution of good quality, commercial, compound feeds.

Unfortunately, in many areas of equine nutrition **good scientific information** is still not available. Confusion and controversy often exist, especially where one research paper's findings directly contradict those of another. There are many reasons for this confusion. Much of the research has been carried out in ponies and then applied to the horse but such extrapolations may not always be applicable. In other instances, the data available have been extrapolated from another species such as a ruminant. Largely for financial reasons, most of the nutritional research in horses has been carried out on relatively few animals and has concentrated on the effects of short-term alterations in intake.

The **adaptive changes** that occur over longer periods are therefore not well understood. Differing experimental protocols, basal diets, and exercise regimens may all contribute to the conflicting results. In addition, the normal daily nutrient requirements vary according to several factors, depending on the nutrient involved, and include age, body weight, exercise and environmental conditions. The availability of a particular nutrient may vary not only with the nutrient, its nature in that feedstuff (e.g. of organic or inorganic source) and the presence of other nutrients, but also with the individual animal's **absorptive ability**. Nutrition cannot be considered to be an exact science. Considerably more information on the dietary requirements and digestive physiology of domestic ruminants is available than for the horse, however, and more basic and applied scientific research is needed into most aspects of equine nutrition.

Optimal feeding of horses uses both **art and science**. The science provides the information about the digestive and metabolic processes, the nutrient requirements and the principles behind feeding practices. The art is the ability to convert this theory into practice for the individual horse, its needs, likes and dislikes. In this chapter, a general and, it is hoped, practical guide to equine nutrition is given. Wherever possible, recommendations are based on sound research but interpreted practically. It aims to provide a guideline to follow and to highlight some of the reasons behind the basic rules of feeding. Although, wherever possible, discrepancies between various authors' recommendations have been removed, some remain because in a number of instances "correct" values are simply not known and the best that exists at the present time is a range of acceptable levels.

GUIDE TO TYPICAL FEEDSTUFFS

Domestication and our increasing demand for horses to perform repeatedly have resulted in energy requirements that, for some horses, are above those able to be provided by their more "natural" diet of fresh forage. Cereals provide more net energy than hay, which in turn provides more than twice the

net or usable energy of straw. However, the upper part of the gastrointestinal tract (GIT) has a relatively **small capacity** and the horse has **digestive and metabolic limitations** to high grain, starch and sugar based diets. Large grain meals may overwhelm the digestive capacity of the stomach and small intestine leading to **the rapid fermentation** of the grain carbohydrate in the hindgut. This potentially can result in one of a number of disorders including colic, diarrhea and laminitis.

Therefore, there has been increasing interest in the use of **alternative energy sources** for horses, especially alternative fiber sources, which do not cause such marked disturbances in the hindgut and yet provide more energy than typical forages. In addition, because vegetable oils provide proportionally more net energy than the cereals, yet contain no starch or sugar and may provide other advantages, there is an increasing use of supplementary **vegetable oils**.

Table 3.1 provides figures for the typical composition of some common feedstuffs. Individual samples may vary within a range and, for complete accuracy when evaluating a dietary regimen, **individual analyses** must be undertaken. Pasture and hay analyses vary according to season, soil type, geographic location and other variables such as harvest date. For accuracy, a number of actual representative forage (fresh or preserved) samples must be analyzed when reliable results are required.

The importance of calculating the actual **elemental levels** of the required mineral from the selected source cannot be overemphasized. The **bio-availability** of certain minerals will be affected by many factors such as the levels of any antagonistic minerals present. In addition, there will also be variation in utilization between individual horses.

When assessing the nutrient value of particular feedstuffs, it must be remembered that modern methods of feed production have had two major effects on the composition and feed value of equine rations. First, they have allowed a **wider range of ingredients** to be used as modern production methods destroy many of the harmful substances that might prevent the feedstuff being used in its raw state. Second, they have affected the **nutrient availability and digestibility** of certain traditional and recently introduced feedstuffs. Moreover, there are several methods of preparation or treatment of feedstuffs that have differing effects on palatability, digestibility and stability in storage.

CEREALS, SUGAR BEET AND OIL SEEDS AS FEEDSTUFFS

Major cereals fed to horses

Oats are the traditional cereal fed to horses in work. They contain significantly higher fiber and lower starch levels than most other cereals and the nature of their starch particles helps to promote a high pre-cecal starch digestibility in contrast, for example, to corn and barley. As with all cereals and cereal by-products, oats provide a low level of calcium and a moderate level of phosphorus (which may be bound in phytate compounds, reducing its availability), giving a reversed **calcium to phosphorus ratio** (*q.v.*). Also, in common with most cereals, the level of the essential amino acid lysine is

Table 3.1 Guide to the typical composition of common feedstuffs (assuming 880 g DM/kg), in part derived from the NRC[1]

	Crude protein (g/kg)	Crude fiber (g/kg)	Ca (g/kg)	P (g/kg)	DE (MJ/kg)	Mg (g/kg)	Lysine (g/kg)	Starch (g/kg)
Dried milk	340	0	10.5	9.8	15.1	1.2	29.0	–
Oats	96	100	0.7	3.0	10.9–12.1	1.4	3.2	385
Barley	95	50	0.7	3.3	12.8	1.3	3.1	515
Extruded soya bean meal	440	62	2.4	6.3	13.3	2.7	26.0	50
Field beans	255	74	0.8	4.8	13.1	1.5	17.0	360
High protein grass meal	160	220	6.0	2.3	9.6	2.7	8.0	15
Wheat bran	155	110	1.0	12.0	10.8	5.6	6.0	165
Sugar beet pulp	70	174	10.0	11.0	10.5	2.5	4.5	10
Cane molasses	30	0	7.2	1.0	11.4	4.0	0	–
Limestone flour	–	0	365	0	0	20.6	0	–
Dicalcium phosphate	–	0	238	187	0	5.9	0	–
Steamed bone flour	–	0	323	133	0	3.3	0	–
Grass hay	45–90	330	2.9	1.7	7.6	1.1	2–4	V
Grass/clover hay	60–110	330	4.0	1.7	7.8	3.0	3–5	–
Full fat soya beans	360	44	1.7	4.7	15.5	2.9	24	45
Linseeds	320	90	4	7.4	14.6	3.7	12.9	36
Flaked maize	80	15	0.2	2.9	15.2	1.0	2.6	610
English alfalfa	180	260	12	3.8	11.5	2.6	7.3	30

	Oil (g/kg)	Cu (mg/kg)	Zn (mg/kg)	Mn (mg/kg)	Fe (mg/kg)	Na (g/kg)	K (g/kg)	Cl (g/kg)
Dried milk	10	10	41	2	4	5	17	11
Oats	45	4	35	38	65	0.2	4	1
Barley	17	4	15	16	7.3	0.1	4	1
Extruded soya bean meal	18	13	50	31	160	0.2	17	0.1
Field beans	1.5	9	N/A	N/A	N/A	0.1	12	0.7
High protein grass meal	30	7	16	30	200	1	22.5	0.8
Wheat bran	35	12	98	120	145	0.1	4	0.9
Sugar beet pulp	5	10	1	34	250	3	17.5	2.2
Cane molasses	–	20	15	44	200	2	26	25
Limestone flour	–	–	–	–	–	–	–	–
Dicalcium phosphate	–	–	–	–	–	–	–	–
Steamed bone flour	–	–	–	–	–	N/A	N/A	N/A
Grass hay	21	3	12	20	150	–	10–35	–
Grass/clover hay	–	–	–	–	–	–	–	–
Full fat soya beans	180	12	N/A	N/A	N/A	0.1	16	0.4
Linseeds	340	7	N/A	60	90	0.6	6.8	0.2
Flaked maize	36	2	19	5	31	0.1	3	0.4
English alfalfa	25	12	28	25	250	1	21	5

[1] *National Research Council, NRC (1989)* Nutrient Requirements of Horses, *5th ed, National Academy Press, Washington DC.*
N/A, data not available; V, variable.

relatively low. There are now varieties of oat produced without husks, colloquially often called **naked oats**. They have a better amino acid profile, higher oil levels, and thus considerably higher energy levels than the husked varieties.

Barley has a higher energy level than oats and is generally fed rolled or cooked (cooking increases **pre-cecal starch digestibility**; *q.v.*). However, the amino acid profile, low calcium level, and phytate-bound phosphorus need correcting when barley is the major ingredient in horse rations.

Maize tends to have the lowest crude protein (CP) of the common cereals fed to horses and the highest energy value. In the UK it is generally micronized or steam flaked before feeding but in the USA and mainland Europe it is often simply cracked to open the outer husk.

Wheat has traditionally not been fed to horses. However, with the introduction of efficient cooking methods, the resultant alteration in the structure of the starch has made it a useful high energy feed for inclusion in commercial coarse mixes and home-mixed cereal rations. Large amounts per meal should be avoided, however, as they may lead to a sticky consistency in the stomach which may favor **dysfermentation** (*q.v.*).

Triticale is a hybrid resulting from crossing wheat and rye. In a ground form it should have a feeding value slightly greater than that of barley and evidence indicates that triticale may be better digested by the horse than is wheat. Both rye and triticale are subject to **ergot** infestation (*q.v.*), so clean samples should be sought.

Regardless of how triticale, wheat, barley or maize are mechanically processed, the starch will be less well digested in the small intestine than when cooked grains are fed.

Oil seeds

The **soya bean** is an excellent source of protein in an equine diet, providing good levels of essential amino acids. It must be properly cooked before feeding to help destroy the protease inhibitors as well as potential allergenic, goitrogenic and anticoagulant factors. However, in practice, most soya available in retail outlets has been suitably treated.

Soya is available as an **expelled meal**, with the oil removed; as the **full fat meal**, which has added advantages of providing good levels of essential fatty acids; and as the **full fat flake**, which has usually been micronized. This latter form is the most common to add as a top dressing, as the physical consistency of the meals can be unpalatable to some horses.

Linseed must also be cooked before feeding to destroy the glycoside, which, after soaking, could potentially release **hydrocyanic acid**. Linseed also has a good amino acid profile and in some methods of processing, where the oil is not extracted, also provides good levels of certain key fatty acids.

Vegetable oils

Horses have been shown to be able to digest and utilize high amounts of oil, but for practical purposes approximately 0.75–1 g of oil/kg BW/day may be considered to be the upper limit. Levels of 5–8% in the total diet are more

common in some high performing horses and many performance horses can be fed up to 100 mL/100 kg BW daily in divided doses without any problems provided that it has been introduced gradually, is not rancid, the horse requires such an energy intake, additional vitamin E is provided and the overall diet is re-balanced.

Adding oil to existing feed has the potential to create **multiple** imbalances (including an inadequate vitamin E intake and a calcium imbalance) and therefore could be considered less safe than feeding a diet where the oil has been balanced in relation to all of the essential nutrients in the feed. Any supplemental oil or oil-supplemented feed should be introduced **slowly**.

Supplemental fat or oil diets can be supplied in four main ways:

1. As an **oil supplemented, manufactured diet**. The advantage here is that such diets should be balanced with respect to the protein, vitamin and mineral intake that they provide when fed with forage (and salt as required). This can be a simple, practical and convenient way to feed high oil diets.
2. **High oil supplemental feedstuffs**, such as rice bran, which are also high in fiber and usually low in starch. However, many of the rice brans available have the same disadvantages as wheat bran in that they have a very imbalanced calcium-phosphorus content.
3. **Supplemental animal fat**. Many horses find most animal fats to be unpalatable and these fats seem often to be more likely to cause **digestive upsets**. Their use is not to be recommended.
4. **Supplemental vegetable oils**. The exact type of oil that may be preferred will depend on the individual horse and the nature of the processing to which the oil has been subjected. **Corn oil** and **soy oil** are probably the most commonly used vegetable oils in Europe.

It has been suggested that feeding oil supplemented diets, with appropriate training, can result in a range of effects on a variety of physiologic, metabolic parameters as well as on performance. These include:

1. Increased mobilization of free fatty acids (FFA) and increased speed of mobilization; increased speed of uptake of FFA into muscle—often considered to be rate limiting.
2. A glycogen sparing effect so that fatigue is delayed and performance improved (this could be especially important in endurance activities).
3. Increased high intensity exercise capacity.
4. In horses with a high energy demand, helping to reduce feed volume so that the roughage intake can be maintained (oils have also been suggested to help reduce the extent of bacterial dysfermentations in the stomach and small intestine).
5. Behavioral advantages over high cereal starch diets.

In order to have the potential to obtain metabolic benefits from the feeding of oil or oil supplemented diets, in addition to those associated with its high energy density and lack of starch content, the oil needs to be fed for **several months**.

Linoleic acid and **alpha-linolenic acid** are considered dietary essential fatty acids. However, no evidence of deficiency has been described for the horse and it must be assumed that a normal diet of cereal grains and natural forage, or of pasture herbage, will provide the dietary requirements.

FORAGES AND OTHER FIBER SOURCES

The choice of fiber source is now much wider with the advent of new methods of grass preservation, improved grass and other forage plant species as well as other technological advances. There are two equally important aspects when selecting the most appropriate fiber source:

1. The nutrient levels in the selected forage, and thus the percentage of the horse's total daily nutrient requirements that will be met through the fiber source.
2. The effect that forage may have on other aspects of the horse's health, especially the respiratory system.

Hay

Hay is the most commonly used long fiber source and may be divided into several types.

Meadow hay is generally made from permanent pasture and has a great diversity of species, including several different grasses, herbs and other plants. This hay is often termed "soft", as the diversity of plants results in different rates of growth and stages of maturity at the time of cutting.

Meadow hay will, on average, also provide higher protein (typically 8–12% dry matter [DM]) and digestible energy levels (typically 9–11 MJ/kg DM) than most seed hays. Meadow hays also often have higher mineral levels than seed hay, as they contain a greater proportion of deeper rooting herbaceous species.

Seed hay is produced from specially seeded leys, usually 1–3 yr old, and contains predominantly one or two grass species (often rye grass or timothy). This hay is more uniform and, due to the growth rate and cutting time, is usually fairly mature, with a lower proportion of leafy material and higher proportion of stalk than meadow hay. Typically, seed hay has lower energy (for example approximately 8–10 MJ/kg DM) and protein levels (approximately 4–8% DM) and a lower digestibility than meadow hay. The mineral levels in seed hay also tend to be lower than for meadow hay, although this will depend on the soil upon which the hay was grown.

Legume hay (usually alfalfa or lucerne, clover or sainfoin) has, due to **nitrogen-fixing properties**, higher protein levels than seed or meadow hay. Legume hay may be grown as a pure stand, but can be difficult to dry in cool wet climates as the stalks are very moist and thick so that cutting is often left until later in the season, when temperatures increase. However, by then the hay may have become very mature and stalky, with low energy and digestibility values. An exception to this is alfalfa, which can be cut earlier, barn dried and packaged in a short chopped form in plastic-covered bales. Clover and sainfoin are commonly mixed with grass species such as timothy to make

conventional hay, but care must be taken with the leys, as competition between the species will alter the relative proportions over a number of years.

Barn-dried hay is wilted in the field for 2–3 days when weather conditions are good and loose packed into special buildings; air of a particular temperature and humidity is then blown through the stored grass for 7–10 days before baling. When correctly practiced, this results in hay with a high DM, thus limiting the development of fungal spores.

Sometimes hay is baled with too high a moisture content due to unsuitable weather conditions at cutting time, insufficient turning in the rows, or other factors. A high moisture content will allow the development of large quantities of **fungal spores** (*q.v.*), which can be inhaled by the horse. Hay with a DM ⩽87% should always be assessed for spore level.

Soaking hay before feeding

The practice of soaking hay with the aim of reducing the number of airborne particles is popular in some areas. It has been reported that soaking a 2.5 kg hay net for 30 min reduces respirable particle numbers by approximately 90%. The water used for soaking must be fresh and increasingly it is recommended that soaking for >30 min may not be advisable due to the potentially negative effect of **prolonged soaking** on the soluble **carbohydrate and nitrogenous content** of hay and the pollutant nature of the effluent. Alternative solutions include the practice of steaming hay or the use of semi-wilted forages, silages or vacuum packed dust-free fodder.

Semi-wilted forages

In an attempt to reduce the level of fungal spores in forage for horses, methods of preserving grass have diversified. "Dust-free" grass and other forage plants such as alfalfa are wilted to approximately 50–60% DM and packaged in semi-permeable plastic, where a mild lactic fermentation occurs owing to the limited amounts of oxygen present. This lactic fermentation stabilizes at approximately pH 4.5–5.5, depending upon the amount of oxygen and substrate available for the microbial fermentation and helps to inhibit the proliferation of fungal spores. (Water activities <0.985 combined with a low pH may help to control in particular the sporulation of *Clostridium botulinum*, *q.v.*).

These forages exert a lower challenge to the horse's respiratory system and may be a valuable way to provide long fiber to a horse suffering from allergic respiratory disease (*q.v.*).

Damage to packaging allows the influx of oxygen, permitting further microbial activity to occur. This can be identified as a patch of mold, which is limited by the extent of the oxygen diffusion through the hole in the packaging. There may also be an increase in temperature as a result of the microbial activity. Bags in which this has occurred should be discarded.

Silage

Some larger horse keepers now find it economical to use silage. The rapid pH drop, the greater water activity, the decrease in available oxygen and soluble

carbohydrates as fermentation progresses all can help inhibit the development of fungal spores. There are, however, several important factors to be considered before using silage.

First, the DM content is very important to help inhibit **clostridial activity**. Horses also find very low DM material unpalatable, therefore it is recommended that silage for horses should have a DM >35% and preferably >40%.

Second, pH should ideally be <6.0 in order to inhibit undesirable microbial activity. At pH values between 5.0 and 6.0, the DM should exceed 40% as an added inhibitory factor to clostridial activity. Horses may find very low pH material unpalatable, and silage with a pH <4.5 may be rejected by some horses. There are also anecdotal reports that low pH silage may be **extremely unsuitable for donkeys**.

Third, it should be appreciated that if the silage was made to meet the nutrient requirements of dairy cattle the nutrient levels may be unsuitable for horses: for example, lactating dairy cattle require a higher daily protein intake than most horses. Finally, once a "big bale" of silage has been opened it should be used within 2–3 days in order to prevent **secondary microbial activity** from occurring.

Where large amounts of silage or haylage are used, supplementary vitamins D and E are necessary as ensiling destroys vitamin E and vitamin D_2 is not synthesized during the ensiling process. It is always advisable to get professional help when considering producing silage for horse feeding.

Straw

Straw provides a low nutrient level forage, which may be used to provide a portion of the daily forage intake for some horses, although problems with **spores and dust** must be taken into consideration. In addition, due to the high silica and indigestible fiber content there is a risk of **impactions** (*q.v.*) especially in Thoroughbreds and Thoroughbred crosses.

Chemical treatment of straw with **sodium hydroxide** and **ammonia** may increase nutrient value but this requires specialized equipment and expertise and the practice has not gained widespread popularity. Straw may be sprayed with **molasses** to increase its palatability but the nutrient values are still very low. There have been some concerns expressed regarding the various chemicals that may be used in grain production (e.g. to restrict the growth in height and to prolong the vegetative stage). It has been thought, for example, that they may leave unwanted residues on the straw; however, currently there is no evidence to support this concern.

Significant intakes of straw should also be **avoided in young animals**, where the hindgut microflora may not be fully established and the highly indigestible straw may lead to impactions.

Hydroponics

A hydroponic culture is the practice of germinating seeds (usually barley) in water-filled trays in a humidity- and temperature-controlled, enclosed environment.

Correct maintenance of the hydroponic unit is vital to ensure optimal conditions for germination—usually 20/24 h of light and a temperature of

19–20°C. **Routine hygiene** is important to prevent the build-up of mold spores. The barley seeds used should be of the highest quality and must not be treated with mercurial or other seed dressings. The feeding of hydroponic barley is not commonly practiced today.

Soya hulls and sugar beet pulp

It has been suggested that certain fiber sources (sometimes referred to as **highly digestible fibers**) such as sugar beet pulp practically provide more digestible energy to the horse than their traditional crude fiber, protein, fat, etc., analysis would suggest. This is in part because sugar beet pulp contains major fractions of pectins, arabinans and galactans, etc., which are lost during the crude fiber analysis, yet these carbohydrates can be fermented and thereby utilized by the horse. In addition, the fiber or more specifically the non-starch polysaccharide (NSP) in beet pulp is highly digestible over the total tract with a significant proportion being degraded in the small intestine during transit to the hindgut.

Various digestibility studies suggest that not only is sugar beet pulp well fermented in the horse (>60% digestibility of organic matter) but that this degradation occurs to a large extent within the time period that such a feedstuff would remain within the gut. This explains why sugar beet pulp and a similar feedstuff, **soybean hulls**, are increasingly being used as fiber-based energy sources in modern horse feeds.

In the UK, **sugar beet** is usually molassed and presented as **dehydrated shreds** of compressed pellets. When rehydrated, there is a considerable increase in volume, and thus the practice of soaking sugar beet shreds or pellets in at least twice their dehydrated volume of water is essential before feeding. Small quantities of extruded unmolassed sugar beet in compound mixes need not be soaked before feeding, as the extrusion process has already expanded the material.

METHODS OF FEED PROCESSING

Mechanical rolling, bruising or grinding of cereal grains aims to break open the outer husk, thereby releasing the floury kernel for enzymic digestion. The disadvantages include a greater predisposition for oxidation and an increase in dust. In addition, **mold growth** occurs more readily in grains where the kernel has been broken.

Micronizing cereal grains and vegetable protein seeds is a rapid method of cooking and rolling the grains to gelatinize the starch and improve enzymic digestibility within the small intestine.

Steam flaking of cereal grains is a method of mechanically and biochemically altering the structure of the starch molecules in order to improve digestibility.

Extrusion of cereal grains and vegetable protein seeds involves grinding and increasing the moisture of the cereal grains and "cooking" the resultant slurry at very high temperatures and pressures before forcing the cooked material through a die, where the resultant drop in pressure forces a rapid expansion of the material as air enters the mixture. Typically this process leads to a moisture content of 8–10% (or DM of 90–92%).

Oil extraction and "roasting" of high oil seeds is an industrial process. The resultant oils extracted are then available for use in human or animal feeds, depending upon the degree of refinement.

Grinding and steam pelleting: individual ingredients are ground, mixed, steamed and forced under mechanical pressure.

Coarse mixing combines feedstuffs, often processed by one of the above methods, usually mixing them with a sugary syrup such as molasses or glucose.

FEED STORAGE

Correct storage of feedstuffs is essential to preserve their nutrient value, ensure palatability is retained, and help prevent fungal or bacterial contamination, which may affect the horse's health. In order to help **prevent fungal growth**, feedstuffs should be of the correct moisture level; cereals with a moisture content >16% must be considered suspect. The treatment of high moisture cereal grains with **propionic acid** to act as a mold inhibitor and preservative has been practiced, although the effects of this compound on horses have not been widely studied.

Oxidation is a potential problem in rolled, cracked or bruised cereals. This rancidity will clearly affect palatability and may also affect nutrient availability, especially of certain vitamins. There may also be metabolic implications such as an increased level of peroxides. Storing feed at low humidity and low temperatures will reduce the rate at which oxidation occurs. The importance of maintaining feedstuffs at a suitable temperature, humidity and with adequate ventilation must therefore be strongly emphasized.

Infestation with **mites** is another common cause of feed spoilage. The practice of keeping feeds in galvanized bins can be useful, but care must be taken to ensure the bins are fully emptied and cleaned of all the previous material before a new bag or load is tipped in. In hot weather, high moisture feeds may cause condensation in the galvanized bins, so caution should be exercised.

FEEDSTUFFS ANALYSIS

From time to time it may be necessary to undertake more detailed analyses of specific feedstuffs. Such costly analysis will only be of value if representative samples, especially of pastures or roughage, are taken. Sampling may be required because of a suspected nutritional involvement in a particular disease or disorder where typical, tabulated analyses do not provide the necessary degree of detail or accuracy. Analysis may also be required in order to confirm that dietary ingredients meet the required or designated specification, or to assist with future purchases. If there is any suspicion of a feed related problem the samples should obviously be taken from the feedstuffs that have been fed.

Caution should be exercised as to whether the analyses are given on the fresh **as fed** material, or on a **dry matter basis**. "*Dry matter*" basis refers to the feed or forage after the moisture has been taken out, whereas the term "*as fed*" refers to a feed as it would be fed to a horse. Most concentrate feeds such as

cereals, cubes, pellets, etc., contain approximately 10% moisture with a dry matter content of 88–92% and fresh forage from 20% to 60%. It is important to realize that only the dry matter contains nutrients, so more feed will need to be fed, on an as fed basis, to match requirements if the feed contains more water.

Box 3.1 gives suggestions for routine analyses in order to assess general feed quality and major nutrient levels. In special circumstances, more detailed analyses will be required.

Box 3.1 Suggestions for routine analysis in assessing general feed quality

Cereal grains and by-products, vegetable and animal proteins

1. Dry matter.
2. Crude protein (CP).
3. Digestible crude protein (often based on ruminant data so caution needed with interpretation); or, as a guide,

   $$\text{DCP (g/kg DM)} = -27.2 + 0.917 \times \text{CP (g/kg DM)}.$$

4. NDF (and ADF).
5. Ash (as a possible guide to soil contamination).
6. Oil (various methods available, ether extract is usually adequate).
7. Energy (check if given in terms of ruminant ME [metabolizable energy], and conversion coefficients to horse DE should be used—current suggested conversions: divide by 0.9 for high fiber material, divide by 0.85 for low fiber material—very approximate). Many equations are available to estimate DE (i.e. there is no definitive equation) e.g.:

   $$\text{DE (MJ/kg DM)} = -3.54 + 0.0209 \times \text{CP} + 0.042 \times \text{Oil} + 0.0001 \times \text{CF} + 0.0185 \times \text{NfE}.$$

8. Micronutrient levels for these ingredients may be obtained from published tables.
9. Certain feedstuffs in the above category contain anti-metabolites in their raw state, and where toxic effects are suspected, analyses for the presence of the anti-metabolites should be made.
10. Results should be interpreted in terms of units per day intake (e.g. g/day protein, or MJ/day DE), rather than percentages as, unless intake quantity is known, the figures are meaningless in terms of effect upon the animal.

Forages (including hay, haylage, silage, straw)

1. The level of fungal contamination in hay should be assessed before purchase.
2. Dry matter.
3. Crude protein.
4. Digestible crude protein (is likely to be based on ruminant data so caution on interpretation).
5. Modified acid detergent (MAD) fiber (other more accurate methods may soon be available). NDF and ADF may also be of value.

Box 3.1 continues on page 164

Box 3.1 Suggestions for routine in assessing general feed quality [continued]

6. Digestibility or D value (based on cattle data, but provides useful comparative data when several samples are assessed.
7. Energy (see under cereal grains).
8. Calcium, phosphorus, magnesium. Other minerals may be assessed as required.

Where forages are the main source of nutrients, further mineral analysis may be advisable. In addition to the above, for silage and haylages:

(a) pH (see text).
(b) Ammonia to indicate the nature and suitability of the fermentation. Ideally NH_3–N levels $<$3.0% although up to 6.0% are probably acceptable. $>$6.0% may affect palatability.

N.B. If abnormally high levels are suspected, nitrate levels should be assessed. Caution should be taken with the interpretation of the nitrate data, as laboratories describe nitrate levels differently.

Pasture and soil
Whilst it may be necessary sometimes to determine the protein and energy levels in pasture, mineral levels are required from both pasture and soil; in the former to ensure any necessary deficiencies are corrected in the concentrate feed, and in the latter to ensure correct fertilizer programs are maintained. Several standard texts on soil analyses and fertilization programs are available.

ADF, acid detergent fiber; NDF, neutral detergent fiber; NfE, nitrogen free extract.

THE DIGESTIVE TRACT

PHYSIOLOGY AND PATHOLOGY OF DIGESTION

The empty alimentary tract accounts for about 5% of the total BW of a horse. The weight of the gut contents varies according to feeding, from 5% (concentrate) to 10% (roughage). In the small intestine, digestion is primarily by the body's own enzymes, while in the voluminous large intestine the feed components are fermented by microorganisms. It is important to appreciate, however, that some fermentation will occur in the stomach and the small intestine. The approximate sizes of the various sections of the gastrointestinal tract are shown in Table 3.2.

Mastication

The duration of feed intake (Table 3.3) depends on the type of feed and the size of the animal. By feeding mainly concentrates, the time taken to ingest the feed and the number of chewing movements are greatly reduced. This may lead to a change in behavioral patterns: for example, animals may bite

Table 3.2 Guide to the size of various parts of the gastrointestinal tract in horses as well as the duration of ingesta passage (500 kg BW)

	Length (m)	Fill (kg/100 kg BW) when feeding		Duration of passage
		Hay	Concentrates	
Esophagus	Up to 1.5	–	–	10–15 s
Stomach	–	2.5	1.8	1–5 h
Small intestine	16–24	2.2	2.2	1.5 h
Cecum	1	3.5	1.5	15–20 h
Colon	6–8	12	6.0	18–24 h
Rectum	0.2–0.3	–	–	1–2
Total		20.2	11.5	35–50 h

Table 3.3 Guide to the duration of feed intake in horses and ponies (min/kg feed)

	Approximate BW (kg)	
	Horse 500	Pony 240
Hay	40	80
Straw	50	–
Milled hay, pelleted	8–10	–
Oats	10	50
Pelleted feed (diameter 4–8 mm)	10	40
Chewing movements/min	80–90	100
Chewing movements/kg hay	3400	–
Chewing movements/kg oats	850	–

and lick objects within their reach. Horses should be fed sufficient amounts of roughage (preferably long fiber or chop) daily in order to help prevent such abnormal behavior.

During chewing, the feed is thoroughly ground by the molar teeth; at the same time the secretion of saliva is stimulated. The **grinding** of whole grains is necessary for their optimal digestion in the small intestine. The intensity of the grinding of the roughage may be important for the passage of digesta through the ileocecal orifice and the large intestine. Short chopped straw or hay (≤20 mm) as well as very fine grasses (e.g. wind bent grass [or silky bent-grass], *Agrostis spica-venti*) may be swallowed without intensive chewing and grinding. This increases the **risk of obstructions** as well as increasing the risk of dental enamel points and hooks developing due to restricted chewing movements. The ingestion of lawn mower cuttings increases the risk of colic either due to an obstruction (*q.v.*) or dysfermentation (*q.v.*).

The ground feed is mixed with varying amounts of saliva depending on the duration of the feed intake (Table 3.4). This means that the DM of the boluses swallowed is higher after feeding concentrates than roughage. The occurrence of esophageal obstructions depends not only on the swelling capacity of the feedstuff (for example, dried sugar beet pulp), but also the speed of the feed intake and the size and DM content of the boluses swallowed.

Table 3.4 Principal differences between feeding roughage and concentrate feed

	Roughage	Concentrate feed
Duration of feed intake	Long	Short
Salivation	Heavy	Less intensive
Dry matter of swallowed boluses (%)	<15	>25
Filling of the stomach	Slowly	Quickly
Content of the stomach (temporary)	Moderate	Moderate to high[1]
Dry matter of stomach content (%)	20	30–40
pH reduction in region of pylorus	Normal	Retarded
Microbial activity in stomach and small intestine	Moderate	Moderate to high[1]
Production of organic acids in the large intestine	Continuously	Discontinuously with the risk of low pH in the cecum
Feces dry matter (%)	20	20–45

[1] *According to the amount of feed offered per meal.*

Stomach and small intestine

The horse has a small, simple stomach, which is suited to the intake of rather small quantities of feed per meal. The cranial region of the stomach is non-glandular and is lined by stratified squamous epithelium similar to the esophagus. As this region fills, bacterial fermentation of the feed starts. This principally involves **lactobacteria**, which convert easily soluble carbohydrates to lactic acid.

Microbial activity and degradation is stopped when the gastric contents reach the fundic gland region and mix with the acid stomach juice containing pepsinogen.

Large quantities of digestive fluids are secreted into the small intestine, in particular from the liver (bile) and the pancreas into the duodenum. The main functions of the pancreatic secretion are to neutralize the acid chyme and to provide proteolytic, amylolytic and lipolytic enzymes. Bile also helps to alkalize the digesta, and the bile acids are required for emulsification and digestion of lipids.

Although the pancreatic enzyme **amylase** hydrolyses starch to disaccharides and trisaccharides, these have to be further digested by the mucosal enzymes before the resultant hexoses can be absorbed. Mucosal enzymes are also important for protein digestion and absorption.

In the small intestine of the adult horse, the digestive processes (i.e. the enzymatic degradation of proteins, fats, starch and sugar) are similar to those of other monogastric animals. However, the activity of most of the enzymes in the chyme, especially amylase, is lower than in other monogastric animals. The type of feedstuff affects the amount of soluble carbohydrate absorbed as glucose: up to 85% of the starch content of whole oats will be digested by the end of the ileum but only 30% of the starch from whole maize (for heat processed maize grains digestibility increases to approximately 90%).

Adult horses (500 kg BW) secrete >100 L fluid/day into the pre-cecal gut at approximately 70–100 mL/min. The DM content of the small intestine is about 5% so that even indigestible fibrous particles can be easily passed to the

cecum. At the ileocecal junction, the chyme flow is stopped and the contents are discontinuously pressed into the cecum (5–7 times/h; up to 1 L at a time), which means that **obstruction** is a potential risk.

For the commonly fed diets consisting of hay and oats, approximately two thirds of the completely digestible parts of the feed will have been broken down and absorbed by the time the ingesta reaches the large intestine.

Large intestine

The large intestine does not possess mucosal enzymes and does not have active transport mechanisms for hexoses and amino acids. Digestion and absorption of residual carbohydrates and proteins relies instead on microbial action and absorption of the end products of microbial fermentation. The intensity of this process depends on the amount and the temporal influx of fermentable material arriving from the small intestine.

This **bacterial degradation** mainly produces **volatile fatty acids** (VFA), i.e. acetate, propionate and butyrate, plus amino acids, ammonia, sulfides, etc., and, after a high influx of easily fermentable carbohydrates, lactic acid. The rate of VFA absorption increases with decreasing pH. Disturbances of the digestive processes in the large intestine are marked on the one hand by insufficient microbial activity and on the other hand by accelerated degradation rates, particularly in the cecum.

Excluding **damage to the flora** (e.g. by antibiotics or mycotoxins) low microbial activity in the large intestine occurs when animals are fed rations consisting mainly of poorly fermentable components such as straw or late harvested hay. If large amounts of these feeds, which are difficult to break down, are ingested, **obstruction of the colon** (*q.v.*) may occur due to slow and incomplete microbial activity. This will be aggravated by any factor that decreases the rate of the passage of ingesta, such as lack of water, little exercise, parasites, and intake of soil and toxins which influence the flora of the large intestine, as well as gastrointestinal motility. On the other hand, if large amounts of easily fermentable substances that escaped digestion in the small intestine flow into the cecum, **abnormal fermentation in the cecum** may result in digestive disturbances and acidosis. This may happen with large amounts of mixed feed per meal or if carbohydrates such as maize starch or lactose are fed. Disturbances are especially likely if the animal has not adapted to a high grain diet.

Undigested proteins and urea that enter the large intestine are broken down by microbial enzymes. The main end product is ammonia, which is absorbed particularly at alkaline pH. **Microbial protein**, which is synthesized in the large intestine, fundamentally cannot be utilized by the horse. Animals with a high demand for protein (e.g. foals or lactating mares) must therefore be fed high quality protein that can be broken down and absorbed primarily in the pre-cecal section of the gut.

Most water-soluble vitamins as well as the fat-soluble vitamin K are synthesized in the large intestine. The horse appears to be able to utilize these so that oral supply is only necessary under certain circumstances (*q.v.*).

Table 3.5 Guide to the daily intake and turnover of water (L/100 kg BW) and electrolytes (g/100 kg BW)[1]

	Intake	Secretion(s) ■ Saliva ■ Gastric juice ■ Secretions into small intestine	Flow from ileum into the cecum	Absorption ■ End of small intestine ■ Hindgut
Water	3–5	20–25	10–14	9–12
Sodium	5	~50	30–42	28–35
Chloride	15	~60	10–14	10–14
Potassium	10	~9	5–7	2–3

[1] *Based on Meyer, H., Coenen, M. (2002)* Pferdefütterung *(Horse Nutrition), 4th ed, Blackwell Scientific Publications, London.*

Water and electrolytes

There is a large water and electrolyte turnover in the gastrointestinal tract. While considerable amounts of water, sodium (Na) and chloride (Cl) enter the small intestine via the saliva, stomach juices, pancreatic juice and bile, only about 50% of water, 35% Na and 80% Cl will be absorbed by the end of the ileum. Therefore a large ileocecal flow of water and Na (and to a lesser extent chloride) takes place (Table 3.5), but most of the water and electrolytes that enter the large intestine will be absorbed.

Absorption of calcium (Ca) and magnesium (Mg) mainly takes place in the small intestine, while phosphorus (P) absorption occurs predominantly in the large intestine. Therefore a high P intake disturbs Ca absorption to a greater extent than a high Ca intake affects P absorption.

The large water and electrolyte turnover in the intestine has two consequences:

1. With an **ileus** (*q.v.*) in the small intestine, the intestine will fill up very quickly proximal to the blockage. The liquor may possibly reach back to the stomach while the animal becomes dehydrated.
2. **Diarrhea** (*q.v.*) in adult horses is mainly related to dysfunction of the large intestine because an elevated flow of water from the small intestine can usually be reabsorbed in an intact functional large intestine.

The importance of microbial fermentation in the gut

Several types of microorganisms are present within the gut contents; the exact make-up is influenced by a number of factors including substrates that have been fed in the past and are currently being fed, the passage time, the pH and organic acid composition at the various sites as well as extent of the various interactions with the horse's own digestive secretions (such as the gastric juices), etc. There are marked individual differences in the amount and type of the organisms throughout the GIT but the lowest numbers are found in the fundus region of the stomach.

Normal fermentation in meal-fed horses

Ingesta is propelled quite rapidly through the small intestine in a fluid form in the adult horse, some appearing in the cecum within 45 min and much of it reaching that point within 3 h of eating. Protein that escapes digestion in the small intestine is degraded to ammonia by bacteria in the ileum and to a much larger extent in the large intestine. The carbon skeletons are utilized as energy sources by the bacteria yielding acetic, propionic and butyric VFA as by-products. Starch that escapes digestion in the small intestine and most structural carbohydrates are subjected to fermentation by the large gut bacteria, again yielding VFA.

Bacterial fermentation also produces some longer chain fatty acids, as well as lactic acid. These acids and some of the ammonium ions are absorbed from the large intestine and enter the systemic circulation. Much of the ammonia, however, is reutilized by bacteria in the synthesis of **bacterial protein**, stimulating rapid bacterial growth. The bacterial population therefore ebbs and flows between the surges of ingesta reaching the large intestine.

It is important to note that there is a **fluctuation** in the hindgut bacterial populations in any meal-fed horse. The microflora population within the hindgut does adapt to a certain extent to the type of feed being fed. However, if the dietary fluctuations are too marked, or excessive starch or rapidly fermentable carbohydrates reach the hindgut even in the concentrate adapted horse, this will result in a significant change in the **microbial population**, which may have clinical consequences.

Dysfermentation

As well as obstructions, conditions associated with dysfermentation are the main cause of digestive upsets. Mistakes in feeding technique, selecting incompatible feeds or insufficient preparation of some feeds may induce inappropriate microbial growth and/or dysfermentation (*q.v.*), potentially with severe consequences for the health of the horse.

After ingestion of large meals of starch or sugar, fermentation is more extensive in the first part of the stomach, because the stomach contents have a higher DM content and the mixing of feed and gastric juice is therefore slower. This means that either the normal reduction in pH is delayed or the pH remains >4.5. Large amounts of lactic acid will be produced. The same process can occur with feeds that have a sticky consistency or potentially whenever gastric acid secretion is reduced. A further risk comes from feeds that are contaminated, especially with yeasts, when gas production may be so extensive that there is a risk that a **stomach rupture** (*q.v.*) may occur.

Mistakes in feeding technique and the selection of incompatible feeds may also have consequences in the small intestine. Again, inappropriate microbial fermentation (e.g. of easily digestible starch provided in large amounts) may produce high amounts of organic acids, resulting in a reduction in the pH and disruption of normal digestion. **Spasmodic colic** (*q.v.*) may be the final clinical result. All factors that reduce passage in the small intestine (excitement, stress, parasites, etc.) favor microbial activity and potentially increase the risk of colic.

As described above, large amounts of starch and, to a lesser extent, protein, ingested in a single meal may have an effect on digestion both in the stomach and the small intestine. In addition, significant amounts reach the large intestine, stimulating an almost **explosive growth of microorganisms**. Gas production can exceed the rate at which the methane, hydrogen and carbon dioxide are normally absorbed into the blood and expelled through the lungs so that the lumen of the large intestine becomes **distended**. Moreover, the rapid production of VFA and lactic acid in particular causes a rapid **decrease in pH** of the fluid, increases the permeability of the mucosa and upsets the microbial balance. This favors the growth of organisms that can withstand a lower pH, stimulating more lactic acid production and causing the death of certain bacteria that cannot survive under such conditions, thereby releasing **endotoxins** (non-protein lipopolysaccharide fragments of the cell wall of Gram-negative bacteria) and other compounds. These endotoxins, together with the other unwanted compounds produced as a consequence of this change in the conditions of the hindgut, may be absorbed into the blood and have further adverse effects. The blood flow to the feet, for example, may be particularly sensitive to some of these factors that may in turn trigger the development of **laminitis** (*q.v.*).

The importance of fiber

In addition to functioning as a source of energy, the **fibrous components** of feed have other values. In the **long form** (pieces in excess of 2–3 cm in length), fiber occupies the stabled horse's time in chewing, so that it is less inclined to what are often referred to as "boredom-related" stable vices. The gastric contents have a higher moisture content and are more friable, allowing more immediate penetration of gastric juices, including HCl, and promoting better digestion further down the digestive tract. Also the microbial fermentation of fiber (fed as short or long material) proceeds at a slower pace than does the fermentation of starch or protein. This in turn has two advantages:

1. The ebb and flow of the microbial population of the hindgut, in numbers of organisms and in their species distribution between meals, is less marked than when starch and protein are the principal substrates.
2. By diluting readily fermentable material, wild fluctuations in the pH of the hindgut are prevented and thus the likelihood of acidosis is reduced.

Gastric ulceration

Modern management practices that include meal feeding, low fiber/high concentrate diets, early weaning and intensive training programs help to produce a poorly buffered, acidic environment in the stomach. This has been linked to the high prevalence of **gastrointestinal ulcers** (*q.v.*) particularly in intensively managed horses such as performance horses.

Foals are highly susceptible to ulceration because they start secreting gastrin just after birth before the gastric mucosa has fully developed. In addition, stressful weaning programs may act as an exacerbating factor in the development of gastrointestinal tract ulcers. There is a strong correlation between the

diet fed and the pH of the stomach. Concentrate diets have always been implicated but ensuring that these are fed in small amounts, possibly in combination with forages such as alfalfa hay, may help. A **high forage intake**, which encourages chewing and stimulates salivation, may also be advantageous. Turning out to pasture can be very beneficial for those that are affected. Medical treatment is often required.

NUTRIENT REQUIREMENTS

INTRODUCTION

The principal function of feed is to provide the nutrient requirements of the horse and its symbiotic gastrointestinal microorganisms. Maintenance requirements can be defined as the daily intake that maintains constant body weight (BW) and body composition as well as the health of a healthy adult horse with zero energy retention at a defined level of low activity in comfortable surroundings.

Nutrient requirements are typically stated as an amount per kg of feed or amount per kg BW daily. These amounts are the minimum needed to sustain normal health, production and performance of an average healthy animal. The amounts vary widely amongst horse groups with differing physiologic demands, i.e. growth, age, lactation, physical activity and workload (rider weight and ability, terrain and intensity of activity). They will also be affected by other factors including the environmental conditions. For example, energy requirements increase in animals exposed to very **low temperatures**, particularly where there is considerable air movement, and rain decreases the insulation properties of the coat.

As well as varying according to breed, body composition, stage of training, etc., it is also very important to remember that horses are individuals and differ in their metabolic efficiency (e.g. some horses are "good doers"), temperament, health status (including level of parasitic burden), appetite, likes and dislikes and other variables. It should be noted that there can be a difference between what a horse **can eat** and what it **might need** for maintenance, which in practice means that many mature horses will gain weight if fed free choice hay and not exercised.

Guidelines to requirements only can be provided; these then need to be tailored to the individual circumstances. It is important to note that one of the main reference materials used and referred to are the National Research Council (NRC) requirements, which recommend **minimal** rather than **optimal** requirements.

Imprecision in the assessment of nutrient requirements is compounded by uncertainty in feed analysis. The bioavailability of nutrients also varies between feed sources. The values given in Table 3.6 assume a high bioavailability from the ration.

Requirements can be given in a variety of ways. Two of the most common are per kg DM feed intake, and amounts per day on a dry matter or as fed basis. It is important to check what units are being used. Either can be suitable but obviously the DM intake guidelines rely on horses being fed appropriate amounts of feed for their workload, age, reproductive status, etc.

Table 3.6 Guide to the minimum daily nutrient requirements of horses[1]

	Digestible energy (MJ)	Crude protein (g)	Lysine (g)	Ca (g)	P (g)	Mg[2] (g)	K (g)
1. Mature weight 500 kg							
Maintenance (adult)	69	656	23	21	14	7.5	25.0
Stallions (breeding)	86	820	29	26	18	9.4	31.2
Pregnant mares							
9 mo	76	801	28	36	26	8.7	29.1
10 mo	77	815	29	36	27	8.9	29.7
11 mo	82	866	30	38	28	9.4	31.5
Lactating mares							
Foaling to 3 mo	118	1427	50	57	36	10.9	46.0
3 mo to weaning	102	1048	37	38	22	8.6	33.0
Working[3]							
Light	86	820	29	29	18	9.4	31.2
Moderate	103	880	31	32	21	11.3	37.4
Intense	137	1050	37	40	29	15.1	49.9
Foal growing at 1.0 kg/day[4]							
4 mo	60	730	30	37	19	4.0	11.3
6 mo	71	864	36	40	20	4.6	13.3
Yearling							
growing at 0.6–0.8 kg/day	87	956	40	40	20	5.7	18.2
24 mo old							
Not in training	79	820	32	28	14	7.0	23.1
In training	110	1050	41	35	19	9.8	32.2
2. Mature weight 200 kg							
Maintenance	31	296	10	10	6	3.0	10.0
Stallions (breeding)	39	370	13	11	8	4.3	14.1
Pregnant mares							
9 mo	34	361	13	16	12	3.9	13.1
10 mo	35	368	13	16	12	4.0	13.4
11 mo	37	391	14	17	13	4.4	14.2
Lactating mares							
Foaling to 3 mo	57	688	24	27	18	5.0	21.2
3 mo to weaning	51	528	18	18	11	4.0	14.8
Working[6]							
Light	39	370	13	11	8	4.3	14.1
Moderate	46	410	14	14	10	5.1	16.9
Intense	62	450	16	18	13	6.8	22.5
Foal growing at approx 0.5 kg/day							
4 mo	31	365	15	16	9	1.6	5.0
Yearling							
growing at 0.2–0.3 kg/day	43	462	19	15	8	2.5	7.9
24 mo old							
Not in work	33	337	13	9	5	2.8	9.4
In work	48	485	16	13	7	4.1	13.5

[1] *Based on National Research Council, NRC (1989)* Nutrient Requirements of Horses, *5th ed, National Academy Press, Washington DC.*
[2] *Assumes availability of 35%.*
[3] *See also Tables 3.15 and 3.16.*
[4] *See also Tables 3.17 and 3.18.*

Table 3.7 Guide to the minimum[1] water needs (kg) of horses per kg of feed DM consumed and the water (kg) provided by pasture herbage per kg herbage DM (1 kg water is equivalent to 1 L)

	DM	Water
Water requirements of horses per unit of DM consumed		
Last 90 days of gestation	1	3
First 3 months lactation	1	4
Breeding stallion	1	3
Weaned foal	1	3
Barren mare	1	2
Maintenance		
Grain/hay diet	1	2–3.5
All hay diet	1	3.5–4
Water content of herbage per unit of DM		
Spring growth	1	4
Dry summer	1	2.5
Mild winter	1	3

[1] *Quantities of water given assume ideal environmental conditions.*

BODY WEIGHT ESTIMATIONS

Many nutrient requirements are proportional to body weight. Unfortunately, judgment by eye can be inaccurate; calibrated weighbridges are the most accurate but are not commonly available. Weigh tapes and estimations based on linear measurements provide an approximation but these can only be taken as a guide or used for monitoring purposes where standardized procedures are followed.

There are a number of equations available such as that to **estimate body weight** in kg (w) from heart girth in cm (hg) and length of the body in cm (l) from the point of the shoulder to the point of buttock for the *adult* horse only:

$$w = [(hg)^2 \times l]/11\,877$$

This will tend to overestimate the weight, for example, of those horses with reduced gut fill in hard work such as the fit racehorse and is not reliable for the pregnant mare in late gestation or for young, growing animals, etc.

WATER

The requirements for water are given in Table 3.7. The water content of the body should remain within the approximate limits of 68–72% of fat-free mass. Values below this represent a dehydrated state. Water is lost by excretion in urine, feces and sweat, as well as by evaporation from the lungs and in milk. Lactation can increase needs by 50–70% above maintenance.

The requirement for supplementary water is influenced both by the amount of DM consumed and by the moisture content of feeds available. Cereals and hay contain approximately 10% moisture whereas pasture herbage contains 40–80% moisture depending on season and rainfall. These sources affect the supplementary amounts of water required (Tables 3.7 and 3.8). Dry mares (or

Table 3.8 Guide to the minimum[1] supplementary water requirements of mares (liters daily per mare)—refer to Table 3.7 for maintenance levels

Body weight (kg)	200	400	500
Last 90 days of gestation[2]			
In stable	13	22	26
On pasture	0	0	0
First 3 months of lactation			
In stable	28	42	50
On pasture	7	11	12

[1] These amounts are minimum. They assume ideal conditions and will be insufficient for mares on parched pasture with environmental temperatures >30°C.
[2] Needs of the breeding stallion are similar to those of the pregnant mare.

other non-lactating horses) on lush pastures with shade, undertaking no work, can thrive without additional water, although it is always advisable that a clean supply be made available. **Pregnant and lactating mares** should be provided with supplementary water at all times (see Tables 3.7 and 3.8). Foals should have adequate access from around 2 weeks of age. The requirements of the **breeding stallion** are similar to those of the pregnant mare.

Maintenance needs are usually met by providing 2–3.5 L/kg DM intake on a mixed diet of grain and hay in temperate conditions. For all hay diets, 3.5–4.0 L/kg DM may be needed. Environmental temperature has a large effect on the amount consumed. Values of 2 L/kg DM at 18°C and 8L/kg DM at 38°C have been reported. **Sweating** involves losses in particular of sodium, potassium and chloride in addition to water so that severe sweating also necessitates the replacement of these electrolytes.

Sweat production

Unfortunately, the conversion of chemical energy provided by the feed to mechanical energy in the form of **ATP** that can be used by the muscles is not very efficient, and the "waste" heat that is produced has to be removed from the body. One of the main mechanisms for heat removal is via the **evaporation of sweat**. The amount of sweat produced depends on the environmental conditions, nature of the work (which in turn will depend on the rider's ability and the terrain) and the animal's fitness. Under favorable climate conditions, sweat loss can be around 2–5 L/h if the work is a run at a low pace (approximately 2–4 m/s) or in the order of 7–8 L/h in long distance rides at a faster pace or in difficult terrain (Table 3.9).

In hot humid conditions where sweating is partially ineffective, production can be as high as 10–15 L/h. Sweat production seems to decrease only after extreme water loss; although there may be some changes in sweat composition with time, basically sweat production is accompanied by an obligate loss of electrolytes. When the sweat loss is low, much of the loss can be made up by absorption of water contained in the large intestine, but if water losses are greater (3–4% BW) a decrease in circulatory volume as well as **loss of skin elasticity** occurs.

Table 3.9 Sweat production

Work	Amount of sweat (L/100 kg BW)[1]	Average	Average water requirement (L/100 kg BW/day [including maintenance])
Light	0.5–1	0.75	5
Moderate	1–2	1.50	5–7
Heavy	2–5	3.50	7–10
Very heavy	>5	5.00	>10

[1] *Depending on duration and intensity of activity and environmental temperature. Rule of thumb: 1 L/100 kg BW/h with light trotting at 18–20°C.*

Table 3.10 Guide to the composition of sweat

Electrolyte/element	Amount lost per L sweat	Approximate amount needed to be ingested to replace amount lost per L sweat (g)
Sodium	3.1 g/L	3.45
Potassium	1.6 g/L	2
Chloride	5.3 g/L	5.5
Calcium	0.12 g/L	
Magnesium	0.05 g/L	
Phosphorus	<10 mg/L	
Zinc	11 mg/L	
Iron	5 mg/L	
Copper	0.3 mg/L	
Selenium	Traces	

Horses participating in **endurance rides** over distances of 50–200 km typically lose 3–7% of their body weight during the competition—some horses may lose 10% or more. These losses are only partially compensated for during overnight stops, perhaps due to persistent loss in the GIT content, which takes longer than an overnight period to recover to pre-race levels.

Sweat contains relatively low levels of calcium (approximately 0.12 g/L), magnesium (approximately 0.05 g/L) and phosphate (<0.01 g/L) but relatively high levels of sodium, potassium and chloride as shown in Table 3.10. There are also small amounts of various trace elements, e.g. iron at approximately 4.3 mg/L and Zn at 11.4 mg/L. However, the main electrolytes lost with sweat are **sodium, potassium and chloride**.

ENERGY

Energy is supplied to the horse via its diet, but fundamentally energy is not a nutrient. The chemical energy or gross energy contained within feeds needs to be converted into a form of energy that the cells can use for work or movement (usable or **net energy**). Dietary energy is provided by the four principal dietary energy sources.

1. **Hydrolyzable carbohydrates,** e.g. simple sugars and starch. These can be digested by mammalian enzymes to hexoses that are absorbed from the

small intestine (SI) or, if they "escape" digestion in the SI, are rapidly fermented in the hindgut.

2. **Fermentable fibers**: component of dietary fiber—cellulose, pectins, hemicelluloses, etc. These are not digestible by mammalian enzymes but can be fermented by the microorganisms predominantly located in the hindgut. Speed of fermentation as well as site may play an important role in the energy value to the horse.
3. **Oils/fats**, utilized as fatty acids and glycerol. Despite their more "evolutionary traditional" diet containing relatively low concentrations of oils, horses in general appear to be able to digest and utilize up to 20% of their diet as oil if suitably introduced.
4. **Proteins**. Although much of the constituent amino acids will be utilized in protein synthesis, depending on the dietary level and the balance of the amino acids, a significant proportion of the carbon skeletons of many amino acids are combusted as energy sources or converted into fat or glucose. Not an efficient energy source (see below).

With the exception of feeds that contain a lot of fats or ash, the gross energy content of feeds tends to be similar. Differences arise mainly from differences in digestibility. Hay has a lower digestibility than cereals; it produces much more spare "lost" heat so is much more "internally heating" and is therefore especially useful in winter. In addition, the efficiency of conversion of digestible to usable or net energy differs widely.

Cereals have more net energy than hay, which in turn contains more than twice the net or usable energy of straw. Vegetable oils contain proportionally more net energy than the cereals and 2.25–3 times the amount of digestible energy. Replacing forage with cereals and/or oil decreases the amount of feed the animal has to eat in order to obtain the required amount of energy (important as horses have a finite appetite).

Energy requirements

Critical to feeding any horse for health and vitality is the appropriate and adequate supply of energy, especially during the **training** phases (*q.v.*). If a horse is fed too little energy for its needs it will tend to become **dull and lethargic**, lose weight and/or become clinically ill. If a horse is fed too much energy or inappropriate energy it may become **hyperactive**, gain weight and/or become ill.

Adult horses in particular tend to be fed primarily for energy; the diet is then balanced for protein, vitamins and minerals.

At present, the energy potential of a horse feed is described in two main ways: digestible energy (DE) and net energy (NE). Each of these has been determined in a number of ways over the years. The DE system is the most commonly used in UK, Germany and the USA; the NE system and its variants are gaining popularity in the rest of mainland Europe.

The French (who pioneered the value of the NE system for horses), for example, base their system on the horse feed unit (UFC), a net energy system of values relative to the NE values of barley. Net energy is considered to be

that portion of the feed energy that is actually available for use—be that movement, production of milk, fetal growth, etc. However, the efficiency of conversion of the feed energy to available energy varies according to use: for example, approximately 25% efficiency when converted to kinetic energy, approximately 70% for milk production, but only approximately 20% for fetal growth. Figures that have been derived from one use may therefore not be appropriate for another. It is also important to realize that the DE and NE systems are not easily interchangeable and therefore one system should be used throughout to calculate both requirements and the rations to fulfill such requirements.

Two units of energy are in common use in the horse industry: the SI unit of energy, the joule (J where kilojoule [kJ] = 10^3 J, and the megajoule [MJ] = 10^6 J), a unit of electrical work used predominantly in Europe, and the calorie in the USA (4.184 J approximates to 1 calorie).

Requirements and intake are given either as the amount per kg of DM (zero moisture) or the amount in air-dried feed (assumed to contain 12% moisture). Depending on the system and the country, recommendations are given for estimated metabolic body weight and others for actual body weight. Various equations have been used around the world to predict energy requirements. The NRC (1989), for example, uses for **maintenance** (up to 600 kg BW):

$$\text{Maintenance} = 4.184 \times (1.4 + 0.03 \times \text{Body weight}) \text{ MJ DE/day}$$

An adult horse not doing any work typically requires, very approximately, about 13–15 MJ DE/100 kg body weight. The amount of total feed in the daily ration should be adjusted according to the amount of **work performed** and the **condition** of the individual horse. It is therefore important to monitor body condition and weight regularly. Obese or underweight horses are unlikely to perform optimally, and certain clinical conditions may result in a loss of weight.

As energy is stored by the horse there is no requirement for energy needs to be fully met on a daily basis. Indeed it is unlikely that they will, or should be. The immediate energy requirements are met almost entirely from energy stored as glycogen, fat, circulating glucose and high energy phosphates.

Energy deficiency and excess

A protracted deficiency of dietary energy causes a **loss of depot fat** and of **muscle mass**, whereas excess dietary energy leads to fat deposition at subcutaneous abdominal and intra- and inter-muscular sites. Both can result in clinical signs as well as changes in temperament.

PROTEIN

Dietary protein is normally measured as crude protein (CP: nitrogen × 6.25, for most common feedstuffs). **Digestible crude protein** (DCP) is defined as the proportion of dietary CP that is **apparently** digested. Frequently this is a calculated value rather than a value derived from digestibility studies in horses, and it varies considerably from approximately 40% to 80% of CP. The digestibility appears to vary in relation to the protein content of the feed

(e.g. low protein grass hay will have a lower protein digestibility than high protein alfalfa hay) and to the concentrate–roughage ratio (increasing the concentrate–hay ratio from 1:1 up to 3:1 will tend to increase digestibility; above this range the digestibility may decrease).

Protein sources

Most feedstuffs contain some protein but, as indicated in Table 3.1, there is considerable variability in the amount of protein and amino acids, especially lysine (limiting to the rate of tissue protein synthesis). The oil seed meals are generally good sources of protein whereas cereal grains contain less protein and are also generally poorer in their amino acid profile. Grass hay typically provides less digestible protein than cereals, whereas the protein value of legume roughages depends considerably on the care that has been taken to preserve **plant leaf**.

Dietary protein requirements

Requirements vary in proportion to tissue demands for protein synthesis and are, therefore, much greater during lactation or during growth than for adult working horses. The requirements are set (see Table 3.6) as those that meet the minimum needs of approximately 95% of healthy horses, accepting that individual differences exist. During ill health, such as recovery from trauma and infection, **protein needs increase** considerably.

Again, recommendations vary according to the various systems. The NRC recommends approximately 10 g CP/MJ of DE per day for horses at rest and in work.

Protein deficiency

Insufficient dietary protein causes a **negative nitrogen balance**, loss of protein from tissues, restrictions in milk production of lactating mares and growth failure in foals. There are no specific symptoms of deficiency other than a **gradual loss of muscle and liver mass**, with a decline in blood plasma albumin concentration, failure of suckling foals, or of weaned foals, to grow and some loss of appetite. A protein deficiency is possible especially where poor roughages constitute the majority of the diet, when **energy** will also be limiting. This partly results from a decline in the ability of large intestine microorganisms to degrade dietary fiber when nitrogen intake is severely restricted.

Amino acid balance

A **protein deficiency** implies an amino acid deficiency. Few natural protein sources contain the optimal proportion of dietary essential to non-essential amino acids, and few potential feed proteins contain an ideal distribution of the 10 dietary essential amino acids (based on experimental work on growth in the rat). Thus, in biologic terms, a protein deficiency can be most efficiently rectified by giving initially supplements containing the amino acid(s) that

is/are the principal limiting amino acid to tissue protein synthesis (including growth, milk production, etc.).

In the horse, **lysine** has been established as the first limiting amino acid for most diets. Of the other dietary essential amino acids, only six of the 10 have been demonstrated to change in respect of their blood plasma concentration when a protein deficiency is induced. These are isoleucine, leucine, phenylalanine, threonine, tryptophan and valine. Few of these have been adequately examined, although it is believed that for growing horses **threonine** may be the second limiting amino acid.

The practical solution for supplying additional limiting amino acids is to add **soya bean meal**, or other good quality protein, to the diet. It could then be assumed that the need for the limiting amino acids would be met (providing extensive synthetic sources alone have not been used, see below).

Protein excess

A moderate excess of dietary protein (up to approximately 50% above the requirements of the individual) has no observable adverse effect in healthy horses. More than this may cause a slight reduction in the performance of racehorses and possibly some reduction in appetite. It has been recommended not to feed >2 g DCP/kg BW to exercising horses, especially endurance horses.

Protein, however, is not a nutritionally preferred option as an energy source as it is inefficiently converted to usable energy with proportionally higher amounts of waste energy (heat) produced; the nitrogen must be removed, as excess protein is not stored. Excess protein is degraded in the liver with the formation of urea. This is excreted by the kidneys (urine) and is secreted back into the lumen of the gut. There are potentially higher **ammonia levels** in the stable as the urea in the urine is converted by bacteria in the environment to ammonia.

The process of degradation and excretion of the products requires the expenditure of energy and increases basal water requirements. Where there is loss of either hepatic or renal function, large excesses of dietary protein may cause an accumulation of protein degradation products and even cause **ammonia toxicity**, although under normal circumstances this is unlikely.

Protein excess may result in increased renal losses of Ca and P, although evidence regarding this is conflicting. Despite a link in many horse breeders' minds, there have not been any conclusive studies demonstrating adverse effects of high or low protein intakes on the incidence of **developmental orthopedic disease (DOD)** (*q.v.*) in the horse.

Deficiencies and excesses can also occur where total protein intake is within the normal range, but where dietary amino acid imbalances exist. The most likely situation is when growing horses receive diets providing poor quality proteins deficient in lysine. Another possibility exists where synthetic amino acid supplementation occurs of some amino acids only or in the incorrect proportions.

MINERAL AND TRACE ELEMENTS

The macro- and micro- (or trace) elements required in the diet for normal cellular function can be provided inorganically or organically. **Macroelements**

are required in quantities in the range of several grams per day and include sodium, potassium, chloride, calcium, phosphorus and magnesium. Sulfur is normally considered a macromineral and is provided organically from proteins containing sulfated amino acids such as methionine and cystine. The **electrolytes** (Na, K, Cl, Ca, Mg—substances that exist as positively or negatively charged particles in aqueous solution) principally affect intra- and extracellular ion and acid-base balance. **Microelements** are required in milligrams per day and include iodine, iron, manganese, zinc, selenium, cobalt and copper.

The elements that are most frequently **deficient in natural diets** are calcium, sodium, chloride, copper, zinc, iodine and selenium. Others that could be deficient in some areas of the world include cobalt and chromium. It is also possible that some of these elements could be present in toxic quantities.

Utilization of dietary sources

The availability, i.e. the proportion of an element that can be absorbed (**true digestibility**), differs considerably amongst sources of the same element, and also amongst elements; for example, the availability of common calcium sources may vary from 35% to 60% whereas the extent to which some trace elements are absorbed may be <5% of that consumed. In addition, there may be marked individual variability in the availability from different sources. Thus it is often not possible to give exact values for required dietary content.

Interactions

There are **many interrelationships** amongst the macro- and micronutrients. Few of the possible interactions have been thoroughly investigated in the horse and in practice only a few of the possible interactive effects appear to require practical measures to avoid adverse consequences. For example, while little evidence exists that moderate excesses of dietary Ca have any deleterious effects on P or Zn utilization, an excessive dietary concentration of P with Ca:P ratios ⩽1.0 may depress calcium absorption and may cause skeletal problems.

Mineral requirements

The minimal maintenance requirements of minerals depend on their endogenous (inevitable) fecal, renal and cutaneous losses and their availability (Table 3.11).

Calcium, phosphorus and magnesium

In adults, the rate of **calcium** absorption seems not to be regulated at the gut wall, so that the amount of calcium absorbed increases proportionately with intake. Renal excretion therefore increases with intake. Calcium absorption appears to be higher in younger than in older animals. It is, however, reduced with high intakes of oxalic acid and phytate. Greater than 0.5% oxalic acid in

Table 3.11 Guide to endogenous mineral losses by horses, average availability and the minimum mineral requirements for maintenance per kg BW/day

	Ca	P	Mg	Na	K	Cl
Endogenous losses (mg/kg BW/day)	30	12	5	18	40	5–10
Assumed availability (%)	60	40	35	90	80	95–100
Requirements for maintenance (mg/kg BW/day)	50	30	15	20	50	80[1]

The endogenous losses include a safety margin to allow for variations resulting from the type of feed, the individual animal and the amount supplied.
[1] *According to influence on acid-base balance.*

the feed may reduce calcium absorption when the calcium–oxalate ratio is <0.5 (weight to weight basis). With a ratio ⩾1, higher oxalic acid levels (up to 0.87%) may be tolerated. **High phosphorus intake** (especially in the form of phytate) may disturb calcium absorption, especially when the Ca:P ratio is ⩽1.

Major natural **sources of calcium** are leafy forages, particularly legumes, while supplementation may be achieved for example with limestone flour, calcium gluconate or dicalcium phosphate.

The greatest requirements for calcium arise in the young foal where bone mineral is being accreted. Inadequate calcium intakes by developing foals are characterized by poor mineralization of the osteoid tissue (*q.v.*). Mares at the peak of lactation use considerable quantities of calcium for **secretion in milk** and therefore their requirements are higher than those of other adult horses. At peak lactation they are usually in negative calcium balance, drawing on **bone calcium reserves**. In working horses, low calcium intake or high oxalate or phosphorus content in feeds can lead to **nutritional secondary hyperparathyroidism** ("big head disease") (*q.v.*).

Although there is no conclusive evidence that excessive calcium intakes are harmful to skeletal development in the horse, it is considered inadvisable to exceed 3–4 times the requirements as shown in Table 3.12.

Phosphorus absorption, which mainly takes place in the large intestine, is not affected significantly by high calcium intakes. Phytate P of plant origin is less well absorbed than inorganic P, but it may be partially available because there is some phytase activity in the large intestine.

Cereal grains and their by-products are the principal sources of phosphorus. Phosphorus from cereal sources is approximately half to two thirds as available as that in dicalcium phosphate, the common supplementary source.

Protracted and inadequate intake of phosphorus may produce skeletal abnormalities in growing horses similar to those produced by inadequacies of calcium and vitamin D. Deficiency may also cause **abnormal appetite**.

Excessive phosphorus reduces calcium absorption and potentially leads to **nutritional secondary hyperparathyroidism** (*q.v.*). Dietary phosphorus should conform to the amounts indicated in Tables 3.6 and 3.12, and the calcium–phosphorus ratio should lie between 1:1 and 2:1.

Magnesium absorption is slightly higher from organic compounds (e.g. magnesium aspartate) than from inorganic sources (e.g. MgO). No negative effects on absorption have been reported with oxalates. Hay feeding has

Table 3.12 Guide to the mineral and vitamin requirements of horses per kg feed (DM) for a horse of mature weight 500 kg. NB The maximum tolerated is the level at which signs of toxicosis are more likely to occur; this may mean that under certain circumstances unwanted signs may be seen at lower levels. Lower limits, e.g. for selenium, also may be set by relevant legislation

	Maintenance	Pregnancy/lactation	Growing[1]	Maximum tolerated
Typical daily intakes (kg)	8	9–14		
Calcium (g)	2.5	5	6	(15%)[2]
Phosphorus (g)	1.5–2.0	3.4	3.5	(10%)[2]
Magnesium (g)[3]	1.2–1.5	1.5	1.5	(6%)[2]
Sodium (g)	1.25	1.5	1.0	12.5
Iron (mg)	40	50	50	750
Manganese (mg)	40	40–60	40–60	750
Copper (mg)	10–15	15–20	15–20	400[4]
Zinc (mg)	40	45–80	60–80	500
Selenium (mg)	0.1	0.2–0.3	0.2	2.0[5]
Iodine (mg)	0.1	0.2	0.2	4–5[6]
Cobalt (mg)	0.1	0.15	0.15–0.2	20
Vitamin A (IU)	2–4000	4–6000	4–5000	20 000
Vitamin D (IU)[7]	3–600	800	900	2200
Vitamin E (IU)	50–100	80–160	80–160	1000[8]
Thiamin (mg)	3	3–5	3–5	3000
Riboflavin (mg)	2–4	2–4	2–4	

[1] Typical allowances for growing horses are 400 g/day DM per individual per mo of age up to weaning. Heavy topped foals may require a smaller intake of energy and protein, but mineral and vitamin allowances should be maintained. After weaning, daily intakes of air-dried feed should be equivalent to 2.5–3.0% BW daily up to around 18 mo depending on breed. If protein and energy allowances are decreased, mineral and vitamin intakes must be maintained. After 18 mo, feed allowances can be reduced if growth rate has become minimal.

[2] A very approximate guide.

[3] Assuming availability of 35%.

[4] Less may be tolerated by growing horses, particularly if zinc intake is not also elevated.

[5] European legal limit of 0.5 mg/kg DM ~ 1 mg/100 kg BW.

[6] In pregnancy advised not more than 1 mg/kg DM.

[7] Allowances of up to 1500 IU vitamin D have been recommended by some authorities.

[8] No evidence is currently available that more than this level will produce adverse effects in the horse, see text.

been said to favor calcium and magnesium absorption (in contrast to pure concentrate feeding). Major sources are oil seeds, rice grains, legume forages, sugar beet pulp and sugar beet molasses. Most good quality mixed natural diets contain at least 0.1% magnesium. This will meet the requirements of the majority of horses. Nevertheless many manufacturers provide supplements of magnesium as calcined magnesite (MgO), in commercial feeds. The availability of magnesium in MgO of various origins has been shown to differ for the ruminant, but no equivalent studies have been undertaken for horses.

Muscular tremors and **ataxia** resulting from acute hypomagnesemia are unlikely to occur in horses given good quality natural feedstuffs, but may occur in horses receiving magnesium-deficient feedstuffs although not proven to date.

No evidence has been produced that excessive intakes of magnesium are harmful, except **sulfates**, which are **purgative**. Although there is a potential risk of magnesium toxicity where dolomite limestone is used, the lack of evidence for this may indicate low availability of magnesium from this source.

Sodium, potassium and chloride

With a low sodium or potassium intake the endogenous losses will be reduced to <10 mg/kg BW/day for sodium and around 5 mg/kg BW/day for potassium. However, this does not appear to be the case for chloride. Low intakes may increase the true absorption rate for sodium and potassium. In horses with diarrhea or dysfermentation in the intestine, the fecal losses and, therefore, the total requirement will increase.

The maintenance requirement of chloride is not only related to the Cl balance but also to the acid-base metabolism. Intakes of <80 mg/kg BW/day may result in lower plasma Cl concentrations (≤100 mmol/L), alkaline urine, and a tendency for the development of metabolic alkalosis (*q.v.*).

Sodium and chloride are commonly provided by common salt, milk products and sugar beet molasses. Nutritionally improved straw is also a source. The main sources of potassium are leafy forages, sugar beet molasses and milk products.

The provision of forage and water in the last meal before extended exercise increases the fluid and electrolyte contents of the large intestine, which it is believed can act as a reservoir of these nutrients.

Possible clinical signs associated with deficiencies

Forages are generally rich in potassium, and diets containing adequate forage of good quality are unlikely to be potassium deficient. Acute water and potassium depletion may occur in foals with chronic diarrhea, or in adult horses subjected to extended exercise, especially when being fed low forage intakes and/or in hot weather. In both cases, **water and electrolyte supplements** are required to bring about immediate rectification.

Whereas most good quality rations provide sufficient potassium for normal maintenance, **supplementary sodium** in the form of common salt is generally advised, and is necessary for horses given rations based on cereals and undertaking extended exercise in hot weather. Sodium, potassium and chloride are major constituents of sweat, and depletion of these electrolytes by heavy sweating suppresses thirst and the desire to drink despite dehydration.

Possible clinical signs associated with excess

The horse has little capacity to store water or potassium and excessive dietary intakes are rapidly excreted, although in the case of potassium this assumes that water intake is adequate. Potassium toxicity is unlikely except when given parenterally in excess, when it can cause **cardiac arrest** (*q.v.*) or **hyperkalemic periodic paralysis** (*q.v.*). Sodium toxicity is unlikely under normal circumstances, except where a dehydrated horse is given access to salt water ad libitum.

Micro- (trace-) mineral requirements

Principal sources of microminerals

The adequacy of most natural plant materials as sources of microminerals depends to a large extent upon the soil on which the plants are grown. However,

soil content and plant content, especially for certain trace elements such as selenium, do not always closely correlate. It is common practice to supplement feeds with inorganic sources. These should be prepared by competent organizations, as there is a risk of providing excess. Synthetic sources are the most practical alternative for copper, manganese, zinc and selenium. Seaweed meal or potassium iodide can be used as sources of iodine, although toxic intakes have occurred where users have not been aware of the risks of excess.

The most critical trace elements in typical horse diets are iodine, selenium and copper (see Table 3.12 for information on requirements).

Deficiencies and excesses of microminerals

Signs of **iodine** deficiency and excess are similar, and are observed under practical conditions only in foals. Diets for the dam that provide <0.5 mg or >50 mg iodine per day, with a daily dry feed consumption of 10 kg, are likely to cause goiter. Some reports suggest that even lower intakes may increase the risk of **goiter** (*q.v.*) and therefore it has been recommended that pregnant mares are in fact fed <1 mg iodine/kg DM intake and preferably not >1 mg of iodine per 100 kg BW. Excess iodine is also a possible cause of bony abnormalities in foals. Excesses are commonly caused by feeding large amounts of **seaweed meal** or supplementation with excessive potassium iodide or iodate.

Horses apparently can tolerate high levels of dietary **copper**. Dietary deficiencies of copper, including **copper-deficient pastures**, especially for the dam during gestation, are thought to be a factor in the pathophysiology of certain developmental orthopedic diseases (*q.v.*). It has been suggested that diets containing approximately 20 mg/kg DM may be preferable both for the pregnant and lactating mare as well as the growing foal. Moreover, copper availability in pastures may be adversely influenced by heavy metals.

Zinc deficiency in foals is accompanied by inappetence, reduced growth rate and parakeratosis (especially of the lower limbs). Zinc deficiency and excess have been linked to DOD, although there are limited data to support this assertion. Excessive intake can depress plasma copper concentration.

Manganese is required in the synthesis of chondroitin sulfate and deficiencies in other species have led to abnormalities in **cartilage development**. **Cobalt** is required by intestinal bacteria in the synthesis of vitamin B_{12} and therefore is likely to be of most importance to breeding mares and growing foals. **Iron** is essential for the synthesis of hemoglobin, myoglobin and the cytochromes. Natural diets containing 50 mg/kg iron should be adequate for growing foals, and therefore a deficiency should not occur where good quality natural diets are given. There is a risk of toxicity (**nutritional siderosis**) where excessive supplementation occurs.

Selenium deficiency is seen particularly in foals of mares grazing **selenium-deficient pastures**. This may lead to nutritionally associated myopathy (**white muscle disease**) (*q.v.*), which occurs in both skeletal and cardiac muscle. Selenium deficiency may also lead to **depressed immune responses** and **lowered thyroid hormone availability**. Diets containing <0.05 mg/kg DM are likely to depress blood glutathione peroxidase (GSH-px) activity below an acceptable limit.

The margin of safety for selenium is relatively narrow and selenosis can occur. While **acute toxicosis (blind staggers)** (*q.v.*) tends to result in blindness, as well as gastrointestinal, cardiovascular and respiratory signs, it is the more chronic form of toxicity (alkali disease) (*q.v.*) that is more common and causes problems for the feet. The signs include **hair loss**, especially in the mane and tail, and **sloughing of the hooves**. This is seen in particular in areas of seleniferous soils/plants and when supplementation is miscalculated. It has also been suggested that moderately high intakes of selenium, which are not toxic enough to cause the signs described above, may affect the frog horn and be a factor in some cases of persistent thrush.

There is a current legal European limitation to the amount of selenium that can be fed to horses (maximum of 0.5 mg/kg diet at 88% DM) which approximates to around 1 mg/100 kg BW as fed.

Horses are more tolerant than are cattle to excess dietary **fluoride** and adults seem to be able to tolerate 50 mg fluoride per kg DM for extended periods of time.

VITAMINS

Introduction

Vitamins are a heterogeneous group of organic substances, essential for life, that have metabolic functions and are not degraded as sources of energy. They are arbitrarily divided into those soluble in fats and fat solvents, and those soluble in water. Most vitamins are represented by more than one compound, which may have different potencies. Certain **pro-vitamins** exist, e.g. β-carotene and 7-dehydrocholesterol, that do not possess vitamin activity but which can be converted into active vitamins by the body.

The ability of the body to store reserves of vitamins varies. For example, enough vitamin A can be stored by the liver to last for 2–6 mo and reserves of vitamin B_{12} can last for a year through enterohepatic cycling, whereas reserves of thiamin may be sufficient for only 1–2 wk. The healthy horse, however, requires no dietary source of ascorbic acid (vitamin C) as it is synthesized in adequate quantities from glucose in the liver.

Each vitamin may have many functions with differing demands on reserves. It is possible that greater dietary amounts of certain vitamins than are necessary to sustain life may, therefore, have metabolic advantages under certain circumstances.

Vitamin requirements (see Table 3.12)

Similar to other nutrients, vitamin requirements can be affected by a number of factors including age, amount of exercise and reproductive status. However, many are also influenced by the health status of the individual and in particular that of the kidney and the gastrointestinal tract. The need for vitamin supplementation can also depend on external factors such as the type and quality of the diet and the amount of access to sunlight. Today many horses do not have access to good quality green forage all year round and therefore **vitamin supplementation** is often required. Relatively little research has been carried out into the vitamin requirements of the horse, in particular the amounts needed

not just to prevent or correct deficiency symptoms but to promote optimal growth rate, health and performance.

Fat-soluble vitamins: sources and possible clinical signs of deficiency and excess

Vitamin A

The principal source of vitamin A is β-carotene, contained in green herbage and to a lesser extent in carrots, yellow maize and legume seeds. Principal supplementary sources are the partly water-soluble retinyl esters of palmitate and acetate (synthetic). During the winter, herbage contains less pigment and may be deficient in β-carotene. Research has suggested that the use of certain synthetic β-carotenes as the sole source of vitamin A cannot meet vitamin A requirements of horses and is not to be recommended (always check the bioavailability). Heat, light and oxidation can destroy β-carotene content of feed and therefore the content is significantly reduced with storage.

Possible clinical signs associated with deficiency include night blindness, poor growth, excessive lacrimation, reduction in disease resistance and reduced appetite. Clinical signs associated with excess may include bone fragility and malformations, plus there have been suggested teratogenic effects. In adults there is unthriftiness, poor muscle tone, ataxia and loss of hair. Hypervitaminosis A is unlikely to result from the provision of rich sources of β-carotene, such as artificially dried alfalfa, as the horse is thought to be able to reduce the conversion of β-carotene to vitamin A.

Vitamin D

Vitamin D is provided as vitamins D_3, through ultraviolet (UV) irradiation of 7-dehydrocholesterol in the skin, and D_2 through exposure of ergosterol, found in plants, to the action of UV light during desiccation after cutting. It occurs in significant amounts only in naturally cured hays. **Ergosterol** also occurs in other plant forms, e.g. fungi, yeasts, etc. Irradiated yeast is used as a commercial source of vitamin D_2 (**ergocalciferol**). Commercial supplements of vitamin D_3 and D_2 are widely available. **Vitamin D is not believed to be essential for the absorption of calcium in the horse**. Vitamin D may be destroyed by heavy metals and alkaline components of feeds.

The dietary requirement for **vitamin D** is considerably influenced by the extent of exposure to **direct sunlight** and its angle of incidence. In winter there is almost no UV light at latitudes above 50°. The requirement is also influenced by the degree to which dietary minerals (Ca, P and Mg) are balanced and the extent to which the current year's sun-cured hay is given.

Possible clinical signs associated with deficiency include **skeletal abnormalities in foals** and **osteomalacia** (*q.v.*) in adult horses. Potential signs of a deficiency can include a decrease in appetite, food intake and growth rate as well as impaired mineralization of growing bone with a reduction in bone ash content, bone cortical area and bone breaking strength. True 'rickets' and osteomalacia as seen in other species have not been confirmed in foals or adult horses.

Possible clinical signs associated with excess vitamin D include hypercalcemia, hyperphosphatemia, bone resorption, soft tissue calcification, anorexia

and poor performance. When given in large oral doses, vitamin D_3 is approximately twice as toxic as vitamin D_2.

Vitamin E

Vitamin E (α-tocopherol) occurs naturally as several isomers of tocopherol and tocotrienol. The highest potency, as a vitamin, is possessed by the α-isomer of tocopherol. Research has suggested that the d-alpha form may result in higher plasma concentrations than the equivalent amounts of dl-forms. The richer sources are oils of green plants. Wheat germ oil is the richest source, containing 0.85–1.28 mg/g α-tocopherol. Synthetic supplements of α-tocopherol acetate are widely available. Natural sources are believed to be more bioavailable than the synthetic.

Whether **athletic performance** is improved by high dietary concentrations of α-tocopherol is unproven. However, there is some evidence that exercising animals may benefit from additional supplementation. Large doses accumulate in muscle and liver tissue, and the stability of polyunsaturated fatty acids of tissues is affected by their vitamin E content. Vitamin E is believed to be important for the immune system in general, and intakes of 160 IU/kg DM in gestating mares have been shown to specifically increase the **immunoglobulin concentrations of the colostrum** and subsequently in the suckling foals.

The requirement is currently considered to be between 1.5 and 4.4 mg/kg BW daily and even up to 6 mg/kg BW in the intensively exercising animal. Therefore, levels of 160–250 IU/kg DM feed have been recommended for the performance horse with an additional 100 IU/100 mL of any supplementary oil. This is higher than the level of supplementation of many rations and may be higher than the total vitamin E content, i.e. natural plus supplementary, of some rations. In particular, supplementation needs to be considered carefully for horses in work, gestating mares, sufferers of the **equine rhabdomyolysis syndrome** (*q.v.*), those being fed supplementary oil and those without access to green pasture.

Possible clinical signs of deficiency include vitamin E and selenium responsive myodegeneration "white muscle disease" (*q.v.*)—a common manifestation of vitamin E and/or selenium deficiency in young foals in particular. Possibly more important potential signs of deficiency are **depressed immune status**, poor performance, reduced fertility and fetal death. **Equine motor neuron disease** (*q.v.*) is believed to be caused by a lack of vitamin E, which may predispose the type 1 oxidative neurons to oxidative injury and death. It tends to occur in horses that are either stabled or have access to dirt paddocks and are only fed grass hay with a high grain ration. However, this is not always the case.

Possible clinical signs of excess have not been produced and are likely to require very high intakes. However, it has been suggested that very high doses may interfere with absorption or utilization of other fat-soluble vitamins.

Vitamin K

The horse appears to have **no need for supplementary sources** as the intestinal bacteria seem to synthesize the menaquinones (vitamin K_2), which are absorbed in adequate quantities. If there is chronic use of sulfonamides, or of other antibiotics, in amounts adequate to disrupt this synthesis then supplements may become necessary. Vitamin K status affects **bone metabolism** as

well as **blood coagulation** and it has been suggested that the requirement may increase during times of increased bone metabolism, but there is little work to support this in the horse.

It has been suggested that an increased risk of prolonged bleeding may be seen with the ingestion of certain plants, or if hindgut fermentation is severely depressed, or if liver function is compromised (as vitamin K is converted to its active form in the liver).

The plant form is not thought to be well absorbed and is therefore unlikely to cause toxicity; however, grossly excessive intakes of synthetic vitamin K_3 may be toxic and cause fatal anemia and jaundice. Injectable forms may be toxic and have been suggested to have the potential to result in depression, kidney failure, loss of appetite and laminitis.

Water-soluble vitamins: sources and possible clinical signs of deficiency or excess

Vitamin C (ascorbic acid)

Ascorbic acid is synthesized in adequate amounts by the liver and other tissues from glucose under normal circumstances. It has been suggested that the requirement may increase in times of stress and disease when natural production may not meet demand. Recently it has been shown that ascorbic acid is a key antioxidant in the fluid lining the lungs and that levels are reduced in horses with **recurrent airway obstruction** (RAO; formally known as COPD, or heaves) (*q.v.*) as well as with lung inflammation in general. Additional supplementation may be of value under such circumstances. Synthetic forms are sometimes used as supplements but the efficiency of intestinal absorption is very poor for some forms and their stability through processing varies.

The needs of the healthy horse for ascorbic acid are met by tissue synthesis, but horses that have been subjected to trauma, disease (especially of the respiratory system) or major surgery may require additional supplementation.

Vitamin B_1 (thiamin)

Thiamin is synthesized in the intestinal tract and is present in natural diets. The richest source is brewer's and baker's yeast, containing 150–160 mg/kg. The cereal grains are good sources, thiamin being contained in the scutellum and germ, so that cereal by-products contain 10–15 mg/kg. Synthetic thiamin salts are widely available.

Some feeds may contain insufficient amounts of **thiamin**, and supplementation to bring the dietary concentration to 3 mg/kg air-dried feed has been suggested to increase growth rate in young stock. Amongst exercising horses 4 mg/kg air-dried feed may be insufficient and it may be prudent to ensure that the level is approximately 5 mg/kg air-dried feed.

Signs suggested to be associated with deficiency include a reduced growth rate and appetite, leading to anorexia and loss of weight, ataxia, bradycardia, missing heartbeats, muscular fasciculations and decreased erythrocyte transketolase activity. Bracken fern poisoning (*q.v.*) (bracken contains thiaminase) causes nervousness.

As to excess, there have been unconfirmed reports that parenteral doses $\geqslant$5 mg/kg BW may have a **tranquilizing** effect.

Biotin

Biotin sources differ in bioavailability. Reasonably good sources include brewer's yeast, oil seed meals (especially rapeseed meal), alfalfa meal and maize grain, although availability in other cereal grains is low. Synthetic supplements are widely used. Biotin is synthesized by gut microorganisms in amounts adequate to supplement the diet for most horses. There is some evidence that certain types of **equine hoof defect** may be aided by biotin supplementation over many months or years. Biotin in wheat, barley, sorghum and bran is said not to be very available due to phytate binding.

Biotin has been identified as a key component of the metabolic pathways of cornification, and in cattle biotin has been shown to be specifically required for the normal production and cornification of hoof horn tissue. A deficiency of biotin, therefore, has often been related to poor skin, poor coat condition and/or poor hoof quality in other species.

Although evidence of biotin deficiency per se has not been published in the horse (and depressed activity of biotin-dependent carboxylase has not been investigated), there is some scientific research to suggest that when supplemental biotin is added to the diet of horses with poor hoof health, an improvement may be seen in some but not all horses. However, other defects do not respond to biotin and require adequate calcium, protein and possibly zinc. As it is not possible by eye to determine which horses have which type of defect, it may be that a **good balanced diet** with additional biotin is the initial route forward for horses with problem hooves.

The amounts of biotin that are recommended to be of value vary: levels of 3–4 mg/100 kg BW/day have been recommended in the literature (for a minimum of 6–9 mo). It is, therefore, important to recognize that biotin is not a panacea for all horses with poor hooves but that it may be worth considering for some.

Currently no recommended upper daily intake limit has been set for biotin but it has been suggested that horses are not given >3 times the levels recommended above.

Folic acid and vitamin B_{12}

Reasonably good sources of folic acid include brewer's yeast (15 mg/kg), green forages (alfalfa meal 1–5 mg/kg), wheat bran (0.8 mg/kg), oilseed meals and whole wheat (0.5 mg/kg). Synthetic supplements are widely available. Vitamin B_{12} is found only in animal products. For foals, fishmeal, milk products and synthetic supplements are used. The **foal** has the greatest need for dietary sources of **folic acid and vitamin B_{12}** as it does not have a fully functioning hindgut for some time after birth. Some evidence indicates a need for supplementation of horses in training with folic acid.

Synthetic supplements of folic acid providing 20–200 mg daily have been used, but there is little scientific evidence as to their efficacy. Suggested levels for folic acid are 0.55 mg/kg DM feed for adult horses at rest and in light to moderate work, approximately 1.1 mg/kg DM in pregnant and lactating mares, and approximately 1.7 mg/kg DM for those in intensive work and young growing horses with the greatest demands. **Vitamin B_{12}** levels of 5 μg/kg feed as fed for performance horses and 15 μg/kg feed for young growing horses have also been suggested.

Possible clinical signs of folic acid deficiency include **megaloblastic anemia with macrocytosis**. However, this has not been confirmed for folic acid in the horse. In other species differentiated from vitamin B_{12} deficiency by the absence of methyl malonyl CoA accumulation but with homocysteine accumulation in the blood.

Signs due to excesses of folic acid and vitamin B_{12} have not been produced in the horse.

No dietary supplementary requirement appears to exist for other water-soluble vitamins.

PRACTICAL NUTRITION AND PRACTICAL RATION FORMULATION

GENERAL ASPECTS

General information about rations and feeding technique is provided in several specialist books about horse feeding; in this chapter only an overview is given.

Horses are individuals and vary in many of the areas that influence their needs with respect to nutrients and energy. Owners and riders also have individual requirements with respect to the condition of their horse and the nature of the ride, some of which may be influenced by the diet fed. Some horses seem to be "extremely lively" whatever they are fed, others remain stoical, but what might make one horse fat or excitable may be ideal for its stable mate.

Although BW can be a useful guide to requirements, **feed conversion efficiency rates** vary significantly. Daily feed intakes determined as a percentage of BW must be used as a guide only, and adapted to suit the individual's metabolism. Regular monitoring of BW and condition scoring can be a very valuable tool.

Appetite

Horses have a **finite appetite**, which influences what they can be fed in order to meet their energy requirements. This ranges from approximately 1.5% to 3.0% of BW on an as fed basis for most adult horses, although nursing and weaning foals may eat significantly more. On average, most horses eat approximately 2–2.5% BW/day (at 88% dry matter), i.e. 10–12.5 kg for a 500 kg horse (corresponding to approximately 2% of BW on a dry matter basis, i.e. 10 kg DM for 500 kg BW).

Number of meals

Feeding rations based on roughage or silage in the stable causes few problems because the ingestion time is long (see Table 3.4). Feeding roughage twice a day is satisfactory. On the other hand, **horses eat concentrate feed very quickly** (see Table 3.3). To prevent disturbances in the stomach (gas production, ulcers) and/or in the cecum (acidosis) and to have the highest energetic utilization of the feed, horses should, ideally, not be fed >0.5 kg concentrate

feed/100 kg BW/meal. This means that horses (500 kg BW) that need >5 kg concentrate feed/day should be fed three times a day and performance horses with requirements for 8–10 kg concentrate feed/day should be fed four times a day.

When to feed and water

There has been considerable debate over the years about when and what to feed horses before they are exercised or at a competition. Should they be fed or fasted and when should the hay be fed in relation to the grain or exercise? Some studies have concluded that, at least in horses undertaking **event type work**, feeding large amounts of hay along with grain may result in a lowered plasma volume and an **increase in body weight**, which may be detrimental to performance. Recently it has been recommended that grain should be withheld from many types of performance horses for at least 3 h before exercise, but **repeated small quantities of hay** should be fed to ensure proper gastrointestinal tract function and psychological well-being.

After physical activity and sweating, horses should have water (**before feeding**) to restore their water losses. Initially small quantities (not too cold) should be offered soon after intensive exercise and during cooling out. Water may be offered ad libitum to a fully recovered horse. At other times it is not necessary to provide water only before feeding—it should be available constantly.

Protein digestibility may be improved by feeding a small amount of roughage a few hours before feeding concentrates.

Forage: concentrate ratios

Forage (fresh or preserved) should be the **foundation** of any horse's diet, even those in hard work. Many horses and ponies do not require any other core feed, and those animals with maintenance or low energy needs may be satisfied by feeding plenty of forage at 1.5–2% BW. As energy needs increase, hays with higher energy levels and greater digestibilities should be considered. If this is not sufficient then additional feeds will be needed to meet the energy needs. Protein, vitamin and mineral supplements are likely to be needed to supply the essential nutrients not contained in the forage, or the forage and additional energy source(s), especially if manufactured compound feeds are not being fed.

Those horses in little or no work or those that are extremely efficient feed converters may benefit from being fed lower energy containing roughages but care must be taken that this does not increase the risk of impactions (*q.v.*).

For the majority of horses, even those in work, at least 50% of the diet, on a dry matter basis, should be suitable forage (approximately 1 kg DM/100 kg BW). Even fit, very intensively working horses should be fed at least 35%, and preferably 40%, of DM intake as forage. This may be as "long" fiber, such as hay, or may be chopped or ground and pelleted. Under most circumstances it appears to be beneficial to provide a significant part of the fiber intake as either "long" fiber or as a long chop. Depending upon the season and land available for grazing, pasture may provide a significant proportion of the

forage requirements. Forage type should not be changed rapidly and poor quality forage should be avoided.

For accuracy of formulation, and particularly where nutritional problems are suspected, the forage must be **analyzed**. In practical situations where hay is purchased in small quantities, visual assessment of the leaf–stalk ratio coupled with knowledge of the typical analysis for that type of hay may provide a rough guide to nutrient content.

During certain times of the year the fiber levels in grass and other fresh herbage are low, the moisture content high, and the soluble carbohydrate level high. During these periods, restricted access to pasture is necessary for some animals (especially those prone to the **equine rhabdomyolysis syndrome** and **laminitis**) if such a nutrient composition is undesirable (*q.v.*). Where access to pasture is restricted, or animals are being kept on "starvation paddocks" for example, alternative sources of forage of an appropriate nutritional content (plus vitamins and minerals) must be provided to maintain key nutrient intake and to help avoid disorders such as **hyperlipemia** (*q.v.*).

Pasture

It must not be assumed that abundant pasture will meet all nutrient requirements. Pastures over the winter months are generally poorer sources of protein, energy and phosphorus. Moreover, with **wet winter weather** the calcium content can be low. Caution should be exercised where the pasture appears to meet energy, crude protein and fiber requirements (as judged by the animal's bodily condition) as the mineral and amino acid intakes may in fact be deficient. This is particularly important in brood mares, weanlings and yearlings turned out on abundant pasture. Other minerals, such as copper, zinc, and in some areas manganese and/or selenium, can also be very low.

As well as nutrient deficiencies some further risks should be taken into account, for example very short grass (golf grass) may lead to **ileal obstructions** while **high fructan** contents, especially in spring and harvest, may induce laminitis (*q.v.*).

For horses at risk, such as brood mares, young stock and laminitis cases, **herbage analysis** should ideally be used to provide the necessary data to indicate whether supplementary minerals and amino acids are required. Additional protein and energy from concentrate feed may not, however, be required.

CONCENTRATE FEED DESIGN AND SELECTION

There are two main options when selecting a concentrate regimen:

1. To use a manufactured compound feed (either cubes, coarse mixes or extruded feeds), or
2. To mix "straights" or individual raw materials and mineral and vitamin supplements to the desired specification.

The latter includes the practice of feeding cereals and a cereal "balancer".

Compound nuts, coarse mixes and extruded feeds

If a compound feed is used, it is vital that it is chosen to meet the requirements of the horse or pony in question. In most cases, these feeds are designed to be fed as virtually the sole concentrate feed, with hay, water and sometimes additional salt or other electrolytes. Additions may therefore cause **significant imbalances**. Owners should be discouraged from adding to the selected compound feed, in particular micronutrient supplements, as minerals and vitamins can be fed in excess. **Reduced performance** and possibly **clinical toxicosis** may result.

Most compound feeds contain a broad-spectrum mineral and vitamin supplement designed to meet the requirements of a normal, healthy horse for which the feed was designed, when fed at the minimum specified level. If higher levels of feed are required, larger amounts of micronutrients will also be consumed. These amounts are unlikely to be toxic, but this depends on their concentration and what other supplements are being fed. It is usually advisable to change to a feed with a higher energy density that is more suitable to that individual's requirements.

When the level of compound feed drops below the required minimum, either a lower energy and protein specification ration should be offered (at the required minimum level), or additional micronutrients should be added to the reduced concentrate intake.

"Straight" rations

Many owners still like to mix their own materials. This is often referred to as "traditional feeding". Unfortunately, much of the "tradition" has been lost or distorted. In addition, the nutrient composition of traditional feedstuffs may have altered as a result of changing agricultural methods. However, it is of course possible to use home mix rations very satisfactorily. Tables 3.6 and 3.12 can be used to help to determine the nutrient requirements of the horse in question. With knowledge of the raw materials, a mixture of these ingredients may then be selected to meet these nutrient requirements. It is likely that a broad-spectrum mineral and vitamin supplement will be required; these are readily available but must be assessed for their efficacy.

Mineral and vitamin supplements

Several mineral and vitamin supplementary feeds are available. The correct dose depends on ration calculation and the requirements of the horse. Most times they are only necessary to complete rations of roughage or roughage and grain. Industrially produced feeds from reputable manufacturers usually contain sufficient amounts of minerals and vitamins (when fed as recommended). Consequently there is normally no need for additive feeding of single minerals or vitamins unless for a specific reason, e.g. biotin and poor hooves.

Specific micronutrient supplements

Many supplements target specific potential deficiency areas or cases where limited research indicates that a higher level of a certain micronutrient may

enhance performance. These supplements include those said to provide higher levels of the antioxidant micronutrients vitamin E and selenium; the so-called "hematonics" which claim to provide elevated levels of the B complex vitamins, and perhaps iron and copper, for their roles in the hemoglobin molecule; or elevated levels of certain microminerals known to be important in musculoskeletal development such as copper, zinc and manganese. Although there may be cases where the use of these supplements is indicated (e.g. biotin for horses with poor hooves, vitamin E and selenium in gestating mares), in most horses they are not necessary.

Items to avoid

Items such as lawn clippings, large amounts of **rapidly fermentable feeds** such as apples, or feeds designed for other types of animals should not be given to horses.

FEEDING THE PERFORMANCE HORSE

The main specific problems in working horses result from their high energy, water and electrolyte demands.

ENERGY

Energy is supplied to the horse via its diet but fundamentally **energy is not a nutrient**. The chemical energy or gross energy contained within feeds needs to be converted into a form of energy that the cells can use for work or movement (usable or **net energy**).

The energy demand, above that of maintenance, required for various physical activities is suggested in Table 3.13. The average estimated requirements for working horses of energy and digestible protein are presented in Table 3.14.

The energy turnover in muscle during maximum exercise is high. According to recent figures, racehorses need 40–60 MJ digestible energy (DE) above maintenance during training or racing. Assuming the maintenance requirement of such animals is similar to that of other animals (see Table 3.14), the total requirement of DE is in the range of 100–130 MJ DE/day. However, individuals can vary considerably in how much energy they require to maintain condition and provide the rider with the type of ride they require, and all diets should be adjusted to the individual.

Tables 3.13 and 3.14 may be useful for estimating the specific energy demands of horses maintaining submaximal speeds over longer distances. For example, horses of 500 kg BW require for maintenance approximately 65 MJ DE; for 1 h walking (including tack and rider of 75 kg: total BW = 575 kg) = 5.75 MJ DE; for 1 h slow trotting, 14.4 MJ DE; for 10 min galloping 14.4 MJ DE, giving a total requirement of approximately 100 MJ DE/day. Cold weather may increase energy needs by 10–15% to maintain warmth. Exercising up hills or under heavy wet or deep soil conditions may also increase energy needs.

Table 3.13 Guide to the energy requirements above maintenance for various activities (kJ DE/kg BW)[1]

Activity	Speed (km/h)	Requirements		
		Per km	Per 10 min	Per h
Walking	4	2.5	1.7	10
Slow trotting	10	2.5	4.2	25
Fast trotting/cantering	15	3.4	8.3	50
Galloping	25	6.0	25	–
Top speed	40–50	Up to 40	30[2]	–

[1] *Horse and rider.*
[2] *Per min.*

Table 3.14 Guide to the recommendations for the supply of working horses with digestible energy (DE) and digestible crude protein (DCP). Note that this excludes rider and tack weight. (DCP intake from a ration will be approximately 40–80% of the CP content depending on the diet.)

Degree of work	Additional requirements in % of maintenance requirements (MJ)	Kg body weight					
		200		500		600	
		DE (MJ)	DCP (g)	DE (MJ)	DCP (g)	DE (MJ)	DCP (g)
Maintenance		31.9	160	65	318	72.6	363
Light	Up to 25	38	190	76	380	87	435
Moderate	25–50	44	220	87	435	100	500
Heavy	50–100	56	280	111	555	127	635
Very heavy	~100	64	320	127	635	145	725

The daily DE intake of **3-day event** horses (average 600 kg BW) during intense training (2.9 h/day) will be in the range of 150–170 MJ DE, but again many individual animals will not need anywhere near as much energy as this.

When horses work very hard for several days the energy requirements often cannot be covered by the energy ingested because their feed intake may be reduced and requirements are high. Such horses mobilize energy from the **fat stores** in the body. Therefore, before starting **long distance rides**, horses must be in **good condition**.

Recent work has suggested that at least in the more difficult endurance rides, thin horses with a **condition score** (CS) <3 (on a 1–9 scale) might be at a disadvantage because of lower energy reserves, whereas over-conditioned horses could have problems, for example due to the insulating effect of a thicker fat cover.

PROTEIN

If the energy intake or energy stores are adequate, exercising horses need only small amounts of protein above the maintenance requirements. An **additional**

protein supply should, however, be provided to cover the **endogenous fecal nitrogen losses** (which are about 3.6 g N/kg DM intake), the nitrogen loss in sweat (1–1.5 g N/kg sweat) and the building of new muscle mass after a period with low activity (bodybuilding).

In exercising horses, the protein intake (digestible crude protein: DCP) per energy unit (MJ DE) can be the same as in horses at maintenance metabolism, approximately 5 g DCP/MJ DE. With increasing energy demand the proportional increase in protein intake will fulfill requirements and maintain protein stores in muscle and organs and, by keeping the ratio of protein to energy at 5:1, even with a very high energy intake (150 MJ DE/day), an excess of protein does not occur (750 g DCP/day).

In **exercising horses**, especially endurance horses, an intake of >2 g DCP/kg BW/day should be avoided.

WATER AND ELECTROLYTES

As discussed above, sweat contains relatively low levels of calcium (approximately 0.12 g/L), magnesium (approximately 0.05 g/L) and phosphate (<0.01 g/L) but relatively high levels of sodium, potassium and chloride as shown in Table 3.10. There are also small amounts of various trace elements, e.g. iron at approximately 4.3 mg/L and zinc at 11.4 mg/L. However, the **main electrolytes lost** with sweat are sodium, potassium and chloride.

The water and electrolyte requirements of working horses are mainly related to losses in sweat and via the respiratory tract (water). Some figures for sweat production are presented in Table 3.9.

Horses do not reduce their sweat production even with extreme water deficiency. At maintenance level, horses need approximately 4–5 L water/100 kg BW/day (depending on diet and environment; see also Tables 3.7 and 3.8). The amount required increases proportionally with activity and sweat production (Table 3.9).

The total requirement of electrolytes depends on the amount of sweat produced and its composition. The **composition of sweat** does not change even with low intakes of electrolytes. Therefore the electrolyte requirement increases proportionally with higher activity and sweat production (Table 3.15).

Losses of calcium and phosphorus in sweat are small (see Table 3.9). Therefore the requirements of exercising horses are only slightly higher than maintenance (see Table 3.15). After a prolonged period without activity, calcium and phosphorus supply should be increased to approximately 20% above the recommended figures to compensate for the losses from the skeleton during inactivity. An excessive calcium intake (more than three times the recommended figures) should be avoided because the absorption of other nutrients (e.g. zinc, copper and iron) may be reduced. Excessive intakes have to be excreted by the kidney and the large intestine.

The magnesium requirement of performance horses increases because magnesium is lost in sweat (see Table 3.15), although it has been suggested that the magnesium concentration of sweat decreases approximately 30–60 min after the onset of exercise. Higher supplies of magnesium compounds have been recommended to improve performance but this measure is open for discussion.

Table 3.15 Recommendation for the minimum daily mineral requirements of adult working horses[1] (g/day): Based on Tables 3.9 to 3.11

Degree of work[2]	200 kg BW				500 kg BW				600 kg BW			
	1	2	3	4	1	2	3	4	1	2	3	4
Calcium[3]	10	11	11	12	26	26	28	30	31	32	34	36
Phosphorus[3]	6	6	6	6	15	15	15	15	18	18	18	18
Magnesium[4]	3.2	3.4	3.9	4.3	8	8.5	9.7	11	9.6	10	12	13
Sodium	9.2	14	28	38	23	37	70	96	27	45	84	115
Potassium	13	16	24	30	32	40	60	75	39	48	72	90
Chloride	25	33	55	71	61	81	136	178	73	98	163	213

[1] Assumed sweat production as per Table 3.9, i.e. light work ~0.75 L per 100 kg BW, moderate ~ 1.5 L per 100 kg BW, heavy ~ 3.5 L per 100 kg BW, very heavy ~ 5 L per 100 kg BW.
[2] 1, light; 2, moderate; 3, heavy; 4, very heavy.
[3] In young growing animals (2nd and 3rd year) increase supply by 20–30%. Some workers recommend that phosphorus requirements increase slightly with increasing work loads, with a corresponding increase in Ca intake to maintain a Ca:P ratio of between 1.5:1 and 2:1, see Table 3.6.
[4] Some recommend slightly higher magnesium intakes for working horses, see Table 3.6.

TRACE ELEMENTS

Iron is important for synthesis of hemoglobin and for replacing iron lost in sweat (see Tables 3.10, 3.12 and 3.16). With most rations, the iron intake of horses is adequate. Suboptimal hemoglobin values are usually not due to marginal iron intake. There are possible risks of inducing problems due to excessive iron given either nutritionally or via injection.

In exercising horses, the requirements for **copper** and **zinc** increase only slightly because only small amounts are excreted with sweat (see Tables 3.10 and 3.16). Because **iodine** requirements increase with heat production, and some iodine is lost in sweat, the supply of exercising horses should be higher than during maintenance.

Traces of **selenium** have been found in sweat and it has been suggested that there may be increased losses via the urine in exercising horses (perhaps dependent on selenium source). The supply of selenium to exercising horses should therefore be higher than for maintenance. Selenium in combination with vitamin E is important for integrity of muscle tissue.

VITAMINS

Fat-soluble vitamins

Vitamin E is important for exercise capacity. The tissue levels of vitamin E should be sufficiently high to prevent production of lipid peroxidation products. To obtain maximal tocopherol contents in various tissues, exercising horses need approximately 4–6 mg α-tocopherol/kg BW/day. Intakes from around 160 IU to 250 IU/kg DM intake are currently typically recommended for performance horses.

Vitamins A and **D** are not involved in energy turnover in muscle. Intakes higher than those needed for maintenance are therefore not justified (see Table 3.16). Since a moderate excess of vitamins A and D might affect performance negatively, intakes of >5–10 times the maintenance requirement should be avoided.

Table 3.16 Guide to the recommendations for the daily supply of working horses with trace elements and vitamins (based on allowing between 10 and 12.5 kg DM intake for a 500 kg horse)

	Per kg total feed DM	Per kg BW
Trace elements		
Iron	50–70 mg	1.0 mg
Copper	10–20 mg	0.2–0.5 mg
Zinc	40–60 mg	0.8–1.5 mg
Manganese	40–60 mg	0.8–1.5 mg
Cobalt	0.1–0.15 mg	2–4 μg
Selenium	0.2 mg	4–5 μg
Iodine	0.15 mg	3–4 μg
Vitamins		
Vitamin A	4000–6000 IU	80–150 IU
Vitamin D	400–600 IU	8–15 IU
Vitamin E	150–250 mg	3–6 mg
Vitamin B_1	3–5 mg	0.06–0.125 mg
Biotin[1]	0.05 mg	0.001–0.00125 mg

[1] *Note that this not the level that would be recommended for specific hoof support, see text.*

Vitamin K is sometimes used to prevent exercise-induced pulmonary hemorrhage. There is no evidence to support this practice.

Water-soluble vitamins

Racehorses, in comparison with other types of horse, appear to be more susceptible to marginal **thiamin** deficiency (*q.v.*). It is thought that this occurs as thiamin is required for energy utilization and the racehorse requires such a large amount of energy. Furthermore, the gut synthesis may be lower in racehorses fed low roughage diets. Thus the recommendation of 3 mg thiamin/kg feed for maintenance may not be adequate for performance horses, and approximately 5 mg/kg air-dried feed has been suggested.

It has been suggested that animals in hard work that go "off feed" may be beneficially treated with a thiamin supplement (e.g. brewer's yeast); however, this is anecdotal. Stabled racehorses may require a **folate** supplement, but horses on pasture usually do not. Pasture is an excellent source of folate, although weathered pasture may have lower levels. High intakes of biotin (up to 20 mg/day for a 500 kg horse) might only be useful in horses that have a disposition for poor hooves. Doubt must be placed on the practice of giving regular doses of **vitamin B_{12}** to horses before racing.

ANTIOXIDANT SUPPLEMENTATION

Free radicals are independent yet unstable molecules that contain one or more unpaired electrons and are formed as the result of normal body processes. In particular they are formed as a result of aerobic metabolism, therefore their production is increased with exercise, but they may also be created following injury, disease or exposure to certain environmental factors such as allergens, pollutants or radiation.

The phrase "**reactive oxygen species**" (or ROS) (*q.v.*) is often used to describe all those free radicals and other molecules that are capable of causing oxidative damage and contain one or more oxygen atoms. "**Oxidative stress**" occurs when the antioxidant defense system cannot cope with the rate of free radical production. Left uncontrolled, the self-perpetuating "chain reaction" production of free radicals and the consequent damage they cause can lead to alterations in the structure of cell membranes, cell DNA and other cellular components, and cause disruption of normal physiologic processes (some of which may be irreversible), i.e. "**oxidative damage**".

In recent years, there has been growing awareness of the role of oxidative damage, at least in humans, in both the **aging process** and the development of a number of diseases or conditions such as asthma, cancer, skin disease, arthritis, muscular atrophy, cardiovascular disease, liver disease and autoimmune disease. It is thought that oxidative damage may also be implicated in similar diseases in animals. **Antioxidants**, often referred to as "**free radical scavengers**" (although not all antioxidants act by scavenging free radicals), are the body's natural defense against oxidative damage. The main dietary antioxidants for the horse are vitamins C, E and β-carotene as well as selenium. It is therefore important to ensure that adequate amounts are provided to all horses, in particular the performance horse.

There is now clear evidence, both in humans and horses, that a mixture of antioxidants (especially from natural sources) may be more beneficial than a single antioxidant in helping to support antioxidant defenses. Feeding of a single antioxidant or unbalanced mixtures of antioxidants may lead to antioxidant depletion, imbalance and a diminished antioxidant capacity; if fed in excessive amounts, some antioxidants may act as pro-oxidants.

FEEDING THE PREGNANT/LACTATING MARE

INTRODUCTION

It is increasingly recognized in the horse, as well as in humans, that nutrition of the mother may have a very important role in the subsequent health of any offspring. The gestation period of the mare commonly lasts 335–345 days but a considerable variation can exist. The pregnant mare should be kept fit throughout pregnancy, but not fat. Even before pregnancy, a lean but healthy barren, or maiden, mare is better where early conception is required. Individuals that are increasing in body weight are thought **more likely to conceive**.

By the seventh month of gestation the fetus will be approximately 17% of its birth weight. The majority of studies have suggested that embryonic development and fetal growth require no additional nutrients throughout the first 8 mo of pregnancy. Feeding a good balanced diet during this period is still very important. However, fetal growth obviously accelerates markedly during the last three months of gestation and this is a **crucial time** in the nutrition of the mare. Nearly half the copper, zinc, and manganese accumulation, for example, occurs in the 10th month.

Postnatally, pre-weaning is the period of most rapid growth (approximately 110 kg gain in the first 3 mo in Thoroughbred foals). Maternal effects (birth

weight, milk yield, etc.) appear to be more important than direct genetic effects during the early postnatal period. However, maternal influence decreases later in life and direct genetic effects become the primary influencing factors for growth.

During early to mid gestation the mare's nutrient needs for maintenance and any change in body condition or her own growth as well as any exercise should be met. Good quality pasture may meet energy and protein needs but it is unlikely to meet all the mineral requirements. Acute malnutrition with maternal weight loss greater than 50 kg has been associated with early embryo loss and it has been suggested that levels of nutrition of either half or double maintenance may have adverse effects on early embryo survival.

Late gestation is a crucial period in the nutrition of the mare. Mares have varying reserves that they can draw on if intakes during pregnancy are inadequate, but at what stage nutritional imbalances might influence the health of the foal or its health as an adult horse is currently unknown. There is an increased risk of inducing **hyperlipemia** (*q.v.*) if a pregnant mare is starved. It is recommended that the intake of feed be gradually increased during the last few weeks of gestation so that there is no sudden change in feed intake when the mare starts to lactate. The dam ideally should be kept in the foaling environment for at least 2 wk prior to foaling so that the antibodies produced and passed to the foal via the colostrum are appropriate.

Birth weight is important because of neonatal viability. In general, the mature number of cells in many tissues will have been achieved by birth or shortly afterwards, so to a large extent mature weight (apart from fat deposition) is determined by birth weight. It depends much more on the size of the mare than upon the size of the stallion or upon the amount of feed given during gestation. The amount of feed given to the mare during the latter part of gestation will, nevertheless, influence the flow of milk in early lactation.

Abundant good quality pasture can meet the energy, protein, calcium and phosphorus needs of **lactation**, even though the minimum dietary protein requirement will have risen to 125 g/kg of dry feed. Increases in milk yield have been obtained by providing a third more than this, but it is unlikely that this is desirable. As many horse pastures contain poor quality herbage species, the yield of good quality forage can be short lived and stocking density may be such that the provision of concentrates and hay is necessary.

Lactating mares will consume large quantities of roughage, but if the quality of this is poor, **milk yield will suffer**. This could be desirable around weaning to encourage the foal in the search of supplementary feeds and more grazing. A deficiency of water, energy, protein, calcium or phosphorus will ultimately bring about a decrease in milk output without altering its composition, so that within limits the foal will remain healthy but small and of slightly abnormal proportions, as for example, physes in the limb extremities may close early.

During lactation the concentrate proportion of the feed required will vary according to the individual and the quality of the feed being provided. A very heavy milker may need 1.75% BW as concentrates (non-forage portion) although more typical may be 0.75–1.25% BW, especially if the mare is being kept on good pasture. Typical feed intakes during lactation are approximately 2–3.0% BW on an as fed basis (approximately 90% DM). According to the NRC, mares produce approximately 3% of their BW as milk for the first 12 wk

of lactation and then an average of 2% BW for the next 12 wk. Other studies have suggested that the rates are higher—at around 4% reducing to 3%. Because of this discrepancy it has been suggested that the energy recommendations of the NRC are approximately 10–12% lower than those actually required.

A guide to the nutrient requirements of the breeding mare is given in Tables 3.6 and 3.12. The requirements of mares of other weights can be approximately gauged by interpolation (or within small limits of extrapolation). If the mare is lactating during the early part of gestation then her requirements during that period will exceed those of later gestation. The most crucial nutrients for mares given traditional diets are sources of energy, protein, copper, vitamin E, selenium, calcium and phosphorus.

ENERGY REQUIREMENTS

The first 8 mo of gestation have no practical impact on nutrient needs over those for maintenance unless the mare is growing, exercising or needs to gain condition. Most of the fetal growth occurs during the last 90 days of gestation. Even so, the nutrient drain incurred to sustain normal fetal growth is much less than that for lactation. Nevertheless, as the fetus occupies an increasing proportion of the mare's abdominal cavity, her **capacity for bulky feeds** declines during the period in which nutrient requirements increase. This may correspond to an increase in the quality of grazing but, if not, mares should be given forage and concentrates of higher quality than hitherto.

In **late pregnancy** some allowance for the energy needs of the fetus is needed. It has been recommended that mares in the 9th, 10th and 11th months of pregnancy (3rd trimester) should receive 1.11, 1.13 and 1.2 times the maintenance requirements respectively (NRC). Certain breeds may require more to maintain condition and optimal fetal development.

For a mare in the first 3 mo of lactation typically producing around 3% BW of milk according to the NRC:

DE MJ/day = Maintenance + allowance for the energy content in milk, i.e. [4.184 × (1.4 + 0.03 × Body weight)] + [(0.03 × BW* × 0.792) × 4.184]

PROTEIN REQUIREMENTS

The protein requirements of the pregnant mare are relatively low; nevertheless, when grass hays form a major part of the diet, supplementary protein is required as such hays typically contain only 5–7% protein. If they constitute 70% of the diet, then the concentrate should contain 16–17% protein for the latter part of gestation. The protein requirements for milk production are considerably higher, but vary with the potential yield at each stage of lactation (see Table 3.6). Where the intention is to reduce, or limit, milk secretion this is best achieved by restricting the total concentrate intake, rather than by lowering the protein content of that concentration.

The ratio of protein and calcium requirements to energy intake are not identical in pregnancy and lactation to those at maintenance, so one cannot

*__NB__ increase to 0.04 × BW if the mare is a heavy milker.

just increase the amount of the basal diet to match energy needs. For many mares a compound, manufactured, appropriately fortified feed (complementary feedstuff) specifically designed for the purpose can be advantageous in the last third of pregnancy and during lactation.

The NRC protein requirements are taken as crude protein intake and calculated for **pregnant mares** at a fixed proportion of the energy intake, i.e.:

> Requirements g/day ca.10.5 g/MJ DE/day or approximately 1.6–1.75 g of CP per kg BW (dependent on the type of ration being fed)

For the **lactating mare** this is calculated by allowing for the milk protein content and the amount of milk produced (and therefore should vary during the lactating period), but as a guide, in **early lactation** (up to 3 mo) for a 400–900 kg horse producing 3% BW in kg each day of milk (which is taken to contain 2.1% protein) plus allowing for the fact that CP is used for milk production at around 65% efficiency and that a reasonable quality ration is being fed with a protein digestibility of around 55%:

> Protein for lactating mares = Digestible protein for maintenance
> + DP for milk production divided by the estimated CP digestibility
> = **ca. 2.85 g CP per day/kg BW**

For heavy milkers this will increase to around **3.45 g CP per day/kg BW**.

In **late lactation**, with a milk yield of approximately 2% BW and a milk protein content of approximately 1.8%, the requirements will be approximately **2.10 g CP per day/kg BW**.

The digestibilities will vary with the diet, being higher than the estimated CP digestibility of 55% allowed for here if more concentrates are fed or high quality protein feedstuffs are used.

CALCIUM AND PHOSPHORUS REQUIREMENTS

During the last 90 days of gestation, mares kept entirely on reasonably good quality pasture or on high quality conserved forage containing some 30–40% leafy clover, alfalfa or sainfoin **require no other source of calcium** and, if the forage contains 10% protein per unit DM, no supplementary protein. The **phosphorus requirements**, however, amount to approximately 3 g/kg of the total dry diet. Although this would be provided by good pasture, it is frequently not provided by the hay typically given to horses in the UK. This hay normally contains <2 g phosphorus/kg and a supplement may be needed. However, there is a need to ensure that the overall intake of both calcium and phosphorus is adequate; the ratio is ideally between 1.5:1 and 2:1. Table 3.6 gives a guide to requirements. Full tables are available in textbooks but if the data are based on NRC recommendations it is important to remember that these are **minimal** requirements.

During lactation, calcium and phosphorus requirements depend on the actual amount of milk produced and the amount deposited within the milk as well as the availability of the nutrient from the diet. For example, heavy milkers produce approximately 4% BW as milk; moderate milkers approximately 3%, and low or late lactating mares approximately 2%. The amount of calcium

deposited in early and late lactation is approximately 1.2 g and 0.8 g/kg milk respectively. Assuming an absorption efficiency of 50%, this would mean a minimum requirement of **approximately 0.11 × BW g Ca/day** for a moderately milking mare in early lactation. However, 50% may not be valid for all individuals and all diets, therefore it has been recommended that more optimal levels may be approximately 0.14 × **BW g Ca/day**.

WATER REQUIREMENTS

The requirements of the mare for supplementary water during gestation and lactation are given in Table 3.8.

SUPPLEMENTARY FEED DURING PREGNANCY AND LACTATION

Supplemental vegetable fat or oil in the diet of pregnant and gestating mares can be beneficially used as an energy source, allowing for the fact that it provides no additional protein, vitamins (available vitamin E content is variable) or minerals.

Pasture and forage vary considerably in their nutritional content and yet in most pregnant and lactating horses these provide the bulk of the diet. These should ideally be monitored regularly so that the diet can be appropriately fortified for the individual circumstances.

Recent research has suggested that dietary supplementation of vitamin E (total intake of 160 IU/kg DM) and selenium (total intake approximately 0.2–0.3 mg/kg DM) to the mare during the peri-parturient period may beneficially influence colostrum concentrations of immunoglobulins.

It is also suggested that providing adequate copper supplementation during gestation in particular may be advantageous (approximately 15–20 mg/kg DM intake).

FEEDING THE FOAL AND WEANLING

REQUIREMENTS

Foals of many breeds have the capacity to grow relatively fast, but the rate of growth per 100 kg BW declines continuously from about 2 wk of age. The rate of growth of long bones and of skeletal muscle declines at an even faster rate and an increasing proportion of the gain constitutes fat, which has much higher demands for feed energy. Thus, the dietary requirements for protein, calcium and phosphorus, in particular, decline fairly rapidly as a proportion of the total diet with increasing age (see Tables 3.6, 3.12, 3.17 and 3.18).

By 12 mo of age, Thoroughbred foals reach approximately 60–70% mature weight, 90% mature height and 95% of eventual bone growth. This can be delayed somewhat, without incurring an ultimate reduction, by slightly reducing the rate of feeding. Foals growing at a rapid rate deposit greater quantities of bone, muscle and fat than their slower growing counterparts and therefore need more calcium, phosphorus, lysine, etc.

Table 3.17 Recommended requirements (based on the NRC, 1989)[1] of DE and CP on a daily basis for growing horses (500 kg mature weight) with varying average daily gains (ADG)

	Age (mo)	Body weight (kg)	ADG (kg/day)	DE (MJ)	CP (g)
Weanling	4	175	0.85	60.0 (14.4 Mcal)	720
	6	215	0.65	63.0 (15.0 Mcal)	750
	6	215	0.75	67.0 (16.1 Mcal)	805
	6	215	0.85	72.0 (17.2 Mcal)	860
Yearling	12	325	0.50	79.0 (18.9 Mcal)	851
	12	325	0.65	89.0 (21.3 Mcal)	956

[1] *Based on the National Research Council, NRC (1989)* Nutrient Requirements of Horses, *5th revised ed. © 1989 The National Academy of Sciences. Courtesy of National Academies Press, Washington DC.*

Table 3.18 Recommended **minimum** requirements (based on the NRC, 1989[1]) of calcium, phosphorus, magnesium, potassium, vitamin A and copper on a daily basis for growing horses (500 kg mature weight)

	Age (mo)	ADG (kg/day)	Calcium (g)	Phosphorus (g)	Magnesium (g)[2]	Potassium (g)	Vitamin A ($\times 10^3$ IU)	Copper (mg/kg)[3]
Weanling	4	0.85	34	19	3.7	11.3	8	10
	6	0.65	29	16	4.0	12.7	10	10
	6	0.75	33	18	4.2	13.0	10	10
	6	0.85	36	20	4.3	13.3	10	10
Yearling	12	0.50	29	16	5.5	17.8	15	10
	12	0.65	34	19	5.7	18.2	15	10

[1] *Based on National Research Council, NRC (1989)* Nutrient Requirements of Horses, *5th revised ed. © 1989 The National Academy of Sciences. Courtesy of National Academies Press, Washington DC.*
[2] *Higher magnesium levels have been suggested by other workers (see Table 3.10).*
[3] *mg/kg Cu in the feed on a DM basis. Higher copper levels have been recommended by other workers (see Table 3.9 and text).*
ADG, average daily gain.

Energy

The large intestine of the foal is relatively small and so it depends to a greater extent on digestible starch and sugars as sources of energy. Nevertheless it is prudent to stimulate the development of the large intestine and a mature digestive function. Thus high quality leafy hay may be provided in small and increasing quantities as a stimulant.

It is important to allow for maintenance plus growth **and exercise**, if appropriate, which means, based on the NRC (1989):

$$\text{DE MJ/day} = \text{DE for Maintenance} + \text{Allowance for growth: where}$$
$$X = \text{age in mo and ADG is average daily gain in kg}$$
$$= 4.184 \times ([1.4 + 0.03\,\text{BW}] + [4.81 + 1.17 - 0.023X^2] \times \text{ADG})$$

There is increasing evidence to suggest that the way energy is provided to the growing foal may be important, especially in relation to DOD (*q.v.*).

Replacing traditional diets high in starches and hydrolyzable sugars with ones high in fat and fiber has been suggested to have a number of **potential advantages**. The feeding of appropriately fortified **fat and fiber based diets** may help to reduce the incidence of certain digestive and metabolic disturbances as well as resulting in a reduced risk of DOD.

Protein

Protein requirements for growth in horses depend to a large extent on the amino acid requirements of the foal, the amino acid content of the feed ingredients and the digestibility of these amino acids. **Lysine**, as for the mare, is believed to be the first limiting amino acid in typical horse rations for growth and threonine is believed to be the second. The mare's milk has this quality, as do fishmeal and properly processed soya bean meal.

Minerals

The foal has particularly high requirements for calcium and phosphorus and, to a lesser extent, for magnesium, reflecting its skeletal growth (see Tables 3.6, 3.12 and 3.18).

Vitamins

The absence of a fully functioning hindgut necessitates a dietary source of B vitamins. Supplements of vitamins A, D_3 and E often should also be provided.

COLOSTRUM AND NEONATAL FEEDING

It is essential that the foal receives colostrum during the first 12 h of life, and the **absorption of the immunoglobulins** depends upon it not receiving other sources of food during that time. Where colostrum is not available from the dam the foal should receive it from another source. The first factor to be determined with the sick newborn foal (*q.v.*) is its immune status. If immunoglobulin levels are $\leqslant$400 mg/dL and the foal is $<$12 h old, then provision of equine colostrum should be considered and be administered by stomach tube (approximately 2 L colostrum or until immunoglobulin level reaches 800 mg/dL). If the foal is $>$12 h old, septicemic and/or hypothermic, the specialized absorptive cells lining the intestinal tract will have a **decreased absorptive capacity** and consideration should be given to providing **equine plasma** (2–4 L at $\geqslant$1600 mg globulins/dL) from a suitable donor or plasma bank. Immunoglobulin levels should be **monitored** and plasma administration can be stopped once levels are approximately 800 mg/dL.

Foals have **low energy reserves** and therefore can rapidly become **hypoglycemic** if undernourished. This is especially the case if they are **premature** or compromised by infection. The mare should be kept in contact with the foal when possible, even if it is too sick to nurse, so there is a greater chance of

the dam accepting the foal at a later date. There are two advantages if the dam can be milked:

1. The foal receives equine milk/colostrum from its dam.
2. The mare's milk supply will not dry up.

At birth, much of the large intestine contains the **meconium**, which is normally completely voided within the first 2–3 days of life. Sucking usually sets up a reflex promoting defecation of this material. If this does not occur, the normal passage of colostrum and milk may become blocked. The foal may then go off suck for an extended period and should be given fluid feed by stomach tube or appropriate IV solutions of glucose and an isotonic electrolyte solution.

SUPPLEMENTARY FEED

Normal foals start to nibble hay and concentrates at 10–20 days of age. If the supply of milk or the amount of grass is inadequate, the provision of a creep feed from this time may well enable a normal growth rate to be achieved. A month or so before the intended weaning time the foal should be given increasing amounts of a dry feed to compensate for a decline in pasture quality and in milk production of the dam and to accustom the foal to the dietary regimen it must expect upon weaning. This should reduce weaning stress. Any product should be adequately fortified with minerals, trace elements and vitamins and it should contain high quality protein.

WEANING

Age at weaning does not appear to influence significantly mature height and weight but nutrition around this time can be crucial. More gradual techniques of weaning seem to be beneficial. If foals are not used to eating solid feed before they are weaned they will show a more prolonged decrease in **ADG** post weaning which is often followed by an undesirable compensatory growth spurt. NRC states that 200–230 kg weanlings consume up to 3.5% BW but practical work suggests that intakes of approximately 2.5–2.9% BW are more likely. The NRC recommends 30% hay or forage in the ration regardless of the growth rate. Others suggest varying the forage–concentrate ratio depending on the desired ADG; however, it would be recommended that at least 30% of the ration was forage or forage equivalents.

Weaning (*q.v.*) should entail **reducing the supplementary feed of the mare**, or removing her from high quality pasture some days before weaning. Foals should have **company** subsequent to weaning but should be out of sight and earshot of the dam. As a proportion of the diet, requirements for protein and calcium are high at weaning, owing to rapid growth of muscles and bones and their mineralization (see Tables 3.6, 3.12, 3.18 and 3.19). The requirement for these declines markedly over the first year of life as the skeleton matures and as fat deposition replaces rapid muscle growth. Clean water should always be available to the foal and provided in an accessible manner from around 2 wk of age (see Table 3.7).

Table 3.19 Typical range in pasture composition (northern temperate) (mg or g/kg DM).[1] Note that individual pastures may be lower or higher than these guide ranges: e.g. ranges for copper were reported by MAFF in 1990[2] for the UK for all grasses as being between 3.0 and 20.2 mg/kg DM with a mean of 6.7 ± 2.6

	May	July–August
Crude protein (g)	170–250[3]	110–180
Crude fiber (g)	190–230	300–330
Calcium (g)[4]	4–12	3–9
Magnesium (g)	1.4–2.2	1.0–2.4
Phosphorus (g)	2.9–4.0	1.9–3.0
Potassium (g)[5]	18–22	17–20
Copper (mg)	4–12	4–12
Zinc (mg)	20–60	30–60

[1] Note that this illustrates how pasture alone may not provide all the macro- and micronutrients for horses at different life stages or with different lifestyles, e.g. calcium for the lactating mare and growing foal; sodium for the exercising horse; copper for gestation and growth. In particular, attention needs to be given to mares and foals out on pasture of unknown nutrient composition.

[2] MAFF (1990) UK Tables of Nutritional Value and Chemical Composition of Feeding Stuffs. Eds D. I. Givencs and A. R. Moss. Rowett Research Services, Aberdeen.

[3] A few pastures may have protein levels up to 300 g/kg DM or more, especially if primarily for cattle and not horses.

[4] Calcium levels may fall below phosphorus levels, giving reverse ratios over the winter and spring months.

[5] Potassium concentrations can be > 35 g/kg DM.

The **yearling's** appetite tends to be approximately 2–3% BW as fed. The maximum non-forage recommended is 60%. On good, lush pastures, only an appropriately **fortified vitamin and mineral supplement** may be required. Levels of approximately 1–1.7 kg complementary concentrate feed per 100 kg BW may, however, be required, especially for foals receiving grass hay based rations and those on poor quality pasture.

The **long yearling's** appetite tends typically to be approximately 2–2.75% BW as fed. It is recommended that the non-forage feed proportion should be a maximum of 50–60% of the total intake, i.e. approximately 1.0–1.35 kg complementary concentrate feed/100 kg BW.

SODIUM, POTASSIUM AND CHLORIDE REQUIREMENTS FOR PREGNANT, LACTATING AND GROWING HORSES

Pregnant, lactating and growing horses probably need approximately 0.1–0.2% of total diet as sodium (on an "as fed" basis). An average of 0.15% may be most useful.

Potassium intakes for the pregnant mare have been given as 0.38 g × MJ intake per day or approximately 0.35% potassium in the total diet at the end of gestation. Early lactating mares require slightly more potassium, depending again on the amount of milk being produced, the level of deposition in the milk and the digestibility, e.g. for early lactation in a moderate milker (=0.05 × BW + (0.03 × BW × 0.7)/0.5) = **ca. 0.092 BW**. These are minimal requirements from the NRC; more optimal requirements may be approximately 1.3 times these levels.

Recently, it has been recommended that the chloride intakes for pregnancy are 80–82 mg/kg BW/day; early lactation, 89–93 mg/kg BW/day; growth until 6 mo, 93 mg/kg BW/day; and growth 6–12 mo, 85 mg/kg BW/day.

EFFECTS OF DIETARY EXCESSES AND DEFICIENCIES

The young foal has higher requirements for nutrients per unit of feed than other horses.

Excesses

Concern exists that an excess of nutrients, and too rapid a rate of growth, may predispose the foal to **abnormalities in skeletal development**. Present evidence suggests that amounts of dietary protein sufficient for the foal to attain its potential growth rate have no significant adverse effect as long as the remainder of the diet is adequately supplemented. A moderate excess of calcium, trace minerals or vitamins also does not appear to have consistent adverse effects. **Excess dietary phosphorus** can, however, contribute to skeletal problems, and an excessive intake of soluble carbohydrate may contribute to the development of **DOD** (*q.v.*). **High dietary concentrations of soluble carbohydrate should be avoided**.

Deficiencies

The most obvious nutritional deficiencies seen in foals at birth are those of selenium, associated with vitamin E and selenium responsive myopathy, and potentially of copper, associated with **bony abnormalities**. These deficiencies reflect deficiencies in the mare's diet. In foals receiving inadequate milk, or in poorly fed weaned foals, general condition and conformation are adversely affected by an insufficient intake of protein and energy.

FEEDING THE AGED HORSE

INTRODUCTION

There is little reliable published information on nutritional needs specific to the aged horse. Nevertheless, the old horse is generally less able to assimilate feeds than are healthy younger animals. **Badly worn teeth** make it difficult to chew and ingest poor quality roughage, and body weight and condition can be difficult to maintain, especially in winter. Ground roughage contained in high fiber pelleted feeds can make a useful contribution.

Maintenance of normal body weight may require some concentrated feedstuffs. Elderly horses, and especially elderly ponies on good pasture, are subject to **laminitis** and **colic**. Therefore concentrated feedstuffs should be split amongst several daily feeds, and a feed of good roughage should be given, and eaten, before old horses are first introduced to pasture. Pelleted feeds are often helpful in avoiding colic, especially if they contain adequate and appropriate fiber (approximately 15%), 10–20% grain and approximately 12% good quality protein; vitamins and minerals are as required by other adult horses (see Tables 3.6 and 3.12). It is important to ensure that good quality protein is fed and that an adequate calcium and phosphorus intake is maintained.

The inclusion of cooked cereal grains as well as highly digestible fiber sources can be of benefit. Several high fiber pellets are available which, when

moistened and fed as mashes with additional salt and oil if required (and no contraindications), can be used as part or all of the diet of older horses with poor or limited dentition.

PROBIOTICS

Probiotics are **live microbial feed supplements** fed with the aim of improving the intestinal microbial balance. Much more work is needed in this area since the evidence for their use is currently conflicting. Certainly, **lactobacilli** have been administered to scouring foals for hundreds of years through the practice of allowing milk to sour in the manger. Similarly, fecal material collected from healthy horses has been used as a drench in cases of diarrhea (*q.v.*), as a way of recolonizing the intestinal flora.

When selecting a probiotic product, it is helpful to choose one that most closely resembles the normal range of flora in the intestine, although the use of selective strains may be beneficial under some circumstances. The product needs to reach its target area of the GIT in sufficient numbers to enable it to function effectively.

In recent years, certain **yeasts** have been included in probiotic preparations for their putative role in improving digestibility of fiber and other nutrients, notably phosphorus—in particular when added to cereal (starch) based rations. The apparent increase in digestibility has been suggested to arise at least in part from the yeasts stimulating the required enzyme-producing bacteria rather than from a direct effect of the yeasts themselves. Yeasts do not appear to be maintained in the established flora, and presumably need to be fed continuously to maintain their effect. Recently a yeast culture has obtained EU registration for use in equine diets and there is some evidence for beneficial effects when fed with high starch diets.

NUTRITION AND MANAGEMENT IN THE FIELD

The horse is less efficient at digesting fiber than domesticated ruminants and it therefore tends to seek out **younger herbage**. The capacity of pastures to maintain horses in good condition will depend on the amount of herbage in the pre-flowering state of growth. Studies that have been undertaken with horses weighing approximately 500 kg show that, with access to good quality pasture for 7 h daily, they can consume an average of 5.5 kg organic DM, sufficient to maintain their body weight. The intake of herbage diminishes with increasing maturity of that herbage and horses therefore eat reduced quantities of less digestible material, rather than more to compensate for its lower digestibility. Consequently the milk production of mares and the growth rate of foals and yearlings decline rapidly as pasture herbage matures to the flowering stage.

One hectare (approximately 2.5 acres) of high quality grassland could provide pasture and hay for 3–4 light horses of approximately 400 kg, or 4–6 ponies. Low quality permanent pasture, however, may support only one horse per hectare, and where rainfall is low many hectares may be required to supply the needs of a single horse throughout the year. Where the annual rainfall is

of the order of 61–64 cm, average quality grassland can produce sufficient growth for 2 horses and, when fertilized, for 3 horses per ha, or when just being used as summer pasture potentially up to double the number.

The productivity and feeding value of all pastures varies considerably with season (see Table 3.19), rainfall, soil fertility and ambient temperature. Pasture grasses that are going to seed, and brown-colored summer or winter (frost-affected) pastures tend to be of low feeding value for horses.

NUTRITIONAL ASPECTS OF METABOLIC DISEASES

INTRODUCTION

A proper assessment of the nutritional status of healthy working or breeding horses is always a difficult matter, but it is far more complex when there is a superimposed medical problem. The relationship of diet to growth and skeletal development of foals and horses, and a series of metabolic problems that commonly affect horses are described below.

DISTURBANCES OF GROWTH AND SKELETAL DEVELOPMENT

The necessity for correct nutrition of foals, weanlings and yearlings cannot be overemphasized, both in terms of productivity and longevity of competitive horses. Despite this necessity, few specific details of nutritional requirements are available and optimal growth rates of young horses have not been precisely established. This may be why problems of overnutrition in young animals appear to be much more prevalent than those associated with undernutrition.

The term **developmental orthopedic disease** (DOD) (*q.v.*) was first coined in 1986 to encompass all orthopedic problems seen in the growing horse and therefore encompasses all general growth disturbances of horses. It is non-specific and the definitions are not uniformly agreed. However, as defined by some, DOD may be taken to include **osteochondrosis (OC)** (*q.v.*), i.e. "a defect in endochondral ossification that can result in a number of different manifestations, depending on the site of the endochondral ossification defect", one manifestation of which is **osteochondritis dissecans (OCD)** and **subchondral cystic lesions (SBC)** (*q.v.*) of cartilagenous origin; **physitis** (*q.v.*) acquired angular limb deformities; flexural deformities; tarsal collapse; juvenile arthritis or juvenile degenerative joint disease; bony fragments of the palmar/plantar surface of the first phalanx of Standardbred horses (believed to be traumatic lesions); and wobbler disease or cervical vertebral malformation (*q.v.*).

It has been suggested that the clinical signs occur only after a progression of events that begin with a disturbance in the normal development of the cartilage (sometimes referred to as **dyschondroplasia** or DYP) leading to OC. At this point physical (i.e. biomechanical) stresses are superimposed, leading to clinical signs. It is also thought possible that the initial defects or lesions may heal or develop into OCD or SBC.

Due to the **multifactorial nature** of DOD, no single cause is likely to result in expression. Factors that may contribute include genetic predisposition,

biomechanical trauma, and mechanical stress through inappropriate exercise, obesity, rapid growth and inappropriate or imbalanced nutrition. Different combinations may be involved in different cases. Environmental or management factors most likely determine whether expression occurs, i.e. provide the final triggering factor(s).

Various nutrients have been highlighted over the years, in particular energy, calcium, phosphorus, copper and zinc and protein. Many studies have been undertaken and suggested to either support or refute the role of a particular nutrient. However, caution needs to be taken when evaluating and extrapolating from these studies. In a survey in Germany, for example, there was no apparent significant link between the feeding management of foals and the incidence of OC, and no relationship was found between the nutritional status of the mares (in relation to digestible crude protein and digestible energy) and the incidence of OC. However, for a number of reasons (e.g. when stabled, foals were not fed separately from the mares, estimations were used to determine milk and pasture intakes, etc.), the nutritional status of the animals could not be determined accurately.

OVERFEEDING FOALS

Energy

A number of studies have suggested that a high intake of energy may result in an **increased incidence of DOD**. A significant increase in incidence was for example found when diets provided approximately 130% of NRC energy intake (see Tables 3.6 and 3.17). However, it should be noted that there has been concern that the lesions produced by some of these studies are not directly comparable to those found in the field and many field studies have reported foals being fed much higher energy intakes without an apparent increase in clinical incidence. This may be linked perhaps to the background level of predisposition within the individuals, the nature of the energy being provided and the balance of the diet. It has been suggested for example that diets which intrinsically produce high glycemic peaks, or individual horses that respond to certain diets to produce high glycemic peaks (and subsequent effects on insulin and other hormones) may have an increased risk of developing DOD. Such diets have the potential to establish a feeding–fasting cycle, which is a perturbation from the hormonal patterns likely seen in grazing animals. This in turn may adversely influence bone development as the cyclical changes in glucose and or insulin may influence bone maturation via effects on the somatotropic axis.

In other species, such as the pig, dog and sheep, evidence of increased **osteochondral lesions** has been found in breeds with **rapid growth rates** compared with the slower growing breeds. Growth rate depends on both genetics and nutrition. A number of studies have linked rapid growth rates (and often, by inference, excessive feed/energy intake—see above) with an increased incidence of DOD. The connection, however, lacks strength because the chain of events between rapid growth and the molecular events that initiate DOD is a long one. Also, the multifactorial nature of this syndrome means that the connection is not always direct; for example, in some animals a rapid growth rate could be a predisposing factor but expression might only

occur when a number of other factors are superimposed (e.g. as a hypothetical example, those foals genetically predisposed to rapid growth whose dams were fed inadequate copper during gestation and who were subsequently fed an unbalanced diet as weanlings).

Rapid growth may affect bone maturation directly or indirectly due to mechanical overload or disturbances in nutritional supply and hormonal balance. These and other factors associated with rapid growth rates therefore may be involved to a greater or lesser extent in individual cases. However, it is generally recommended that rapid growth rates with high energy intakes should be avoided, especially in animals or breeds prone to DOD.

Despite proposals that excessive protein in the diet causes DOD, this has not been confirmed as a causative factor, nor does it appear to have deleterious effects on growth. However, diets with excessive high quality protein are expensive and therefore wasteful. Whether certain diets that contain higher amounts of insulinogenic amino acids are more likely to adversely affect the incidence of DOD is currently unknown.

In a study of Dutch Warmbloods, the incidence of OC in foals fed high intake with high exercise (HH), high intake with low exercise (HL), low intake with high exercise (LH) or low intake with low exercise (LL) was compared. The researchers found that the HL and LH groups had a significantly higher incidence of OC than the HH or LL groups, the highest incidence being found in the HL group. This suggests that it is likely to be a **combination of factors** that influence incidence and that neither low activity nor high intakes will always result in an increased incidence. However, the lowest incidence was in fact seen in the HH group, suggesting that, if matched by intake, appropriate exercise may be of value in reducing the incidence of OC.

The nature and type of exercise that should be taken is still under discussion. However, it has been suggested that **paddock exercise** may be preferable rather than just forced exercise. Several studies have suggested that the time of birth may influence the incidence of particular forms of DOD (positively or negatively) perhaps due to influence of time of year on nature of the pasture, access to land for exercise and the relative hardness of such ground.

Mineral imbalances

Imbalance of mineral homeostasis is another important facet of the pathogenesis of osteochondrosis (*q.v.*). Foals fed excessive amounts of phosphorus (e.g. four times NRC recommendations, with limited exercise) tended to show lesions of dyschondroplasia in one study, although there may be no clinical signs of nutritional **secondary hyperparathyroidism** (*q.v.*) provided adequate calcium levels are fed.

Excessive dietary calcium has been proposed as a cause of **hypercalcitoninism** leading to osteochondrosis and osteosclerosis (*q.v.*) but there is no evidence to support this theory in foals. The levels of calcium recommended by NRC appear to be adequate (see Tables 3.6 and 3.18) and supplementation (e.g. three to four times NRC recommendations) does not appear to be detrimental to the skeletal development of foals. Increasing the calcium–calorie ratio to foals fed excessive energy (e.g. 129% DE and 340% calcium of

NRC recommendations) does not appear to be protective as in one study lesions of dyschondroplasia still developed.

No adverse effects of **magnesium** have been reported in relation to the incidence of DOD. However, little direct work has in fact been done on this in the horse despite the fact that magnesium may compete for copper binding sites and excessive magnesium may inhibit parathyroid hormone (PTH) secretion.

A copper-containing enzyme—**lysyl oxidase**—is involved in the cross-linking of protein chains in elastin and collagen of cartilage. Disruption of these cross-links due to copper deficiency may result in biomechanically weakened cartilage and increase the risk of DOD. A number of studies have suggested a relationship between **copper** and DOD. In discussing the possible inter-relationship it is important to consider that:

1. Milk has a low copper content, which does not fulfill the copper requirements of the suckling foal. Normally the foal is born with high copper concentrations in the liver, which it is thought will compensate for the milk. If the mare does not get sufficient copper during pregnancy (15–20 mg/kg BW/day) then the foal is more likely to be born with low copper reserves in the liver which in turn makes it less likely to be able to compensate for the low intake from the milk.
2. If foals are grazing in an area with low copper values in grass (<5 mg/kg DM) without supplementation, then a copper deficiency may potentially occur.

Feeding high levels of copper does not automatically entail a reduction in the incidence of DOD. In a number of studies it has been suggested that early signs of DOD may resolve, although there may be a time component to this. In fact, recently it has been suggested that rather than low copper being a causative factor, an increased availability of copper may support various degrees of reparation. A study in Holland correlated the liver copper status of mares and foals with OC scores. All animals had the same availability of feed but their estimated intakes of copper ranged from 95 to 153 mg/day and resulted in mean foal liver copper levels of 372 mg/kg at birth. No direct link between liver copper status of mares and foals at birth or radiographic evidence of OC development in foals at 5 or 11 mo was established. However, foals with higher liver copper status at birth showed increased recession of lesions before reaching the threshold age of 8 mo. It could be suggested that a slightly better placental supply and greater liver stores at birth helped in the lesion repair process and that a good copper supply during gestation may be advantageous. This conclusion is supported by work carried out in New Zealand that suggested possible advantages of providing supplements to the gestating mare, although further research on a much larger scale is needed in this area.

In conclusion, more recent work confirms that **copper supplementation** may not be the "magic bullet" suggested by some in the past as far as DOD is concerned. However, reduced copper intake or absorption, especially during gestation, could possibly either be permissive to the development of DOD under certain conditions or reduce the ability to repair lesions.

Horses appear to have a high resistance to **chronic copper toxicity** and it seems they can withstand levels of <800 mg/kg; therefore it seems very unlikely that levels of approximately 20 mg/kg copper in the feed for the mare and foal will have any deleterious effect. No evidence exists that **molybdenum** interferes with copper metabolism in the horse since the persistent, protein-bound thiomolybdates that occur in ruminants have not been identified.

There have been several reports that industrial contamination of grassland with either **zinc** or **cadmium** has resulted in an increased incidence of DOD (sometimes not confirmed histologically) in foals and young stock, suggesting that increased exposure to zinc and possibly cadmium may result in the development of OCD. However, more research is needed to confirm any possible relationship, to determine what the zinc–copper ratio should be and to ascertain what influence this may or may not have on the incidence of DOD.

There has also been some discussion regarding the nature and distribution of lesions caused by chronic **zinc or zinc/cadmium toxicosis** and whether such atypical patterns should be considered in the same way as the more **typical** DOD found routinely in the field. It has been suggested that in fact they should be specifically referred to as "zinc induced osteochondrosis" rather than being "combined under the more general term of DOD".

ROLE OF NUTRITION AND EXERCISE

At present the interrelationship between exercise and feed intake in relation to DOD is far from clear, although there is an indication that there needs to be a balance between these two factors and extremes must be avoided. There also seems to be a "time window" in which the development of lesions may be influenced by both exercise and nutrition either positively or negatively. This may vary with the different joints but is most likely to range from in utero to approximately 9 mo of age.

NUTRITIONAL MANAGEMENT OF FOALS WITH DOD

Foals identified as having lesions of DOD must be carefully managed to prevent any exacerbation and to allow healing to be promoted. Three factors affecting foals with DOD have been identified:

1. **Dietary digestible energy level.** Although few experimental data exist, it appears to be beneficial to decrease the DE level to approximately 85% of that recommended by NRC, with 100% levels of crude protein, calcium, phosphorus and other nutrients. Excessive levels of calcium in combination with high levels of DE have not been effective in protecting foals from osteochondrosis and it is unlikely that high levels of calcium assist in the healing of DOD.
2. **Dietary copper level.** Collagen cross-linking may be enhanced when dietary dry matter (DM) contains higher levels of copper (e.g. 30–45 mg/kg). However, collagen cross-linking is probably adequate at lower levels (e.g. 10 mg/kg). In cases of physitis it has been suggested by some that levels of approximately 30 ppm copper in the dietary DM may be beneficial. Since

horses have a high threshold level for copper toxicity, the level can be increased with relative impunity.

3. **Exercise and feeding.** If a foal is diagnosed with osteochondrosis and/or physitis, then the level of DE fed should be decreased and any joint trauma minimized by confining the foal and allowing only hand-walking exercise. However, the lack of exercise will further decrease the foal's DE requirement and 70–75% NRC DE may then be adequate.

NUTRITIONALLY ASSOCIATED LAMINITIS

Laminitis is the local manifestation of a serious systemic metabolic disturbance (*q.v.*). Laminitis is perhaps most commonly associated with certain feeding and management factors that will increase the likelihood of a potential attack whatever the type or breed of horse. **Grain overload** for example, whether by accident or deliberately induced, increases the risk of developing laminitis.

Administration of a suitably large 85% carbohydrate and 15% **fiber meal** can result in clinical signs of laminitis within 40 h; another potential iatrogenic cause is **constant tube feeding** with a high energy–protein ration. Turning certain ponies out onto **lush pastures** in the spring and autumn/fall is a common triggering factor for the development of laminitis. Currently it is thought that the high levels of water-soluble carbohydrates (which include the simple sugars as well as the more complex storage carbohydrate **fructans**) may be involved in this process. It has recently been shown that giving relatively large amounts of a particular fructan (*q.v.*) can induce laminitis in the horse.

It is thought that, as in other mammals, the horse does not have the necessary enzymes to digest fructans directly within the small intestine. The bulk of the fructans therefore passes into the hindgut where they are readily fermented, in a similar manner to starch that escapes digestion in the small intestine, triggering off abnormal fermentation as discussed above. Under these circumstances any **endotoxins**, together with various other compounds that may be absorbed into the blood, may have further effects, in particular within the feet (not necessarily directly), triggering the development of laminitis. The degree of fermentation within the small intestine when other more rapidly fermentable feeds are fed possibly is also of some importance in this condition.

Reducing fructan intake

The fructan content of grass varies and is largely dependent upon multiple factors including fertilization, light intensity, ambient temperature, stage of growth, residual fructan accumulation from the previous day, and past and present pasture management regimens. It is usually when energy demands upon the plant are high (e.g. during growth) that the fructan concentration is at its lowest (as it is being utilized to provide energy for growth) and vice versa. It is therefore thought that the safest time to turn out the horse may be late at night, bringing it in by no later than mid morning.

Fructan levels tend to be higher in the stem than the leaf due to the role of storage carbohydrate and therefore **grass management** is important. The amount and nature of the fructan stored vary between grasses; for example, timothy and cocksfoot tend to accumulate larger molecules which may be more slowly fermented in the hindgut than the smaller molecules found in perennial rye grass. The fructan content of hay is likely to be lower than that of fresh grass, and is lower still in haylage due to the fermentation process. Overall, the fructan content of grass is likely to be higher during spring, before the development of the flower, when the fructans are being stored.

Current recommendations to help reduce the risk of laminitis due to high fructan intake include:

1. Turn horses out to pasture when fructan levels are likely to be at the lowest, such as late at night to early morning, removing them from the pasture by mid morning.
2. Do not graze horses on pastures that have not been properly managed by regular grazing or cutting. Try to maintain a young leafy sward approximately 4 cm high. Mature, stemmy grasses may contain high levels of stored fructans.
3. Avoid or restrict turning out in spring (before flower development) and autumn/fall when fructan levels are accumulating and plants generally contain relatively high levels of water-soluble carbohydrates.
4. Do not allow horses to graze on pastures that have been exposed to low temperatures (e.g. frosts) in warm, bright, sunny weather.
5. Avoid grazing horses on freshly cut stubble, e.g. after hay harvest, as plant stems are the storage organs for fructans.
6. Consider zero grazing (while providing the horse with suitable forage) if it is essential for the horse to ingest minimal levels of fructans.
7. Graze horses on pastures containing species that produce low levels of fructan, e.g. timothy.

Ponies with laminitis

Prevention is preferred: feed in a similar way to that described for equine rhabdomyolysis syndrome (ERS) (*q.v.*) based on forage with minimal cereals, utilizing oil as an energy source if required (providing there are no contraindications because of liver function). Minimize the intake of fructans as outlined above. As soon as signs of laminitis are noted the animal should be **removed immediately** from the pasture and treated medically. The hoof should be **radiographed** for evidence of pedal bone rotation (*q.v.*) and appropriate treatment and support provided. Feed should not be totally restricted as reduced feed intake and stress may promote **hyperlipidemia** (*q.v.*). Pregnant or stressed ponies should probably be fed approximately 80% of their maintenance requirements to decrease the chance of hyperlipidemia.

High levels of carbohydrate in the feed should be avoided; consequently roughage diets are most suitable.

Ponies with laminitis are frequently **obese** and **glucose intolerant**. As a result severe vasoconstriction and local ischemia may exacerbate the laminitis. Due to the pain involved there is an increased output of glucocorticoids, which potentiates the digital vasoconstrictive effects of sympathetic catecholamines in blood vessels and further compromises vasodilatation.

Horses with laminitis

Horses with carbohydrate (i.e. grain) overload and **endotoxemia** (*q.v.*) always have a poor prognosis, which may be further complicated by the onset of laminitis. There is controversy over the feeding of horses suffering laminitis secondary to endotoxemia. Although some veterinarians maintain that the affected horse should be fed minimal amounts of grain and alfalfa, with the predominant ingredient in any diet being grass hay, others suggest that endotoxemic horses with laminitis should be fed in a different manner to obese laminitic ponies, in which feed intake and DE should be dramatically reduced.

Horses suffering laminitis secondary to endotoxic episodes may therefore require a diet providing approximately 100–130% of the normal maintenance rations. This can be incrementally implemented over the course of week. Sick horses that are in a **catabolic state** may benefit from feeding at 130% of maintenance.

Severely affected horses commonly become **potassium depleted**, when renal loss of potassium is assessed using **creatinine clearance** (urinary fractional electrolyte excretion [FE]) ratios. Potassium has a vasodilatory effect and dietary replacement may be beneficial. Grain has a low potassium content, but levels may be boosted by feeding alfalfa hay, molasses or supplemental potassium chloride in the acute stages. Serum electrolyte levels should be monitored every second day. Oat-based diets are also low in sodium and a complete fiber-based pellet/cubed diet may be more rational. If this is not possible a vitamin–mineral supplement may be required. If voluntary feed intake is still low due to pyrexia or painful episodes, then **parenteral nutrition** should be considered.

Horses with **endotoxemia** need to be supported medically (e.g. IV fluid therapy, antibiotics, flunixin meglumine) and may benefit from the vasodilatory effects of acepromazine and also from appropriate foot support.

EQUINE RHABDOMYOLYSIS SYNDROME

The equine rhabdomyolysis syndrome (ERS: also known as **tying up**, **azoturia**, **exertional rhabdomyolysis** etc.) affects primarily the muscles of horses of apparently any age, breed or gender and results in the partial or complete inability to move. Death can result. Recurrent sufferers are likely to have an underlying susceptibility to the condition, which may then be triggered by one or more factors, usually including exercise, resulting in the clinical signs. The underlying predispositions as well as the triggering factors are likely to differ between groups of sufferers, so the measures that are successful in one individual may not be so successful in another.

Two subgroups with specific and different causes have been identified and others will exist. One subgroup involves a disorder in muscle contractility or excitation–contraction coupling and the other involves a defect in carbohydrate storage and/or utilization (**polysaccharide storage myopathy**, PSSM).

There is no single procedure or set of procedures (including diet and management) that can guarantee against further episodes of ERS (*q.v.*). However, appropriate management procedures and nutrition of susceptible animals may help to reduce the likelihood or frequency of future episodes. The actual diet that will be the most beneficial to an individual sufferer will depend on the horse as an individual and what it is being used for (as influences energy needs), as well as its history with respect to tying up.

Nutritional advice for a horse prone to ERS

The major proportion, if not all, of the daily intake of feed should be **forage**—either fresh (pasture) or preserved (hay). If the energy needs of the individual horse can be met by forage alone then it should be fed approximately 100% forage (non-legume based). An appropriate general vitamin and mineral supplement normally is required to ensure adequate overall nutrition.

Horses prone to ERS should not be turned out onto lush, fast growing pastures but prolonged daily periods outside in a **sparse paddock** are often beneficial. If the horse's energy needs cannot be met by forage alone then add in some highly digestible fiber sources such as **soya hulls** or **unmolassed sugar beet pulp** (appropriately prepared). In addition, either a fiber based complementary manufactured feed (i.e. high fiber, low cereal—*a low oat*—feed; these feeds tend to be "low energy" feeds and if the horse requires either more energy then consider adding additional supplementary oil) or **supplementary oil** may be given, remembering to balance protein, vitamins, mineral and trace element intake. It is advisable in all cases to try to ensure that the diet provides a sufficient intake of electrolytes in an adequate and balanced manner. Ensure that **sufficient salt** is given and that an appropriate electrolyte supplement is given following or during prolonged exercise, especially in hot weather to compensate for sweat losses.

The addition of wheat bran to the horse's diet should be avoided wherever possible, and large amounts should always be avoided (unbalanced calcium to phosphorus ratio). Certain animals might have an individual alteration in their ability to utilize or absorb certain electrolytes and may benefit from having their electrolyte status evaluated using the **fractional electrolyte excretion test** (*q.v.*) followed by appropriate supplementation.

Vitamin E and selenium deficiencies or imbalances (*q.v.*) are unlikely to be the cause of ERS but they may be **permissive or contributory**. It is therefore advisable to ensure that all horses, especially those in hard work, are fed adequate vitamin E (at least 160 IU/kg DM) and selenium (approximately 0.2 mg/kg DM). Energy intake should be reduced during periods of decreased exercise and sufferers should not be fed in anticipation of an increase in workload.

HYPERLIPEMIA

Hyperlipidemia and hyperlipemia (*q.v.*) are the terms used respectively for the subclinical and clinical disorders associated with an elevation in blood triglycerides and lipids. Hyperlipemia describes the clinical syndrome characterized by depression, anorexia and hepatic failure and is associated with dramatic elevations in blood lipid and fatty infiltration of the liver and other parenchymatous organs.

The syndromes are generally precipitated by **stress** (i.e. transport, alteration of diet, pregnancy, lactation, change of paddock/stabling and infection). Most hyperlipemic episodes are associated with reduced dietary intake and, in large horses, an azotemic state, whether pre-renal (most common), renal or post-renal, which exacerbates the condition by inhibiting the peripheral removal of lipoproteins. During fasting, the triglycerides of adipose tissue are broken down into free fatty acids and glycerol, which are then released into the blood.

In horses, fatty acids taken up by the liver are oxidized completely to provide energy or are re-esterified to form triglycerides and phospholipids. These either remain in the liver or are released into the plasma as very low density lipoproteins (VLDLs). In horses, ketone formation is limited, therefore lipemia occurs in response to **aphagia** rather than ketosis as in ruminants.

Fat, unconditioned ponies are much more susceptible to hyperlipemia than large horses because of the innate insensitivity of ponies to insulin. Insulin normally potentiates the peripheral removal of VLDLs and decreases the mobilization of adipose tissue lipid. The condition arises when the animal is in negative energy balance because of depression of food intake or digestion and absorption. This may be associated with a scarcity of feed (e.g. in winter in the northern hemisphere and summer in the southern hemisphere) or inciting stresses such as pregnancy, lactation, parasitism and transportation.

Affected ponies appear dull and anorexic and show rapid loss of bodily condition. The mortality rate can be high if treatment is not initiated immediately. An uncommon presentation of hyperlipemia is related to hormonal imbalance due to a **pituitary tumor** (*q.v.*).

The initial treatment regimen involves the reduction of the negative energy balance by improving feed intake. If the animal will not voluntarily increase its intake of palatable feed and pasture, then tube feeding of a slurry of readily utilizable carbohydrates (Table 3.20) or a slurry of a complete pellet must be implemented. An indwelling nasogastric tube is best if the animal will tolerate it. Concurrently, drugs should be used to remove the lipids from the blood. **Insulin** and **glucose/carbohydrate therapy** (with supportive amino acids) may be used to curtail lipid mobilization and heparin administration may accomplish an acceleration of triglyceride removal from the blood.

Antipyretics and analgesics should be used if the animal is febrile or in pain. The hydration status should also be carefully monitored to avoid pre-renal azotemia (*q.v.*), which greatly exacerbates the hyperlipidemic condition. **Sodium bicarbonate** may be necessary to correct base deficits, which must be assessed by monitoring blood gases and acid-base status. Food intake produces waves of exogenous glycerides which decline so that the delivery of

Table 3.20 Example of a daily tube feeding schedule that has been used for a 200 kg pony with hyperlipemia. The total diet should be divided into four tube feedings per day

Parameter	Day						
	1	2	3	4	5	6	7
Water (L)	8	8	8	8	8	8	8
Dextrose (g)	120	160	200	240	320	320	360
Casein (g) or dehydrated cottage cheese	120	120	180	240	240	300	360
Dehydrated lucerne meal (g)	600	600	600	700	700	800	800
Electrolyte and vitamin mixture (g)	80	80	80	80	80	80	80

dietary glucose is reduced and there is increased movement of free fatty acids from the adipose tissue.

RENAL FAILURE

Although it is preferable to provide adequate nutrition without excessive protein, it is better to maintain energy intake than to over-restrict protein (dietary crude protein should ideally be <10% DM and of **good quality**). Palatable food should be offered with options as it is important to maintain appetite. Good quality grass hay, possibly with 1–2 kg of oats or corn, is one suggestion. Calcium should not be over supplemented; therefore alfalfa should be avoided but, again, if this is the only forage that the animal will eat, it is preferable to starvation.

Vegetable oil can be added (gradually) if weight cannot be maintained and the serum is not lipemic (e.g. up to 100 mL of corn oil in grain twice a day) but it is necessary to watch out for **lipemia** (*q.v.*). The **blood urea nitrogen (BUN) to creatinine ratios** (mg/dL) (*q.v.*) should ideally be maintained at between 10:1 and 15:1 (<10:1 suggests inadequate dietary protein; >15:1 suggests that dietary protein may be excessive and possibly will aggravate the degree of uremia; *q.v.*).

LIVER DYSFUNCTION

The most useful form of treatment for **acute liver damage** (*q.v.*) is good support and feeding. This involves the provision of oral or IV glucose to combat **hypoglycemia**. In acute hepatitis, **fluid therapy** may also be indicated. The value of protein-rich diets to control the faulty production of plasma proteins is controversial. However, some have used amino acids, especially mixtures containing leucine and valine, with apparently good results. B group vitamins are also commonly used.

In less acute cases the aim is to maximize small intestinal starch digestion in order to increase glucose availability. Oats or cooked grains should therefore be considered. It has been recommended that high protein diets (especially high methionine and other aromatic amino acids diets) should be avoided but intake levels of lysine and other key amino acids, including the branched chain amino acids, should be maintained. Micronized or steam flaked corn has a relatively low protein level but a good branched chain amino acid

to aromatic amino acid ratio and a high starch availability. Sugar beet has been suggested as a potential source of branched chain amino acids.

Alfalfa also has a better ratio than grass hay but it has a higher overall protein content so the intake should be restricted to perhaps 0.75% of body weight with supplemental corn to maintain body weight. Also, avoid early cut hay and haylages, clover in pasture, dried grass products, soya bean meal and high protein compound feeds. It is necessary to feed **little and often** to reduce the metabolic load on the liver. A **low fat diet** should be fed wherever possible. It is not known whether providing choline daily is advantageous (it is a methyl donor and may help moderate hyperlipemia) in the horse. However, additional B vitamins and vitamin C have been suggested to be of value.

WASTING CONDITIONS

Protein-losing syndromes

Loss of bodily condition with or without depression of appetite is common in horses and results from many different causes. Significant amounts of plasma proteins may be lost in urine (i.e. protein-losing nephropathy *q.v.*), pleural and peritoneal fluids, and perhaps most commonly from the gastrointestinal tract (protein-losing gastroenteropathy [PLGE]; *q.v.*). Diets should contain high amounts of quality protein to assist in replacement, although in cases of protein-losing nephropathy it is usually best not to increase protein concentration in the diet as it can exacerbate the azotemic condition.

Protein-losing gastroenteropathy

Protein can be lost from the gastrointestinal tract through loss of mucosal integrity or **lymphangiectasia** associated with increased lymphatic pressure. In acute cases a **plasma transfusion** (*q.v.*) is often necessary to provide protein (albeit a low concentration) to improve osmotic pressure transiently and restore vascular volume. The protein requirement is increased in these horses and if total parenteral nutrition is necessary then the maximum percentage of protein energy used in solution should be approximately 12%.

In chronic cases, diets with a high quality (i.e. digestibility, amino acid spectrum and balance) and quantity of protein should be fed (e.g. soya bean meal, sunflower meal, fishmeal, and alfalfa hay as roughage), unless the horse is concurrently azotemic. Anthelmintics should also be administered.

Diarrhea/malabsorption syndromes

Diarrhea (*q.v.*) results from a multitude of different causes including the so-called "**malabsorption syndromes**". Requirements therefore depend on the cause, and the optimal ration also depends on the likely underlying cause. Frequent small meals are usually preferable, however, and probiotics (*q.v.*) may be worth considering. Horses with **chronic diarrhea** often have PLGE as well, usually because of **decreased mucosal integrity**. They therefore require additional protein. Usually they are also in a state of energy, mineral and vitamin malnutrition.

One possible diet worth considering is ad libitum alfalfa hay, as well as a high protein–energy concentrate, plus a vitamin and mineral supplement.

Horses with **chronic salmonellosis** (*q.v.*) usually have impaired fiber digestion, and a diet with an increased proportion of grain/concentrate may help maintain body weight. In some refractory cases of chronic diarrhea the best solution is to turn the horse out onto **pasture**, which may promote normalization of gastrointestinal flora. In other cases of diarrhea removal from pasture may be of benefit.

If the diarrhea is due primarily to small intestinal dysfunction then little or no grain should be fed. Highly digestible fiber is essential in all cases as the volatile fatty acids produced (together with glutamine and aspartate) are primary energy sources for the enterocytes. Sugar beet pulp is a good source of fiber for horses, especially those with an intact large intestine; immature alfalfa may be better if only the small intestine is intact. Avoid overly mature, poorly digestible, hays. If small intestinal fat digestion is impaired for >1–2 wk the fat-soluble vitamins A, D, E and possibly K should be given parenterally.

If the condition is mainly a large bowel dysfunction grain could be beneficial. However, the exact site and extent of pathology is often difficult to ascertain in the live horse making precise recommendations difficult. It is necessary to start slowly and build up to 50% of the ration if this does not exacerbate the diarrhea. A mineral supplement (particularly if not feeding a legume hay) with added oil (up to 20% if introduced gradually and if small intestinal function is adequate) and water-soluble vitamins may also be indicated. Horses with colitis frequently have severe electrolyte imbalances. **Monitoring** is therefore advisable.

Hyponatremia and hypochloremia (*q.v.*) occur primarily owing to dilution caused by replacement of fluid loss with water. Severe hyponatremia usually occurs in cases of acute salmonelloses. Hypokalemia may occur in horses suffering **colitis** (*q.v.*) because of decreased intake and gastrointestinal loss. These horses are also **acidotic** and require **intensive corrective fluid therapy** (e.g. isotonic bicarbonate [1.2% solution]). The horses should be offered fresh water and a separate electrolyte drink. Feed should be restricted to grass hay for approximately 2 wk in convalescence as the normal cecal and colonic flora are likely to be at decreased levels. Grain/concentrate may then be slowly and incrementally introduced (e.g. 0.5 kg/wk). A vitamin B complex supplement may also be used for 2 wk.

Hyperkalemic periodic paralysis

The aim in hyperkalemic periodic paralysis is to **control potassium intake**, maintaining it at <1% potassium in total diet (and being consistent in feeding amounts and time). Forage is the biggest source of potassium but as forages vary tremendously according to type, region, irrigation, stage of cutting etc., it is recommended that likely sources be **analyzed**. In general, grass type forages have approximately half (0.8–1.7% on a DM basis) the potassium content of the legumes (1.5–3%) and the more mature forages have a lower content than those that were rapidly growing.

Satisfactory diets can be made by mixing unmolassed sugar beet pulp, which is low in potassium, with grass hay and a vitamin–mineral supplement. It is best to avoid lush grass, early harvest hay, legumes, alfalfa and soybean meal and sugar beet molasses.

Chapter 4

Toxicology and pharmacology

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Chapter contents

Disclaimer

Throughout this chapter, all possible care has been taken by the authors to include safe dosages. Where dosages of non-registered products are indicated, the authors cannot take responsibility for possible toxicity.

INTRODUCTION

The horse poses problems to the veterinarian in relation to the administration of therapeutic agents. Anatomically and physiologically horses differ markedly from other domestic species and humans. Consequently, it is **unwise to use extrapolated dosage rates in the horse**. This has been borne out in practice where the disposition, metabolism and excretion of many drugs in the horse have been shown to differ from other species.

Horses have a very large capacity for **oxidative metabolism**. Drugs that are metabolized by this route, such as the sulfide benzimidazole anthelmintics, are rapidly inactivated and consequently require to be given at higher dosage rates than in most other species. Another good example is the non-steroidal anti-inflammatory drug (NSAID) phenylbutazone, which has an **elimination half-life** of 5–8 h in the horse and 37–60 h in the cow. It has also been shown that the excretion of amfetamine, which undergoes extensive oxidative metabolism in the horse, is unaffected by urinary pH, whereas it is excreted unchanged in humans as the parent molecule and is highly influenced by urinary pH.

Toxicity may also manifest both severely and frequently in the horse. This may be specific to individual agents such as the ionophores, which cause **cardiac failure** (*q.v.*), or it may be typical of a whole class of drugs. Antimicrobial drugs have sometimes been associated with a high incidence of **enterocolitis** (*q.v.*) in the horse. Antimicrobial-associated enterocolitis is dependent on the concentration of antimicrobial drug achieved in the large intestine, on the commensal and environmental bacterial population, and possibly also on **stress factors** such as surgery and transport.

The use of horses in competitions also poses problems, as the several authorities which control equestrian sports each have their own regulations regarding the presence of drugs that could potentially affect the performance of the

competitors. Veterinarians must be aware of the regulations and of those drug disposition properties that permit effective use without contravening guidelines.

ANTIMICROBIAL DRUG SELECTION AND DOSAGE

INTRODUCTION

The effective use of antimicrobial drugs in treating systemic bacterial infections depends on the **quantitative susceptibility** of the pathogenic microorganism, and on its relation to the disposition and potential of the drug to produce adverse effects. It follows that the selection of an antimicrobial drug should take into account both the microbiologic (quantitative susceptibility) and pharmacologic (pharmacokinetic) properties of the drug. In addition, consideration must be given to the **location and severity** of the infection as well as to **formulation of the dosage** forms that are suitable for administration to horses, since this will determine the route of administration and dosing rate (dose/dosage interval). Other considerations include the margin of safety of the drug, the convenience of administration of the antimicrobial drug preparation (product) and the cost of the anticipated course of treatment.

The objective of dosage calculations is to maintain plasma concentrations of the antimicrobial drug that are several times the **minimum inhibitory concentration (MIC)** for the pathogenic microorganism for much of the duration of treatment. This is especially true for drugs with a concentration-dependent bactericidal mechanism.

The MIC is an in vitro quantitative measure of susceptibility and potency and may be defined as the drug concentration that, under the test condition, prevents (just inhibits) the visible growth of a certain percentage of the bacterial species, e.g. MIC_{90}. When MIC data are used in conjunction with pharmacokinetic parameters describing drug absorption and disposition, it is possible to calculate "reasonable" dosing rates. Cognizance is not given to the "post-antibiotic effect" whereby microbial growth may be interrupted for some time beyond the period when antimicrobial concentrations exceeded the MIC.

MICROBIOLOGIC CONSIDERATIONS

Approach to therapy

Having diagnosed the presence of bacterial infection, specimens for bacterial culture and susceptibility testing should, wherever possible, be collected before administering an antimicrobial drug. Since there will be some delay in obtaining laboratory results it is important to **initiate therapy** (on an informed empirical basis). The choice of drug can be based on **clinical experience** and examination of stained material (apply **Gram stain** to direct smear).

The laboratory results of **bacterial culture** and MIC determination (when required) give precise data that may be used in selecting the antimicrobial drug, its route of administration and dosing rate for continuation of treatment (specific therapy). The usual dosage regimen for an antimicrobial product is based on providing plasma concentrations of the drug that will be effective against the

majority of susceptible microorganisms and will not cause adverse effects in the horse. The assumption is made that the systemic clearance of the drug is not changed by the disease state, even though this may not always be the case.

Quantitative bacterial susceptibility

The need to determine **quantitative susceptibility** depends on the microorganism isolated, i.e. the causative organism of the infection. The antimicrobial susceptibility of bacteria such as β-hemolytic streptococci, *Rhodococcus (Corynebacterium) equi* and *Corynebacterium pseudotuberculosis* is usually predictable, whereas it is generally necessary to determine the susceptibility of other pathogenic bacteria, especially coagulase-positive staphylococci and enteric microorganisms (*Escherichia coli, Klebsiella, Proteus* and *Salmonella* spp.).

Such susceptibility determinations must follow standard laboratory procedures. Quantitative (MIC) data are preferable to qualitative (disk diffusion, Kirby Bauer method) information because of the possibility of tailoring drug dosage to susceptibility of the causative bacterial pathogen.

Location of infection

When selecting the antimicrobial drug with which to commence therapy, knowledge of the pathogenic bacteria that most commonly cause infections at various locations is useful but should be supported by examination of a stained (Gram or Romanowsky-type Wright–Giemsa) direct smear. Bacterial pathogens that have been isolated from various sites of infection are listed in Table 4.1. Because the principal bacterial species isolated from any site of infection may vary with geographic region, specimen collection for bacterial culture **prior** to commencing antimicrobial therapy is of paramount importance.

Drug selection for empirical therapy

The suggested drug of choice and alternative drug for initial treatment of infections caused by various microorganisms are presented in Table 4.2. The information in Table 4.2 should be used in conjunction with direct smear examination for drug selection (empirical therapy) while awaiting the results of bacterial culture and quantitative susceptibility testing (when considered necessary). Selection of the drug to use is influenced by location of the site of infection.

In **mixed infections** with microbiologically diagnosed **anaerobic involvement**, the concurrent use of metronidazole and benzylpenicillin or gentamicin, depending on whether the primary aerobic bacterial pathogen is Gram-positive or Gram-negative, may represent the antimicrobial drug treatment of choice.

The penicillins, cephalosporins (apart from cefadroxil), aminoglycosides and oxytetracycline must be administered parenterally to horses, while trimethoprim–sulfonamide combination preparations, rifampicin, metronidazole and enrofloxacin (to mature horses only) may be administered PO as paste formulations or by nasogastric tube as oral solutions or aqueous suspensions.

Table 4.1 Bacterial pathogens isolated from various sites of infection

Site	Pathogens
Respiratory system	
Upper	*Streptococcus* spp.
Lower	
Adults	*S. zooepidemicus*
	Opportunistic aerobic bacterial pathogens
Older foals	*S. zooepidemicus*
	Opportunistic aerobic bacterial pathogens
	Rhodococcus equi
Neonatal foals	Opportunistic aerobic bacterial pathogens
Pleuropneumonia	Mixed opportunistic aerobic and anaerobic bacterial pathogens
Gastrointestinal tract	
Peritonitis	Mixed opportunistic aerobic (mainly Enterobacteriaceae) and anaerobic (*Bacteroides* spp.) bacterial pathogens
	Actinobacillus equuli
Abdominal abscess	*S. equi*
	S. zooepidemicus
	Corynebacterium pseudotuberculosis
	R. equi (foals)
Liver abscess	β-hemolytic streptococci
	C. pseudotuberculosis
	Opportunistic aerobic or anaerobic bacterial pathogens
Cardiovascular system	
Bacterial endocarditis	*Streptococcus* spp.
	Opportunistic aerobic bacterial pathogens
Bacterial pericarditis	*Streptococcus* spp.
	Mixed opportunistic aerobic and anaerobic bacterial pathogens
Renal system	
Cystitis, pyelonephritis	Opportunistic aerobic bacterial pathogens
Reproductive system	
Bacterial endometritis	*S. zooepidemicus*
	Escherichia coli
	Pseudomonas aeruginosa
	Klebsiella spp.
Placentitis	*S. zooepidemicus*
	E. coli
	Klebsiella spp.
Mastitis	*S. zooepidemicus*
	Staphylococcus spp.
	Other opportunistic aerobic bacterial pathogens
	Mycoplasma spp.
Bacterial septicemia (neonatal foals)	*E. coli*
	Other opportunistic aerobic bacterial pathogens (mostly Gram-negative)

Opportunistic aerobic bacterial pathogens include *E. coli*, *Klebsiella* spp., *Proteus* spp., *Pasteurella* spp., *Actinobacillus* spp., *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Streptococcus zooepidemicus*.
Opportunistic anaerobic bacterial pathogens include *Bacteroides* spp., *Fusobacterium* spp. and *Clostridium* spp.

Table 4.2 Empirical antimicrobial selection based on knowledge of bacterial pathogen

Bacterial pathogen	Drug of choice	Alternative drugs
Gram-positive aerobe		
β-Hemolytic *Streptococcus*	Benzylpenicillin or ampicillin	Cefalotin or ceftiofur
α-Hemolytic *Streptococcus*	Ampicillin	Cefalotin or ceftiofur
Staphylococcus spp.	Benzylpenicillin	Cefalotin
Staphylococcus aureus Penicillinase producing	Cefalotin oroxacillin	Trimethoprim–sulfonamide
Rhodococcus equi	Erythromycin + rifampicin	
Corynebacterium pseudotuberculosis	Benzylpenicillin	Trimethoprim–sulfonamide
Gram-negative aerobe		
Escherichia coli *Klebsiella* spp. *Proteus* spp.	Gentamicin	Amikacin or enrofloxacin
Actinobacillus spp. *Pasteurella* spp.	Gentamicin or ceftiofur	Enrofloxacin or trimethoprim–sulfonamide
Pseudomonas aeruginosa	Amikacin	Ticarcillin–clavulanate ± gentamicin

Interpretation of bacterial susceptibility

There are no agreed guidelines for the interpretation of quantitative susceptibility results for equine bacterial pathogens. Suggested interpretative guidelines for MIC breakpoint values are presented (Table 4.3). The categories are:

1. **Susceptible**, in which an infecting organism is inhibited by concentrations achieved in blood or tissue fluid after the recommended dose including oral administration
2. **Moderately susceptible**, when an infecting microorganism is inhibited only by blood concentrations achieved with maximum doses, up to the limit of toxicity
3. **Resistant**, when an organism is resistant to usually achievable concentrations of the antimicrobial drug in blood or tissue fluid.

Even though the spectrum of activity of individual drugs within each antimicrobial class or subclass in the case of β-lactam antibiotics is, in general, similar, the quantitative susceptibility of microorganisms to individual drugs somewhat differs. Tetracyclines may constitute an exception in that variation among individual tetracyclines in clinical efficacy is largely due to differences in **lipid solubility**, which influences tissue concentrations attained.

The MIC (*q.v.*) is the quantitative value normally used to define the in vitro susceptibility of a microorganism. It is used, in conjunction with pharmacokinetic parameters that describe the bioavailability and disposition of antimicrobial agents, to calculate **appropriate dosing rates**. This approach allows appropriate dosage adjustment to be made for organisms of different susceptibilities. It is the basis for calculating optimal dosage. Even though quantitative susceptibility (an in vitro measurement of activity) generally correlates with clinical efficacy, it cannot be guaranteed to predict the response to therapy.

Table 4.3 Suggested guidelines for the interpretation of minimum inhibitory concentration (MIC) (μg/mL) of antimicrobial agents based on bacterial isolates of equine origin, apart from fluoroquinolones which relate to isolates of canine origin

Antimicrobial agent	Susceptible	Moderately susceptible	Resistant
Benzylpenicillin	≤0.125	0.25–16	>16
Ampicillin	≤1	2–16	>16
Amoxicillin	≤1	2–16	>16
Gentamicin	≤2	4–8	>8
Amikacin	≤4	8–16	>16
Fluoroquinolones[1]	≤1	2–4	>4
Erythromycin	≤0.5	1–4	>4
Tetracycline	≤1	2–4	>4
Chloramphenicol	≤4	8–16	>16
Trimethoprim—sulfamethoxazole	≤0.5/10	1/20–2.5/50	>3/75

[1] *Quantitative susceptibility of bacterial pathogens varies between individual fluoroquinolones.*

Furthermore, use of the antimicrobial agent to which a pathogenic microorganism is most susceptible in vitro might not be clinically indicated because of its potential to produce adverse effects.

Usual dosage regimens aim to **maintain plasma concentrations** that are several times the MIC_{90} for the majority of usually susceptible microorganisms and could be expected to provide effective therapy. At these plasma concentrations, the penicillins, cephalosporins, aminoglycosides, fluoroquinolones, trimethoprim–sulfonamide combinations, rifampicin and metronidazole produce a bactericidal effect, while tetracyclines, sulfonamides (used alone), erythromycin and chloramphenicol produce a bacteriostatic effect on susceptible microorganisms.

Although the terms **bactericidal** and **bacteriostatic** generally apply to the effect produced, they are relative depending on the concentration attained and environmental conditions at the site of infection. For antimicrobial agents that exert a bacteriostatic effect it is especially important that plasma concentrations be maintained **well above** the MIC_{90} for the pathogenic microorganism throughout the course of therapy. For antimicrobial agents that produce a bactericidal effect the relationship between plasma concentration and bacterial killing depends on whether the mechanism depends on concentration or time.

For drugs with a concentration-dependent killing mechanism (fluoroquinolones and aminoglycosides), it is usual to recommend achievement of C_{max}:MIC ratios of 10 or greater, whereas for time-dependent bacterial killing drugs (β-lactam antibiotics) it is desirable to maintain the plasma concentration between 1 and 4 times the MIC for at least half the inter-dose interval.

Impairment of host defense mechanisms is a variable, not generally taken into account in dosage calculations, which contributes to a discrepancy between expected and actual response to therapy, particularly for bacteriostatic drugs. Inadequacy of the type, quality and quantity of the immunoglobulins, alteration of the cellular immune system, or either a qualitative or, more importantly, a quantitative defect in phagocytic cells may result in therapeutic failure despite the use of otherwise appropriate and effective drugs. The effectiveness of therapy may be influenced by **local factors** at the site of infection. These include pus, the presence of a foreign body, and in the case of abscesses penetrative capacity of the drug and the pH or anaerobic environment within the abscess cavity.

Optimal dosage

Optimal dosage of a drug that produces a bactericidal effect is required in severe infections such as meningitis and endocarditis (*q.v.*), and in immunocompromised patients. Because of variations in the state of host defenses, the post-antibiotic effect or acquisition of **bacterial resistance**, and disease-induced changes in the disposition of an antimicrobial agent, optimal dosage cannot be precisely calculated. Disease conditions that may alter pharmacokinetic parameters include fever, dehydration, hypoalbuminemia (e.g. chronic liver disease), uremia and decreased renal excretion (*q.v.*).

The **pathophysiology** of the disease condition determines the changes in volume of distribution, clearance and, depending on the changes in these two parameters, the half-life of the drug may be altered. At least some of the pharmacokinetic alterations can be accommodated by adjustment of dosage. The ultimate criterion of optimal dosage is the effectiveness of therapy, as indicated by bacteriologic cure.

PHARMACOLOGIC CONSIDERATIONS

The absorption, distribution and elimination processes for antimicrobial drugs are largely governed by their chemical character and by certain physicochemical properties. The majority of antibacterials are weak organic electrolytes, either acids (e.g. penicillins, cephalosporins, sulfonamides) or bases (e.g. aminoglycosides, macrolides, trimethoprim, metronidazole), while fluoroquinolones, tetracyclines and rifampicin are amphoteric compounds and chloramphenicol is a neutral molecule. Lipid solubility and degree of ionization, which is determined by the pK_a of the drug and the pH of the biologic fluid in question, influence the extent of absorption, the pattern of distribution and the principal elimination process (hepatic metabolism and/or renal excretion) for antimicrobial drugs.

Routes of administration

The route of administration of a drug is governed mainly by the formulation of the dosage form (antimicrobial drug preparation). Parenteral preparations of antimicrobial drugs that are formulated as aqueous solutions can be administered either by slow IV injection or IM. Those formulated as aqueous suspensions are designed to provide sustained release (slow absorption), and thereby a prolonged duration of effective plasma concentrations, and should be administered only by IM injection. **Prolonged-release products**, which cause tissue irritation, and drugs in oily vehicles should *never* be administered to horses. This excludes the use in horses of some so-called "large animal parenteral preparations".

At the present time, few antimicrobial drugs are available as oral dosage forms that are convenient to administer to horses. **Oral paste** preparations that are palatable and of suitable consistency may represent the best type of oral dosage. The addition of an antimicrobial agent to the feed as a powder is an unreliable method of dosing, due to variability in the dose ingested and to the effect of food on the extent of absorption of the drug.

The action of some antimicrobial agents, whether administered orally or parenterally, on the cecal and colonic commensal microorganisms of horses

can cause **serious digestive disturbances**. This adverse effect makes penicillins **unsuitable** for oral administration to horses other than newborn foals and limits the use of macrolides and, under certain circumstances, of tetracyclines. Foals appear to be less susceptible than adult horses to disturbance in the balance of commensal microbial flora in the large intestine. It is likely that the microbial balance is related to the composition of the usual diet.

BIOAVAILABILITY, DISTRIBUTION AND ELIMINATION

Bioavailability is defined as the rate and extent to which a drug enters the systemic circulation unchanged (as parent drug). The bioavailability of a drug is influenced by the route of administration and formulation of the dosage form while the plasma concentration profile is, in addition, influenced by the dose administered. Significant features of the plasma concentration profile include the peak plasma concentration and the time period that plasma concentrations exceed a desired minimum concentration based on MIC_{90} for commonly isolated susceptible pathogenic bacterial species.

The usual dosage regimen for an antimicrobial drug must take into account **bacterial susceptibility** to the drug and features of bioavailability, extent of distribution and the overall rate of elimination of the drug based on data obtained in clinically healthy animals, representative of the species of interest. The severity of an infection and functional state of the principal organs of drug elimination may require adjustment of the dosage regimen (either size of dose or dosage interval) or the use of an alternative drug.

When the parenteral preparation is a non-irritating aqueous solution of the drug, absorption from IM injection sites in generally rapid, in that the peak plasma concentration (C_{max}) is attained within 30–60 min, and complete (i.e. systemic availability approaching 100% is obtained). This situation applies to the 5% parenteral solution of **gentamicin** sulfate. **Ceftiofur**, as reconstituted aqueous solution of the sodium salt, is administered to horses by IM injection. The drug is rapidly and completely absorbed from the injection site and, following entry into the systemic circulation, is converted by ester hydrolysis to desfuroylceftiofur, which has antibacterial activity similar to that of the parent drug. Even though the apparent half-life of ceftiofur is approximately 3 h, the recommended dosage interval is 12 h.

Long-acting parenteral preparations are formulated in a non-aqueous (such as oil or an organic) vehicle or a poorly soluble salt of the drug is formulated as an aqueous suspension. These preparations decrease the rate of drug absorption, which takes place over an extended period. **Oxytetracycline** formulated in polyethylene glycol is the only long-acting preparation of oxytetracycline that is suitable for IM administration to horses. The horse is the **least tolerant** of the domestic animal species to injection site irritation, and drugs in oily vehicles should never be administered parenterally to horses. The commercially available long-acting parenteral preparations of **amoxicillin and oxytetracycline**, apart from one recently formulated preparation, are too irritant for IM administration to horses.

When the rate of absorption significantly influences the overall rate of elimination of a drug, **flip-flop pharmacokinetics** apply, allowing the use of a

longer dosage interval than that associated with a conventional (immediate release) preparation of the drug. This applies to **procaine benzylpenicillin**, which is an aqueous suspension. Following the administration of a single dose (20 000 IU/kg) of procaine benzylpenicillin at various IM injection sites and SC, the peak plasma concentration (C_{max}) and systemic availability (indicated by area under the curve over a 24 h period) of benzylpenicillin were highest when the long-acting preparation was injected IM in the neck region (*m. serratus ventralis cervicis*) and were lowest when it was injected SC.

Because of differences in the blood flow to various skeletal muscles and in absorptive surface area, location of the injection site influences features of the plasma concentration profile. The lateral neck (*m. serratus ventralis cervicis*) at the level of the fifth cervical vertebra, ventral to the funicular part of the ligamentum nuchae and dorsal to the brachiocephalic muscle, appears to be the optimal site in horses for IM injection of long-acting parenteral preparations. The convenience afforded by the extended dosage interval associated with the use of long-acting preparations is somewhat offset by a loss of flexibility in dosage.

Absorption of antimicrobial agents, like other drugs, takes place by passive diffusion. The absorption process is mainly determined by the physicochemical properties of the drug, namely **lipid solubility** and, in the case of weak organic acids and bases, **degree of ionization** at the principal sites of absorption. In horses, drugs are absorbed from the stomach and proximal (upper) small intestine and, in addition, from the colon. The rate and pattern of drug absorption, which are reflected by the plasma concentration profile, are influenced by the **availability** of the drug for absorption. This, in turn, is influenced by the stability and solubility of the drug in gastrointestinal fluid and binding (adsorption) to the fibrous constituents in feed. When the latter is substantial, the colon may be the principal site of absorption, which occurs following microbial digestion of the fiber.

The pattern of absorption may be **biphasic** with an intervening period of approximately 8 h, during which time digesta move from the small intestine to the colon. The temporal relationship between feeding and oral dosing influences not only the pattern but may also affect the extent of absorption (i.e. systemic availability) of the drug. When rifampicin (5 mg/kg) was administered PO to horses 1 h after feeding, systemic availability of the drug was 26% compared with 68% when the dose was given 1 h before feeding.

Wide individual animal variation in systemic availability is a feature of orally administered drugs that are well absorbed from the gastrointestinal tract (GIT). The systemic availability of orally administered **metronidazole** ranges from 58% to 92% in horses and does not appear to be significantly affected by the time of feeding relative to oral administration of the drug. Several antimicrobial agents that are commonly administered orally to other monogastric species, such as phenoxymethylpenicillin, amoxicillin, cefadroxil and ciprofloxacin, are poorly absorbed in adult horses.

Having traversed the gastrointestinal mucosal barrier, drug molecules are conveyed in hepatic portal blood to the liver, where they are subjected to **the "first-pass" effect** prior to entering the systemic circulation. Hepatic first-pass metabolism can substantially decrease the systemic availability of lipid-soluble drugs that undergo microsomal oxidative reactions (e.g. trimethoprim, metronidazole, rifampicin, enrofloxacin). While the metabolites of most antimicrobial

agents are inactive, some, such as desacetylrifampicin and ciprofloxacin (to which enrofloxacin is converted), have antimicrobial activity at least equal to that of the parent drug. Because the formation of desacetylrifampicin is capacity-limited, the half-life of rifampicin is dose-related in horses. Certain antimicrobial agents (erythromycin and chloramphenicol) inhibit hepatic microsomal enzyme activity, whereas rifampicin is a potent inducer of hepatic microsomal enzymes. Drug-induced changes in microsomal enzyme activity are generally associated with chronic rather than short-term use of activity-modifying drugs.

The **extent of distribution** of antimicrobial agents, which is more important than the rate of extravascular distribution, is mainly determined by their lipid solubility and is influenced by the degree of ionization in the blood and extent of binding to plasma proteins. Lipid-soluble antimicrobial agents passively diffuse through cell membranes, penetrate cellular barriers, enter most tissues of the body and generally reach infection foci. However, since most bacterial infections occur in **extracellular fluids**, poorly lipid-soluble drugs (β-lactam and aminoglycoside antibiotics) are equally effective as lipid-soluble drugs provided they are not extensively bound to plasma proteins.

A high degree of ionization in the blood, extensive binding to plasma proteins and rapid elimination are factors that limit the concentrations attained in **transcellular fluids** (aqueous humor, synovial fluid and cerebrospinal fluid [CSF]). Elimination by the liver, especially by hepatic microsomal oxidative reactions, requires at least a moderate degree of lipid solubility. Examples of lipophilic antimicrobial agents include erythromycin, clindamycin (contraindicated for use in horses), trimethoprim, enrofloxacin, minocycline, rifampicin, chloramphenicol and metronidazole. Individual tetracyclines differ in lipid solubility, which underlies variation between members of the tetracycline class in their disposition (i.e. distribution and elimination) and clinical efficacy.

Most lipophilic antimicrobial agents are organic bases, some are amphoteric (fluoroquinolones, tetracyclines, rifampicin), and chloramphenicol is a neutral molecule. Even though aminoglycoside antibiotics are weak organic bases, their polar nature accounts for their limited capacity to enter cells and penetrate cellular barriers, and their elimination by renal excretion (glomerular filtration). *Mycoplasma* spp. lack rigid cell walls but **lipid solubility** is a requirement for an antimicrobial agent to be clinically effective because the microorganism is often located intracellularly.

Penicillins and cephalosporins (β-lactam antibiotics) and sulfonamides are organic acids. Because of their high degree of ionization in biologic fluids, the distribution of penicillins is limited in that they attain low intracellular concentrations and do not penetrate well into transcellular fluids. In the presence of **fever** associated with an acute inflammatory reaction, penicillins have **increased capacity** to penetrate cellular barriers (such as the blood–CSF barrier). This may arise through one or more of several mechanisms, including (a) increased blood flow (arteriole dilatation) and (b) reduced extrusion of penicillin from the CSF through disruption of an active efflux pump.

Amoxicillin distributes more widely than benzylpenicillin in extravascular fluids and tissues, presumably due to the higher lipid solubility of amoxicillin. Penicillins, with the exception of nafcillin, are eliminated by renal excretion (glomerular filtration and proximal tubular secretion). Nafcillin and a small fraction of amoxicillin in the systemic circulation are excreted in bile.

The β-lactamase inhibitors (clavulanic acid and sulbactam) do not alter disposition of the penicillins with which they are combined in commercially available dosage forms. β-Lactamase inhibitors enhance the activity of aminobenzylpenicillins (amoxicillin, ampicillin) and ticarcillin.

Individual cephalosporins, particularly those within the second and third generations, differ both qualitatively (spectrum of activity) and quantitatively (MIC for susceptible Gram-negative bacteria) in antimicrobial activity. Distinguishing features of third-generation cephalosporins (cefotaxime, ceftizoxime, ceftriaxone, cefoperazone, ceftazidime), all of which must be administered IV, are their **expanded spectrum** against Gram-negative aerobic bacteria and their ability (with the exception of cefoperazone) to penetrate the blood–brain barrier.

Cephalosporins, like penicillins, are eliminated by **renal excretion** (glomerular filtration and proximal tubular secretion) with the notable exceptions of ceftriaxone and cefoperazone, which are excreted by the liver in bile. Ceftiofur differs from other third-generation cephalosporins in that ceftiofur is administered by IM injection and, following absorption into the systemic circulation, is eliminated by metabolism, initially conversion by an esterase in the kidneys and liver to an active metabolite (desfuroylceftiofur) which undergoes conjugation with endogenous substances (including glutathione) in the liver.

The sulfonamides constitute a series of **weak organic acids** with pK_a values ranging from 5.0 (sulfisoxazole) to 10.4 (sulfanilamide). Weak organic acids exist predominantly in the non-ionized lipid-soluble form in biologic fluids of pH below their pK_a values. Although sulfonamides are seldom administered alone to horses, certain sulfonamides (sulfadiazine, pK_a 6.4; sulfamethoxazole, pK_a 6.0; sulfadoxine, pK_a 6.1) in conjunction with trimethoprim (organic base, pK_a 7.3) formulated as fixed ratio (5:1) combination preparations are widely used. Both parenteral and oral (paste) dosage forms are commercially available.

The sulfonamides and especially **trimethoprim**, which is more lipid-soluble, have good tissue penetrative capacity and they act synergistically to produce broad-spectrum bactericidal effect. The half-lives of sulfadiazine (3.6 h) and sulfamethoxazole (4.8 h) are reasonably close to that of trimethoprim (3.2 h), while the half-life of sulfadoxine (14.2 h) is much longer. Trimethoprim and the sulfonamides with which it is combined are eliminated mainly by hepatic metabolism and a smaller fraction of both drugs in the combinations is excreted unchanged (as parent drug) in the urine. The renal excretion processes involved are glomerular filtration, proximal tubular secretion and pK_a/pH-dependent passive reabsorption of the non-ionized moieties from distal renal tubular fluid.

An estimation of the extent of distribution of a drug is provided by the pharmacokinetic parameter, **volume of distribution**, which quantifies the apparent space in the body available to contain the drug following attainment of pseudodistribution equilibrium. It does not reveal the distribution pattern of a drug, which can be described only by measuring the levels (amount) of drug in the various organs and tissues of the body. Knowledge of the volume of distribution is required for calculating the dose (mg/kg) that must be administered to provide a desired concentration in the plasma. Drug administration by an extravascular route (PO or IM) may require upward adjustment of the dose to compensate for incomplete systemic availability of the drug.

Table 4.4 Process(es) of elimination and pharmacokinetic parameters describing the disposition of antimicrobial agents in horses

Drug	Process(es) of elimination	Half-life (h)	Vd(area) (mL/kg)	Cl_B (mL/min × kg)
Benzylpenicillin	E (r)	0.90	195	2.50
Ampicillin	E (r)	1.20	300	2.89
Amoxicillin	E (r)	1.43	556	4.55
Ticarcillin	E (r)	0.94	250	3.10
Cefazolin	E (r)	0.65	291	5.27
Cefadroxil	E (r)	0.77	462	6.95
Ceftriaxone	E (h)	1.62	650	5.22
Gentamicin	E (r)	2.50	254	1.20
Amikacin	E (r)	1.70	180	1.23
Enrofloxacin	M + E (r)	4.96	2495	5.73
Ciprofloxacin	M	4.71	3900	9.70
Trimethoprim	M + E (r)	3.16	1378	5.03
Sulfadiazine	M + E (r)	3.64	465	1.45
Sulfamethoxazole	M + E (r)	4.80	500	1.20
Sulfadoxine	M + E (r)	14.20	390	0.32
Chloramphenicol	M + E (r)	0.92	700	8.80
Metronidazole	M + E (r)	3.92	660	1.97
Rifampicin	M	6.00	635	1.34
Erythromycin	E (h) + M	1.00	2300	26.6
Oxytetracycline	E (r ± h)	9.60	1500	1.25

E (r), renal excretion; E (h), excretion by the liver in bile; M, (hepatic) metabolism.
For drugs that are eliminated both by metabolism and excretion, the principal elimination process is metabolism.

The overall **elimination** of antimicrobial agents obeys **first-order kinetics** when usual doses are administered by IV injection. This implies that 50% of the drug in the body is eliminated (by metabolism and/or excretion) each half-life. Because lipophilic antimicrobial agents are eliminated mainly by the liver (metabolism or biliary excretion) their half-lives vary widely compared with the half-lives of drugs that are eliminated by renal excretion (Table 4.4). Even though oxytetracycline is eliminated by renal excretion, the relatively long half-life of this antibiotic is attributed to **enterohepatic circulation**. An application of half-life is in the selection of an appropriate dosage interval, which may be either approximately equal to or a small multiple of the half-life. This is especially important for antimicrobial agents that produce a bacteriostatic effect (e.g. tetracyclines, chloramphenicol, sulfonamides).

When a drug is administered by an extravascular route, especially as a long-acting preparation injected IM, absorption controls the rate of elimination and allows the use of a longer dosage interval than that associated with a conventional (immediate release) dosage form of the drug (flip-flop pharmacokinetics). Usual dosage intervals do not take into account the "post-antibiotic" effect, which implies a temporally limited suppression of bacterial growth for a variable period (from 1 to 6 h) after susceptible bacteria have been exposed to antimicrobial concentrations above the MIC.

Aminoglycosides and fluoroquinolones induce a post-antibiotic effect on susceptible Gram-negative aerobic bacteria. Because the half-life is a derived (hybrid) parameter, which depends on the relationship between the volume of distribution, determined by the area method, and the systemic clearance of

a drug, its numerical value is influenced by a change in either or both of the physiologically based parameters.

$$t_{1/2} = \frac{0.693 \times V_{d(area)}}{Cl_B}$$

The **systemic clearance** of a drug, which measures the ability of the body to eliminate the drug, represents the sum of the clearances by the various organs (usually the liver and kidneys) that contribute to drug elimination. Systemic clearance is probably the most important pharmacokinetic parameter to consider in designing a dosage regimen with the objective of maintaining a desired average steady-state plasma concentration. The desired average steady-state concentration should be based on the MIC for the causative bacterial pathogen.

$$\text{Dosing rate} = \frac{F \times \text{Dose}}{\text{Dosage interval}} = C_{p(avg)} \times Cl_B$$

where F is the systemic availability of the drug.

This relationship is more applicable to pharmacologic agents for which there is a defined range of therapeutic plasma concentrations but may be applied to antimicrobial agents, especially those that produce a bacteriostatic effect.

A disadvantage of basing a dosage regimen on the average steady-state plasma concentration is that it provides no information regarding the degree of fluctuation in plasma concentrations during the dosage interval. Fluctuation in steady-state plasma concentrations can be avoided only by administering a parenteral solution of the drug by continuous IV infusion. In the treatment of severe Gram-negative infections in neonatal foals (*q.v.*), consideration could be given to administering cefotaxime or ceftazidime (third-generation cephalosporins) by **continuous IV infusion**. These drugs may have high activity against the causative bacterial pathogens, produce a bactericidal effect, are eliminated by renal excretion and have relatively short half-lives (<1.5 h). Usual dosage regimens for antimicrobial agents that may be used in horses are presented in Table 4.5.

CLINICAL APPLICATIONS

Penicillins have several advantages over other classes of antimicrobial agents in the treatment of systemic bacterial infections of horses. They possess high activity against pathogenic bacteria that commonly cause infection in horses, have a uniquely wide margin of safety which applies not only to adult and maturing horses but also to neonatal foals, the incidence of adverse effects following their parenteral administration is low, and the parenteral dosage forms of various penicillins allow optimal therapy to be provided.

More so than with any other class of antimicrobial agent, dosage with penicillins can be tailored to the susceptibility of the pathogenic microorganism. Because of their inability to acquire resistance plasmids, Gram-positive bacteria, with the notable exception of *Staphylococcus aureus*, remain highly susceptible to penicillins, especially **benzylpenicillin**. Penicillins produce a bactericidal

Table 4.5 Usual dosage regimens for antimicrobial agents used in horses

Drug	Route of administration	Dosage regimen	
		Dose (mg/kg)	Interval (h)
Benzylpenicillin sodium	IV, IM	15 000–30 000 IU/kg	6
Benzylpenicillin procaine	IM	25 000 IU/kg	12 (–24)
Ampicillin sodium	IV, IM	20	8
Oxacillin sodium	IV, IM	25	8–12
Ticarcillin–clavulanate[1]	IV (slowly)	50	8
Cefadroxil[1]	PO	25	8
Cefalotin sodium	IV	20	8
Cefazolin sodium	IV	20	8
Cefoxitin sodium	IV	20	8
Cefotaxime sodium[1]	IV	20–40	8
Ceftiofur sodium	IM	2.5–5	12 (–24)
Gentamicin sulfate	IM	2–4	8–12
Amikacin sulfate	IM	4–8	8–12
Enrofloxacin[2]	IV	5	12
	PO	7.5	12
Trimethoprim–sulfadiazine	IV	4/20	12
	PO	5/25	12
Chloramphenicol sodium succinate[3]	IV	25–50	6
Chloramphenicol palmitate[3]	PO	50	6
Metronidazole	PO	20	12
Oxytetracycline hydrochloride	IV (slowly)	3–5	12
Rifampicin	PO	5	12
Erythromycin estolate[1]	PO	20–25	8

[1]*Recommended for use in foals.*
[2]*Administer enrofloxacin only to adult horses.*
[3]*Use 12 h dosage interval in neonatal foals.*

effect on susceptible bacteria by preventing formation of the cell wall through selective inhibition of peptidoglycan synthesis.

Because *Mycoplasma* spp. lack a rigid cell wall, these microorganisms are inherently resistant to penicillins and cephalosporins (β-lactam antibiotics). Intravenous injection of benzylpenicillin or ampicillin, as the soluble sodium salt, rapidly provides effective concentrations at infection sites that are accessible to penicillins. Because of their rapid elimination by renal excretion, the dosage interval is short (6–8 h).

Procaine benzylpenicillin, the long-acting parenteral preparation of benzylpenicillin, should be administered to horses only by IM injection. The procaine in this preparation decreases the rate of absorption of the penicillin and offsets pain at the IM injection site, but inadvertent IV injection of a fraction of the dose would cause central nervous system (CNS) excitement. The peak plasma concentration of benzylpenicillin will vary not only with the dose administered but also with location of the IM injection site. The long-acting preparation allows the use of a 12 h (preferable) or 24 h dosage interval.

Penicillins should not be administered orally to horses because of their low systemic availability, due to poor absorption from the gastrointestinal tract, and the digestive disturbances associated with the imbalance they may cause in commensal microbial flora in the large intestine. In foals up to 4 mo of age, oral administration of amoxicillin or preferably **pivampicillin**, a pro-drug

which following entry into the systemic circulation is converted to ampicillin, may be effective in the treatment of infections caused by susceptible bacterial pathogens. The parenteral combination preparation containing ticarcillin—clavulanic acid, administered by slow IV injection, may be effective in neonatal foals (<7 days of age) for the treatment of infections caused by susceptible Gram-negative aerobic bacteria.

Penicillins produce a time-dependent bactericidal effect on susceptible bacteria. The overall effectiveness of penicillin therapy is influenced both by the height of the peak plasma concentration, which determines the rate of penetration of penicillin to accessible sites of infection, and the aggregate time, though not necessarily continuous, during which effective penicillin concentrations are maintained.

Cefalotin or cefazolin sodium, administered by IV injection at 8 h dosage intervals, may be effective in the treatment of infections caused by Gram-positive cocci including penicillinase-producing *Staphylococcus aureus*, and a single dose administered by IM injection 1 h before surgery may be indicated for prophylaxis in procedures (performed under optimal conditions) where a wound infection rate exceeding 5% is not unusual. The clinical use of cefadroxil (5% oral suspension) is limited to foals up to 1 mo of age. Cefoxitin, a second-generation parenteral cephalosporin, has a wider spectrum of activity than first-generation cephalosporins against Gram-negative aerobic bacteria and many Gram-negative anaerobes, including *Bacteroides fragilis*, are usually susceptible.

In the treatment of infections caused by susceptible bacteria, **cefoxitin sodium** should be administered by IV injection at 8 h dosage intervals. The clinical use of third-generation cephalosporins, with the exception of ceftiofur sodium, is largely limited to treatment of severe infections in neonatal foals. Significant features of third-generation cephalosporins include an expanded spectrum of activity against Gram-negative aerobic bacteria with remarkably high activity against Enterobacteriaceae, and an ability (except cefoperazone) to penetrate the blood–brain barrier. With regard to anaerobic bacteria, *Clostridium* spp. and *Fusobacterium* spp. are susceptible, whereas *Bacteroides* spp. are often resistant.

Ceftiofur sodium, administered by IM injection to adult horses at 12 or 24 h dosage intervals, is an alternative to ampicillin for the treatment of respiratory infections caused by susceptible bacteria. Because ceftiofur has high activity against fastidious Gram-negative aerobic bacteria (*Actinobacillus* spp., *Pasteurella* spp.), it may be used **concurrently with metronidazole** for the treatment of pleuritis and peritonitis (*q.v.*), which are often mixed infections with anaerobic involvement. Stable mutation to derepression of inducible β-lactamases in certain Gram-negative bacterial pathogens is an important mechanism of high-level resistance to β-lactam antimicrobial drugs. Induction of β-lactamases associated with acquired (chromosomal) resistance is caused especially by cefoxitin and third-generation cephalosporins.

Gentamicin and amikacin, which are the most widely used aminoglycoside antibiotics, show similar pharmacokinetic behavior and have a generally similar spectrum of antibacterial activity but differ in that effective plasma concentrations of amikacin are approximately two-fold higher than those of gentamicin; Gram-negative aerobic bacteria that have acquired plasmid-mediated

resistance due to the production of enzymes that inactivate gentamicin may remain susceptible to amikacin. Anaerobic bacteria are inherently resistant, while streptococci have a natural permeability barrier to aminoglycosides.

Synergistic enhancement of bactericidal activity against at least some strains of streptococci may be achieved by the concurrent use of **gentamicin and benzylpenicillin**, and against some strains of *Pseudomonas*, *Proteus*, *Klebsiella* and other Gram-negative rods by the concurrent use of gentamicin and ticarcillin. Since aminoglycosides and fluoroquinolones have concentration-dependent bactericidal activity, both the height of the peak plasma concentration and the area under the inhibitory curve (AUIC), which is the more important for aminoglycosides, influence the rate of bacterial killing.

Because of **rapid absorption** of gentamicin and amikacin from IM (and SC) injection sites, their relatively short half-lives and capacity to induce bacterial resistance, fixed doses of these drugs should be administered at 8 h (preferably), or 12 h, dosage intervals. The plasma concentration profile is not influenced by location of the injection site. The dose administered should be such as to ensure that the trough plasma concentration does not exceed 2 μg/mL for amikacin and 1–2 μg/mL for gentamicin.

All aminoglycoside antibiotics are potentially **ototoxic** and **nephrotoxic** (*q.v.*); due to their selective binding to phospholipid (phosphatidylinositol)-rich tissues, particularly of the inner ear and kidney cortex, they can accumulate in the presence of renal impairment. Calculation of dosage adjustment for gentamicin in horses with renal impairment should be based on endogenous creatinine clearance, which is often impractical.

In neonatal foals (up to 5–7 days of age) and in horses with impaired renal function (specifically, decreased glomerular filtration rate), either the dosage interval should be increased to 24 h or an antimicrobial agent of another class (selected on the basis of quantitative bacterial susceptibility) should be used.

The potential of aminoglycosides to cause nephrotoxicity (acute tubular necrosis) is influenced not only by the dosage regimen applied but also by the duration of therapy, and is enhanced in the presence of dehydration or by the concomitant use of a diuretic, especially furosemide. The activity of aminoglycosides on Gram-negative enteric bacteria is markedly influenced by the pH of the environment; they are most active in an alkaline environment. Increased local acidity secondary to tissue damage may account for the failure of an aminoglycoside to exert its bactericidal effect on usually susceptible bacteria at accessible sites of infection.

Fluoroquinolones have excellent activity ($MIC_{90} < 1$ μg/mL) against Enterobacteriaceae and fastidious Gram-negative aerobic bacteria and have good activity (MIC_{90}, 1–4 μg/mL) against *Pseudomonas aeruginosa*, *S. aureus* and other staphylococci, *Streptococcus equi*, and *Mycoplasma* spp. Fluoroquinolones, in common with aminoglycosides, are more active against Enterobacteriaceae and other Gram-negative aerobic bacteria in an alkaline environment and induce a post-antibiotic effect. Anaerobic bacteria are generally resistant. Maximal clinical efficacy of fluoroquinolones against susceptible bacteria may be achieved when the peak plasma concentration (C_{max}) is approximately 10 times the minimum inhibitory concentration (MIC) of the bacterial pathogen and a 12 h dosage interval is used. Both the administered dose and the dosage interval determine the area under the inhibitory plasma concentration-time curve.

Enrofloxacin, the fluoroquinolone that may be administered orally to mature horses (>4 yr old), is converted by *N*-de-ethylation (a hepatic microsomal-mediated oxidative reaction) to **ciprofloxacin**, which has antibacterial activity at least equal to that of the parent drug. The half-life of enrofloxacin in horses is 5.0 h while that of ciprofloxacin, which distributes more widely than enrofloxacin in body fluids and tissues, is 4.7 h. Ciprofloxacin decreases the systemic clearance of concomitantly administered theophylline to an extent that could be of clinical significance. The basis of the interaction could be a decreased rate of hepatic microsomal oxidative metabolism (*N*-demethylation) of theophylline. Because of their potential to cause degeneration of articular cartilage (*q.v.*) in weight-bearing joints (arthropathy), the use of fluoroquinolones is contraindicated in foals and young horses.

Even though fluoroquinolones, in common with several other antimicrobial agents, especially macrolides, lincomycins, the more lipophilic tetracyclines and orally administered penicillins, have the potential to seriously disturb the balance of **commensal microorganisms** in the colon of adult horses, the use of enrofloxacin at the usual dosing rate does not appear to cause the adverse effect.

Trimethoprim–sulfonamide combinations provide effective concentrations of both drugs in most body fluids and tissues and produce a bactericidal effect against a wide variety of equine bacterial pathogens. These combinations, which can be administered either orally or parenterally, are a useful alternative (second choice) to benzylpenicillin in the treatment of bacterial respiratory infections in older foals (>2 mo of age) and yearlings, whereas ceftiofur may be preferred in adult horses. In the treatment of pleuropneumonia (*q.v.*), which is often a mixed infection caused by **opportunistic aerobic bacteria and anaerobes**, trimethoprim–sulfonamide combination may be used in conjunction with metronidazole.

Another clinical indication for the use of trimethoprim–sulfonamide combination is in the treatment of **placentitis** (*q.v.*). An appropriate dosing rate for trimethoprim–sulfonamide combinations is 24 mg/kg administered parenterally or 30 mg/kg administered orally at 12 h dosage intervals. The higher dose level recommended for oral administration is to compensate for incomplete systemic availability, due mainly to **hepatic first-pass metabolism**, of trimethoprim. Oral dosing close to the time of feeding further decreases the systemic availability, or at least the peak plasma concentration, of trimethoprim and sulfonamides. This is probably due to binding of both drugs to fibrous components of feed.

Tetracyclines have a broad spectrum of antimicrobial activity, produce a bacteriostatic effect on susceptible microorganisms, and the tissue concentrations attained by individual tetracyclines are mainly influenced by their lipid solubility which, in turn, determines their clinical efficacy. The acquisition of plasmid-mediated resistance to tetracyclines appears to be due to a decreased ability of bacterial cells to concentrate the antimicrobial agents intracellularly. Because the effect produced by tetracyclines on susceptible bacterial pathogens is bacteriostatic, it is essential that effective plasma concentrations be maintained throughout the course of therapy.

Oxytetracycline is the drug of choice for the treatment of tentatively diagnosed and confirmed cases of **equine monocytic ehrlichiosis (Potomac horse**

fever) caused by *Neorickettsia risticii* (previously *Ehrlichia risticii*) (*q.v.*). Either a conventional (immediate release) preparation of oxytetracycline hydrochloride may be administered by slow IV injection at the usual dosing rate (3–5 mg/kg at 12 h intervals) or the long-acting preparation containing oxytetracycline formulated in polyethylene glycol may be administered by IM injection at a dosing rate of 6.6 mg/kg at 24 h intervals for 5–10 days. Long-acting preparations of oxytetracycline formulated in other vehicles are **unsuitable** for administration to horses because of tissue irritation caused at IM injection sites.

The concurrent use of oxytetracycline and rifampicin is clinically indicated for the treatment of **fistulous withers** caused by *Brucella abortus* or *Actinomyces bovis* (*q.v.*).

The potential especially of the more lipophilic drugs (minocycline, doxycycline) in this antimicrobial class to affect adversely the **commensal bacterial flora** in the cecum and colon limits their clinical use in horses. Under physiologically stressful conditions, such as following surgery, oxytetracycline can induce colitis X (*q.v.*), with sometimes fatal consequences.

Rifampicin is a lipophilic antimicrobial agent that attains effective concentrations in most tissues of the body. It readily diffuses through cell membranes to attain high intracellular (including phagocytes) concentrations and penetrates the blood–brain barrier. Rifampicin produces a bactericidal effect on susceptible Gram-positive aerobic bacteria, and both Gram-positive and Gram-negative anaerobes are susceptible to rifampicin. Because **chromosomal mutation** of bacterial RNA polymerase (the enzyme which rifampicin inhibits) can develop rapidly, rifampicin should *always* be used in conjunction with another antimicrobial agent selected on the basis that the combination will either produce a synergistic antibacterial effect or have enhanced clinical efficacy. Even though rifampicin is well absorbed from the gastrointestinal tract, hepatic first-pass metabolism (*q.v.*) reduces the systemic availability of rifampicin, which is further decreased by the presence of food in the stomach.

Rifampicin is partly eliminated by conversion in the liver to the desacetyl metabolite. This metabolic pathway has a dual significance in that 25-desacetylrifampicin has antibacterial activity similar to that of the parent drug and at doses above the recommended range (5–10 mg/kg) the capacity of this pathway may be exceeded leading to an increase in the half-life. Enterohepatic circulation contributes to the half-life of rifampicin, which is 6.0 h in adult horses.

Rifampicin is a potent inducer of hepatic microsomal enzymes, which may cause an increase in the rate of elimination (decrease in half-life) of various concomitantly used lipid-soluble therapeutic agents. Rifampicin in conjunction with erythromycin is specifically indicated for the treatment of ***Rhodococcus equi* infection** (pneumonia, lung abscesses) (*q.v.*) in foals aged between 6 and 16 wk. The recommended approach is to treat concomitantly with erythromycin estolate (20–25 mg/kg administered orally at 8 h intervals) and rifampicin (5 mg/kg PO at 12 h intervals) for a minimum duration of 3 wk. Improvement in clinical signs, the return of white blood cell count and plasma fibrinogen concentration to within the normal ranges, and radiographic resolution of pulmonary lesions serve as a useful guide to the duration of therapy.

The advantages of the **erythromycin–rifampicin combination** are that both antimicrobial agents administered orally attain **effective concentrations** at the site of infection, including an ability to **penetrate abscesses**; they appear

to act synergistically, and resistance of the causative bacterial pathogen to rifampicin is avoided.

Coprophagic behavior of some mares housed with their foals undergoing erythromycin–rifampicin treatment leads to ingestion not only of resistant *Clostridium difficile* (*q.v.*) but also of erythromycin excreted by the foals, which could severely disrupt the commensal bacterial flora of the large intestine and result in acute colitis (*q.v.*) in the mares.

Metronidazole is a lipid-soluble organic base that readily diffuses through cell membranes, distributes widely in tissues and body fluids, and penetrates cellular barriers. The drug is well absorbed from the gastrointestinal tract but shows wide variation in systemic availability within the range 60–80% in horses. Metronidazole exerts a bactericidal effect on most Gram-negative and many Gram-positive anaerobic bacteria. *Bacteroides* spp., including *B. fragilis*, *Fusobacterium* spp. and *Clostridium* spp., especially *C. difficile* (*q.v.*), are susceptible. The development of resistance, which could be due to reduced intracellular drug activation, is rare in usually susceptible bacterial species. In addition, metronidazole has high activity against various protozoa (*Trichomonas foetus*, *Giardia lamblia*) (*q.v.*). Both hepatic metabolism and renal excretion are involved in the **elimination of metronidazole**; the half-life is 3.9 h in horses. A dosing rate of 20 mg/kg administered orally (paste formulation) at 12 h dosage intervals is usual.

The use of metronidazole is clinically indicated in the treatment of **mixed aerobic–anaerobic** infections. The approach that should be adopted is to administer metronidazole **concomitantly** with an antimicrobial agent that has bactericidal activity against the **primary** aerobic bacterial pathogen. When the primary aerobe is Gram-negative, gentamicin or enrofloxacin (in adult horses) may be used whereas when the primary aerobe is Gram-positive, benzylpenicillin or ampicillin may be selected. Because the trimethoprim–sulfonamide combination provides a broad spectrum of activity against aerobic bacterial species, with the exception of *Pseudomonas aeruginosa* (*q.v.*), it could be used in conjunction with metronidazole; however, the use of a narrow-spectrum antimicrobial drug, selected on the basis of quantitative susceptibility (MIC for the isolated aerobic bacterial pathogen) and access to the site of infection, would be preferable.

NEONATAL FOALS

The most common pathogenic bacteria that cause infection (septicemia, pneumonia and septic arthritis) in neonatal (from birth to 7 days of age) and young (<1 mo of age) foals include *Escherichia coli*, *Klebsiella pneumoniae* and bacteria of the genus *Actinobacillus*, with the prevalence varying according to the geographic region.

The failure of passive transfer of maternal antibodies is the most significant factor that contributes to the development of neonatal septicemia. β-Hemolytic streptococci are infrequently isolated from septicemic foals but may cause pneumonia and septic arthritis, while *Pseudomonas aeruginosa* can cause septicemia and pneumonia. Approximately 50% of bacterial infections in neonatal foals are **mixed infections** (including *E. coli*).

Blood culture is a valuable, although not invariably certain, technique for making a microbiologic diagnosis of septicemia.

The success of treatment of bacterial infections in **neonatal foals** (*q.v.*) depends upon the prompt initiation of antimicrobial therapy according to an informed empirical approach, continuation with specific therapy based on precise identification of the causative pathogenic microorganism and its quantitative bacterial susceptibility, and the provision of supportive measures.

To avoid overloading **cardiopulmonary function** in neonatal foals, IV infusion of parenteral solutions should always be performed **slowly**. In selecting an antimicrobial agent, consideration should be given to the stage of development of the physiologic processes that affect distribution and elimination of the drug, and the immune status (serum IgG concentration) of the foal. The former is largely dependent on the age, in terms of days after birth, of the neonatal foal, while the latter is related to the ingestion of colostral antibodies. Correction of any deficit in serum immunoglobulins (*q.v.*) should precede and would enhance the effectiveness of therapy.

In neonatal foals, the use of an antimicrobial agent or antimicrobial combination that produces a **bactericidal effect** is preferable. Whenever possible, a parenteral preparation that can be administered IV should be chosen; this ensures that therapy will not be compromised by variations in drug absorption.

Should **gentamicin** be the drug of choice, precautions must be taken to avoid **nephrotoxicity and auditory damage**; dehydrated or fluid-depleted foals are particularly subject to gentamicin toxicity. The dosing rate for gentamicin is 3 mg/kg administered parenterally, usually at 12 h dosage intervals. Should therapy with gentamicin exceed 7 days, it is advisable to measure trough serum concentrations and monitor renal function.

Even though **amikacin** is less nephrotoxic than gentamicin, its use (6 mg/kg administered parenterally at 12 h dosage intervals) should generally be reserved for the treatment of infections in which the bacterial pathogen is susceptible to amikacin but resistant to gentamicin.

Ticarcillin–clavulanate combination has a wide margin of safety and, depending on quantitative susceptibility of the bacterial pathogen isolated, could be used as an alternative to an aminoglycoside antibiotic. A reasonable dosage regimen for ticarcillin–clavulanate combination is to administer 50 mg/kg by IV injection at 8 h dosage intervals for at least 3 days. Even though ticarcillin is active against *Pseudomonas aeruginosa* (*q.v.*), the concurrent use of ticarcillin and gentamicin could be justified in the treatment of severe infections because of their generally synergistic action against some strains of *Pseudomonas*.

Cefoperazone and especially **ceftazidime**, third-generation parenteral cephalosporins, have high activity against *Pseudomonas aeruginosa* and when used concurrently with an aminoglycoside antibiotic a synergistic action is produced. Whereas ceftazidime may penetrate the blood–brain barrier and is eliminated by renal excretion, cefoperazone does not penetrate the blood–brain barrier and is eliminated by the liver in bile. An empirical dosing rate for **ceftazidime** is 25–40 mg/kg administered by IV injection at 8–12 h dosage intervals.

The failure of many antimicrobial agents to attain effective concentrations in CSF and exert a bactericidal effect is a well-recognized problem in the treatment of bacterial meningitis, especially when caused by Enterobacteriaceae.

Either cefotaxime or ceftriaxone may be the antimicrobial agent of choice because each has the ability to penetrate the blood–CSF barrier and has high activity against *E. coli* and *Klebsiella* spp.

The parenteral preparation of **trimethoprim–sulfadiazine**, administered by slow IV injection at a dosing rate of 24 mg/kg at 12 h dosage intervals, is a useful alternative which is far less expensive than a third-generation cephalosporin. The combination has a bactericidal effect on *E. coli*, *Klebsiella* spp. and *Proteus* spp. and is often, although not always, effective in the treatment of **bacterial meningitis** (*q.v.*).

Because **fluconazole** penetrates the blood–CSF barrier and has activity against *Cryptococcus neoformans*, it is the antifungal agent of choice in the treatment of cryptococcal meningitis (*q.v.*). Fluconazole suppresses oral and esophageal candidiasis in immunocompromised foals and may be effective in the treatment of systemic **Candida infections** (*q.v.*). The empirical oral dosage regimen entails the initial administration of 400 mg (total loading dose) followed by maintenance doses of 200 mg at 24 h dosage intervals. Even though fluconazole has lower in vitro activity than itraconazole against *Candida* spp., it is the drug of choice for treatment of systemic Candida infections because it causes fewer interactions with therapeutic agents and least inhibition of hepatic microsomal cytochrome P450 enzymes.

Itraconazole may be the drug of choice for the treatment of mycotic pneumonia caused by opportunistic fungi (*Aspergillus* spp., *Candida* spp., *Mucor* spp.) in neonatal foals (*q.v.*).

ANTIFUNGAL AGENTS

Cutaneous mycotic infections caused by dermatophytic fungi (*q.v.*) are usually treated topically in horses and could be treated systemically. Drugs that may be applied topically include natamycin, various imidazole derivatives and nystatin, while systemic treatment is provided by orally administered griseofulvin, ketoconazole or itraconazole.

Topical antifungal preparations should be formulated to provide **penetration and persistence** of the drug at the cutaneous site of the infection. For topical application, there appears to be no clear preference for the use of one imidazole over others.

Superficial infections caused by *Candida* spp. (*q.v.*) may be treated locally by applying nystatin or an imidazole derivative, whereas soft tissue and gastrointestinal candidiasis are treated by administering orally an imidazole derivative. **Systemic mycoses** caused by dimorphic fungi require oral or parenteral therapy with an **imidazole derivative** usually used alone but could be cautiously used in conjunction with **amphotericin**; the drug is administered IV. Because of its narrow therapeutic index, high potential to cause nephrotoxicity, requirements associated with administration and the high activity of some imidazole derivatives against dimorphic fungi, the clinical utility of amphotericin is limited and decreasing. **Itraconazole** is replacing amphotericin as the drug of choice for the treatment of systemic infections caused by dimorphic fungi and systemic aspergillosis, caused by *Aspergillus fumigatus* (*q.v.*).

Natamycin is a polyene antibiotic with fungicidal activity against a variety of filamentous fungi, including dermatophytes (*Microsporum* spp., *Trichophyton* spp.), and against yeasts (C*andida* spp., *Cryptococcus neoformans*) (*q.v.*). A freshly prepared 0.01% aqueous suspension of natamycin, applied topically by spray or sponge on two occasions with a 4-day interval and again 2 wk later, if required, is often effective in the treatment of **ringworm (dermatophytosis)** (*q.v.*).

It is important that all grooming utensils and tackle be thoroughly cleansed and immersed in the natamycin suspension, which should be prepared in plastic or galvanized containers. Natamycin has been used successfully to treat **filamentous fungal keratitis**, especially when caused by *Fusarium* spp. (*q.v.*). A recommended treatment is to apply 1 drop of a 5% aqueous suspension (natamycin ophthalmic) every 1–2 h, decreasing to 6–8 times daily after a few days. If *Aspergillus* is identified mycologically as the causative organism of a **corneal infection**, the drug of choice is **miconazole**. Miconazole is commercially available as a parenteral solution (10 mg/mL) that can be applied locally at short intervals and administered by subconjunctival injection (10 mg s.i.d. for 5 days). Natamycin is not effective against deep mycotic infections of the eye, because of poor penetration to the site of infection.

Nystatin, a polyene macrolide antibiotic that is structurally similar to amphotericin, is used mainly to treat cutaneous yeast infections caused by *Candida* spp., although some *Candida* spp. other than *Candida albicans* may be resistant. For topical application, nystatin is formulated as a cream and an ointment. Nystatin administered as an oral suspension (100 000 units/mL) is not absorbed from the gastrointestinal tract and may be used for the treatment of gastrointestinal candidiasis. However, itraconazole (oral liquid) may be the antifungal agent of choice. In the treatment of mycotic endometritis caused by *Candida* spp. intrauterine nystatin could be considered second choice to clotrimazole, which is administered as an aqueous suspension (500 mg daily for 7–10 days) by **intrauterine infusion**.

The **azole class** of antifungal agents comprises the imidazoles (ketoconazole, miconazole, clotrimazole and enilconazole) and the triazoles (itraconazole and fluconazole). Based on their greater affinity for fungal than for mammalian cytochrome **P450 enzymes**, the triazoles are relatively more selective in action than the imidazoles, which accounts for the lower incidence of drug interactions and side effects associated with their use.

Azole antifungal agents are generally fungistatic against various **filamentous fungi**, which include *Aspergillus* spp. and dermatophytes (*Microsporum* and *Trichophyton* spp.), yeasts (*Cryptococcus neoformans*, *Candida* spp.), and dimorphic fungi (*q.v.*). Individual azoles differ in their activity against fungal species and in their pharmacokinetic properties, both of which contribute to clinical efficacy. The duration of treatment with azole derivatives should be based on both clinical and mycologic response.

The use of clotrimazole is limited to **topical application**. Absorption of ketoconazole and itraconazole, lipophilic drugs, is increased by low gastric pH. **Ketoconazole** is dissolved in **0.2 N hydrochloric acid** prior to administration by nasogastric tube to horses. In the systemic circulation, ketoconazole and itraconazole bind extensively to plasma proteins and undergo elimination by hepatic microsomal oxidative reactions; ketoconazole especially

causes inhibition of the hepatic microsomal cytochrome P450 enzyme system. **Itraconazole** (oral liquid) is the azole of choice in the treatment of **refractory dermatophyte infections** (*q.v.*) because marked binding to keratin occurs, and is the only azole with activity against *Aspergillus* spp.

Guttural pouch mycosis (*q.v.*), which is most commonly caused by *Aspergillus nidulans*, may be treated by administering **itraconazole** orally (5 mg/kg q 12 h) and irrigating the guttural pouch with a parenteral solution of either itraconazole or miconazole once daily. Itraconazole is the preferred azole for the treatment of systemic infection caused by dimorphic fungi.

Fluconazole differs from the other azoles in that it is soluble in water, binds to a low extent to plasma proteins, readily penetrates the blood–CSF barrier, and is eliminated mainly by renal excretion. It has the **widest therapeutic index** of the azoles and the lowest incidence of drug interactions. Fluconazole is the drug of choice in the treatment of cryptococcal meningitis (*Cryptococcus neoformans*) (*q.v.*) and in urinary tract mycoses, usually *Candida* spp. (*q.v.*). The usual dosing rate of fluconazole for the treatment of fungal cystitis, which may also involve opportunistic aerobic bacteria, is 4 mg/kg administered PO q 12 h in conjunction with trimethoprim–sulfadiazine (oral paste formulation); a long duration of treatment is required.

Griseofulvin is a fungistatic lipophilic antibiotic that is administered orally as a paste formulation or as granules added to the feed for the systemic treatment of cutaneous infection caused by dermatophytes (*q.v.*). Its selectivity of action is due to an energy-dependent uptake of the drug by susceptible dermatophytic fungi (*Microsporum* and *Trichophyton* spp.) The absorbed drug distributes via the systemic circulation to the various layers of the epidermis, including the *stratum corneum* where it selectively binds to **keratinocytes** and persists in the newly forming structures that gradually replace the fungal infected structures. This implies that a **long duration** of treatment is invariably required. The suggested dosage for horses is 25 mg/kg of the oral paste or oral granules (which contain 75 mg/g), s.i.d. for 2 wk followed by 12.5 mg/kg s.i.d. for a further 8 wk. The absorption of griseofulvin is increased when the drug is administered with feed. Because griseofulvin induces hepatic microsomal cytochrome P450 activity during the course of treatment, the rate of metabolism of concomitantly administered therapeutic agents that are mainly eliminated by hepatic microsomal-mediated oxidative reactions is increased.

ANTHELMINTICS

INTRODUCTION

In most countries, several anthelmintics are licensed for use in the horse. The main chemical groupings into which they can be classified include probenzimidazoles and benzimidazoles, tetrahydropyrimidines (pyrantel), avermectins and milbemycins and pyrazinoisoquinolones (praziquantel). In some places, the simple heterocycle, piperazine, the organophosphates and morantel are also available, as are a number of products containing more than one active anthelmintic.

MODE OF ACTION

Febantel is a **pro-benzimidazole** with a phenyl guanidine structure, which is hydrolyzed and cyclized into **fenbendazole** and, while the parent compound may have some neurotoxic effect on parasites, it is likely that the principal mode of action is through the activity of the benzimidazole metabolites.

The **benzimidazoles** have been shown to inhibit parasite metabolic enzymes including fumarate reductase. However, at lower concentrations they attach to nematode tubulin, thus disrupting cytoplasmic microtubules with consequent failure of intracellular secretory granule transportation. This latter effect is thought to be the mode of anthelmintic activity common to all members of the group.

Pyrantel and morantel act as a cholinergic agonist at the parasite ganglion and thus stimulate spastic paralysis of parasite musculature. Preparations of pyrantel are formulated as salts (embonate in the UK, pamoate and tartrate in the USA). The embonate and pamoate salts are less water soluble than the tartrate salt, are less well absorbed from the gastrointestinal tract, and are therefore **less toxic** to the host.

Avermectins and milbemycins affect parasites in many ways, but the most likely explanation for their antiparasitic action is that they increase parasite neuronal membrane permeability to chloride ions. This action, which causes paralysis of the parasites, is mediated by a glutamate-gated mechanism which is potentiated by the avermectins and milbemycins.

The precise mechanism of action of **praziquantel** is unknown but it does affect muscular activity in **cestodes** and causes vacuolation and disruption of the parasite tegument.

Piperazine causes hyperpolarization at nematode muscle cell membranes, which results in flaccid paralysis, and it may act as a GABA agonist within the parasite.

The **organophosphates** inhibit cholinesterase enzymes, particularly acetylcholinesterase, which results in a build-up of acetylcholine in ganglia or at neuromuscular junctions. In the host, the organophosphates initially form a reversible complex with acetylcholinesterase but, with time, the complex becomes irreversible and cholinesterase activity will then recur only when the new enzyme is synthesized. In the parasite, inhibition may be reversible or irreversible, depending on the species involved. Reversible inhibition is usually sufficient to facilitate expulsion of the parasite by peristalsis if its predilection site is the gut.

TOXICITY

The **pro-benzimidazoles** and **benzimidazoles** are very safe drugs in the horse. The therapeutic index (i.e. the dose at which toxic signs are first seen/minimum therapeutic dose) for each drug used is >10 and for fenbendazole is $\geqslant 200$. If toxicity is seen, it is generally first manifest as diarrhea with abdominal discomfort.

Pyrantel has a therapeutic index >6 and the more soluble tartrate salt is slightly more toxic than the embonate or pamoate salts. Toxicity in the horse reflects the likely mode of action of pyrantel on nicotinic receptors, which

results in increased respiratory rate, sweating and incoordination. Consequently some preparations are contraindicated in debilitated animals. The morantel preparations available for horses comprise the tartrate salt, which is highly polar and thus poorly absorbed from the gastrointestinal tract. This confers good safety on this product.

Ivermectin is reported to be safe at up to 10 times the recommended oral dose. However, at very high dose levels (12 mg/kg or 60 times the recommended dose) animals become depressed and ataxic and may display mydriasis and lower lip droop. Where *Onchocerca* spp. (*q.v.*) are prevalent, treatment at the therapeutic dosage rate may result in a hypersensitivity reaction to dead microfilariae with ventral abdominal edema and pruritus. **Ivermectin is not licensed for parenteral administration in the horse and should not be given by injection** since a low but significant incidence of infected injection sites with consequent clostridial myositis (*q.v.*) occurs. Anaphylactoid reactions (*q.v.*) have also been associated with IV administration and attributed to the presence of the excipient polysorbate 80 in the micellar formulation. **Moxidectin** has been shown to be safe at up to three times the therapeutic dose in foals. At higher dosages signs similar to those reported for ivermectin occur.

Piperazine is unlikely to cause toxicity, even at doses as high as 17 times that recommended for therapeutic efficacy.

The **organophosphates** have relatively narrow therapeutic indices, which may depend upon the capacity for enzymatic degradation or inactivation of the drug. Toxicity may also depend upon the formulation, since these drugs are commonly presented in slow release resins that reduce the maximum peak systemic exposure to the drug and thus its toxicity. Of the two organophosphates commonly used in the USA, **trichlorfon** paste and liquid preparations have a narrower therapeutic index of 1 than **dichlorvos resin** pellets which have a therapeutic index of 3.

Acute organophosphorus toxicity is the result of irreversible inhibition of acetylcholinesterase and presents initially as parasympathetic stimulation with diarrhea and colic. Ultimately all muscarinic and nicotinic receptors become stimulated and animals die of asphyxia as respiratory muscles fail to function properly.

PHARMACOKINETICS

There is little information on the pharmacokinetics of many of the anthelmintic drugs used in the horse. Some of the benzimidazoles, avermectins and milbemycins and pyrantel have, however, been investigated. **Fenbendazole** and **oxfendazole** are metabolically interconvertible as a reversible step in the pathway which leads to the formation of a more highly oxidized metabolite, oxfendazole sulfone, which is anthelmintically inactive.

Lower plasma concentrations of fenbendazole and oxfendazole are achieved following administration of fenbendazole than the same dose rate of oxfendazole. This probably reflects the relative insolubility and consequent slow absorption of fenbendazole and its subsequent rapid oxidative metabolism through the oxfendazole intermediate to the sulfone metabolite. If oxfendazole is administered as the parent compound, its rate of absorption exceeds that of its metabolism and therefore higher plasma concentrations are achieved. These

generate higher plasma concentrations of fenbendazole by reductive metabolism than are achieved when fenbendazole is administered as the parent compound. These characteristics of absorption and metabolism possibly explain the very high dosage recommendations for fenbendazole for the treatment of migratory stages of large strongyles and for immature small strongyles. Oxibendazole undergoes extensive **first-pass metabolism** (*q.v.*) and very low concentrations of parent drug are detected in plasma following oral administration.

The comparatively short persistence of benzimidazoles in the plasma of horses compared with ruminant species means that their efficacy may be improved by dosing over a number of consecutive days, since improved efficacy is a feature of prolonged exposure of parasites to benzimidazoles.

Pyrantel can be detected at low concentrations of up to about 0.1 μg/mL in plasma between 1 and 60 h after oral administration of 13.3 mg/kg BW of pyrantel embonate. It is largely excreted unchanged in the feces, in which concentrations >1.0 mg/kg can be detected and in which it is present for approximately 70 h.

Ivermectin has been shown to persist in the tissues and plasma of many species of animal for some time after administration, conferring prophylactic activity against susceptible parasites ingested or otherwise acquired during the period of persistence. In the horse, oral administration of 200 μg/mL of the commercially available paste preparation results in persistence at measurable concentrations >2 ng/mL for 14 days, conferring activity against ingested infected larvae. This accounts for the interdosing interval of 8–10 wk often recommended for this anthelmintic which is derived from the shortest prepatent period of the common equine parasites (6–8 wk for small strongyles) plus the 2 wk period of anthelmintic prophylaxis. **Moxidectin** is highly lipid soluble, and following administration distributes to the lipid compartments of the body from which reservoir it redistributes slowly to the predilection sites of the parasites. It can be detected in horse plasma for at least 80 days following a therapeutic dose and this may account for the suppression of small strongyle egg output for 90 days.

The pharmacokinetics of other anthelmintics used in the horse are less critical since their efficacy is not dependent upon persistence nor do they confer significant prophylactic activity.

SPECTRA OF ACTIVITY

Anthelmintic medication may be indicated for the following common internal parasites of the horse. In the foal, the large ascarid *Parascaris equorum* and the threadworm *Strongyloides westeri* (*q.v.*) which inhabit the small intestine are frequently the cause of unthriftiness and diarrhea, respectively. In adult horses, treatment for the stomach bots *Gasterophilus* spp. (*q.v.*) and the ileal or cecal tapeworm *Anoplocephala perfoliata* (*q.v.*) is often carried out, although the pathogenic significance of these parasites is unclear.

The strongylid worms are, however, pathogenic. These include the large strongyles *Strongylus vulgaris* (*q.v.*), which has a migratory pathway via the cranial mesenteric artery, and *S. edentatus* (*q.v.*), which migrates via the liver and parietal peritoneum, and the small strongyles or cyathostomes (*q.v.*), which

include many species and which invade and develop within the large intestinal mucosa. The predilection site of all the strongylid species is the cecum and colon.

The colon is also the predilection site for the large pinworm *Oxyuris equi* (*q.v.*), which is not pathogenic *per se* but which lays eggs causing perineal irritation.

Lungworm infection in the horse is attributed to *Dictyocaulus arnfieldi* (*q.v.*) and is relatively uncommon, as is infection with the liver fluke *Fasciola hepatica*.

The efficacy of the available anthelmintics against adult stages of most of these parasitic infections is well established. However, larval stages are often less susceptible and there is a paucity of data on anthelmintic efficacy against immature parasites. Parasite resistance to anthelmintic drugs is an emerging concern and is used to describe parasites that are less susceptible to a drug than the original population.

EFFICACY

The following assessment of drug efficacies is for susceptible parasites.

Febantel is >95% effective against adult and larval *P. equorum*, adult large and small strongyles, and adult and larval *O. equi* when used at a dose of 6 mg/kg.

Mebendazole at a dose of 5–10 mg/kg is >95% effective against *P. equorum* and *S. vulgaris* but less so (80%) against *S. edentatus* and the small strongyles. It is highly effective against larval and adult *O. equi* and is effective against *D. arnfieldi* in donkeys if administered at 15–20 mg/kg daily for 5 consecutive days.

The standard recommended dose rates for **fenbendazole** and **oxfendazole** are 7.5 and 10 mg/kg respectively, and both have been shown to be >90% effective against *P. equorum*, large and small strongyles and mature *O. equi*. They are also effective against immature and migrating large strongyle larvae, although the dose of fenbendazole should be increased to 60 mg/kg for these stages. Fenbendazole is effective against *S. westeri* at 50 mg/kg, against immature small strongyles at 30 mg/kg and against *D. arnfieldi* at 15 mg/kg. Administration of fenbendazole and oxfendazole over a number of consecutive days may prove more effective against the more recalcitrant parasites than a single administration.

Fenbendazole has an efficacy claim for the treatment and control of migrating and tissue larval stages of large strongyles and encysted mucosal 3rd and 4th stage small strongyle larvae, when all administered at 7.5 mg/kg BW daily for 5 days.

Oxibendazole is >90% effective against *P. equorum*, large and small strongyles and adult and immature *O. equi* when administered at 10 mg/kg, and has good activity for *S. westeri* at 15 mg/kg. It has also been shown to be effective against small strongyles resistant to other benzimidazole anthelmintics, although these parasites do subsequently appear to develop resistance to oxibendazole rapidly.

Pyrantel is administered at a standard dose of 6.6 mg base/kg BW, which is equal to 19 mg of pyrantel embonate/kg BW. It is >90% effective against *P. equorum*, *S. vulgaris* and small strongyles, but only 65–70% effective against

S. edentatus and adult *O. equi*, respectively. It is recommended for *A. perfoliata* if the dose is increased to 13.2 mg base/kg (38 mg pyrantel embonate/kg).

Ivermectin at 200 μg/kg is >95% effective against *P. equorum*, *S. westeri* and large and small strongyles including arterial (*S. vulgaris*), tissue (*S. edentatus*) and luminal L_4 (cyathostomes) stages. Its activity on mucosal developing L_3 and L_4 has been inconsistent. It is also highly effective against *D. arnfieldi* and *O. equi*. The activity of ivermectin for **arthropods** also makes this an extremely effective drug for both the oral and gastric stages of *Gasterophilus* spp. (*q.v.*).

Moxidectin (400 μg/kg) has similar excellent activity to ivermectin against *P. equorum*, *S. westeri*, adult and arterial/tissue stages of large strongyles and adult luminal L_4 stages of small strongyles. It has been shown to confer between 55% and 84% reduction in mucosal developing L_3 and L_4 stages of small strongyles and has authorized claims for encysted inhibited early L_3 and developing intramucosal L_4 larval stages in some markets. It has an authorized claim for *Gasterophilus* spp. in some markets, although efficacy has been shown to be rather variable (20–99%) against this parasite.

Praziquantel (1 mg/kg) has excellent activity against *A. perfoliata*, the common cestode of horses (*q.v.*), and is exclusively used for this parasite either alone or in combination products designed to extend the spectrum of activity.

Many of the remaining anthelmintics have limitations in their spectra of activity or efficacy and consequently some of the drugs are produced in combinations that complement each other. **Piperazine** is >95% effective for *P. equorum* and for small strongyles at 88 mg/kg but is otherwise poorly effective and is produced in combination with oxfendazole.

The two organophosphates are highly effective against *P. equorum*, *O. equi* and *Gasterophilus* spp. **Dichlorvos** is also >90% effective for *S. vulgaris* and the small strongyles, and >70% effective for *S. edentatus* at a dose rate of 35 mg/kg. The dose of **trichlorfon** has to be increased from 40 to 80 mg/kg to confer activity against large and small strongyles. The organophosphates are marketed alone and in combinations with benzimidazoles.

There are no drugs specifically licensed for the treatment of *F. hepatica* in the horse. However, the benzimidazole **triclabendazole** has been shown to be highly effective at reducing fecal egg output from infected animals when given at 12 mg/kg. The plasma concentrations of triclabendazole and its metabolites achieved following administration at this dose are lower than those achieved in the ruminant and it may be that a higher dose rate is more appropriate in the equine.

STRATEGIC DOSING

Anthelmintic strategies for the horse depend to a large extent on **prevalence and seasonality** of the parasites. In many countries, control is usually based on anthelmintic administration at 4–6 wk intervals to all horses at grass. The persistent activity of **moxidectin** and its activity against immature stages of cyathostomes mean that the dosing interval can be extended to 13 wk.

If treatments are timed to coincide with **highest egg output** then they should be concentrated in the spring when the horses are producing most eggs

and in the autumn/fall when **pasture contamination** with infective strongyle larvae is highest. Suppressive treatment in the spring may lower pasture contamination sufficiently to preclude necessary medication throughout the latter half of the grazing season. In very hot dry climates larval survival during the summer is low.

In the USA, an alfalfa feed preparation containing pyrantel tartrate has been produced to deliver continuous low-level medication to horses for strongyle control.

RESISTANCE

The development of **resistance to anthelmintics** is a well-recognized phenomenon and in horses occurs principally with the **small strongyles**.

In order to minimize the likelihood of resistance developing, **annual rotation** of anthelmintics from different chemical groupings has been advocated. This system means that each generation (assuming one annual generation) of parasites is only exposed to one drug group and subsequent generations are exposed to a different anthelmintic for which they have not had the opportunity to develop resistance. Where this system is adopted it is obvious that some parasites may not be treated for a whole season since the anthelmintics currently available on their own are **not effective** against all species. It may therefore be necessary to include one or more treatments with another drug with a different spectrum of activity.

The factors that increase the likelihood of resistance developing include:

1. More frequent treatment, which increases the selection of parasites with resistant genes.
2. Using anthelmintics with 90–99% efficacy; if efficacy is <90%, sufficient susceptible parasites survive treatment to retain the susceptibility of the population; if >99.9%, there are too few survivors to reproduce effectively.
3. Few parasites existing in refugia (i.e. not exposed to the anthelmintic), for instance free living stages. In droughts, the number of parasites in refugia may be small, thus if treatment is initiated a large proportion of the total population is exposed and thus selection is intense.
4. Using drugs with a long terminal plasma elimination half-life, since parasites are exposed to subtherapeutic concentrations for a prolonged period. However, where drug activity is increased by time of exposure the influence of this parameter is likely to be complex.
5. Dominant rather than recessive mode of inheritance of resistance.

ANALGESIA

INTRODUCTION

While the equine species has been of central importance to the veterinary profession since time immemorial, understanding of behavioral expression of pain in horses remains poor relative to other domestic species. Horses are frequently described as being "very sensitive" to pain, based primarily on

violent behavioral responses to acute painful or frightening stimuli. **Behavioral manifestations** of discomfort (other than those associated with severe acute pain) are less well appreciated. Experimental evidence indicates that domestic animal species, in common with humans, respond to noxious stimuli of similar intensities, and there is no doubt that manifold subtle behavioral indicators of discomfort in horses probably pass unrecognized. Thus it is considered highly likely that pain in horses is **under-diagnosed** and consequently **under-treated**.

ASSESSMENT OF PAIN

Severe pain associated with conditions such as **laminitis** or **colic** is generally easily recognized. However, horses often demonstrate discomfort through more **subtle behavioral indicators** that may include sweating, ears flicked frequently or held back, reluctance to move or increased locomotor activity, restlessness, reduced weight bearing on a limb or a rigid stance, weight shifting, abnormal postures, abdominal guarding, kicking at the abdomen, interrupted feeding patterns, withdrawal to the back of the stable and reduced interest in/interaction with companions, and abnormal postures, particularly head held below the withers. While increased heart and respiratory rates may accompany severe acute pain, they are not reliable physiologic pain indices in other species, in particular where animals are in unfamiliar surroundings or are being assessed by unfamiliar individuals. The presence or absence of one or more of these signs will depend on the location and severity of the pain, e.g. horses with abdominal pain may also paw the ground, roll, stretch and turn their head towards their flanks.

The nature of the pain, as interpreted by clinical signs, may also help in making a diagnosis. In general, the horse exhibiting signs of colic due to an impacted large intestine does not manifest severe signs of pain, whereas a horse suffering with **tympanitic colic** (*q.v.*) will often manifest pain in a more violent manner. In both instances pain arises due to intestinal distension but is manifested by different behaviors. The horse suffering with **spasmodic colic** (*q.v.*) may show intermittent signs of pain with a return to normal behavior in between episodes. These are important observations and influence the diagnosis and subsequent choice of analgesic drug. Thus, there is a need to observe the nature and pattern of pain in the horse, before selecting analgesic drugs for effective pain management.

The assessment of **postsurgical pain** may be difficult due to the superimposed stress of both anesthesia and hospitalization in horses. Knowledge of procedures considered painful in humans is useful in selecting an analgesic agent and, in the absence of evidence to the contrary, it is reasonable to assume that pain will exist in situations in which humans would experience pain.

Orthopedic procedures, commonly carried out in horses, are likely to be associated with severe postoperative pain, in particular as the animal is required to use the affected limb in some manner during recovery. Superficial or body surface surgery, particularly if extensive, also can cause intense discomfort in humans and other animal species, and is likely to do the same in horses. Intra-abdominal surgery can cause a marked degree of postoperative pain, particularly when the animal resumes a standing position.

PHARMACOLOGIC CONTROL OF PAIN

There are many sites along the pathways involved in the transmission of nociceptive/pain information from the periphery to the CNS where activity may be modulated. Drugs that suppress or modulate the animal's response to pain which act centrally in the brain and spinal cord include the opioids, the α_2-adrenoceptor agonists, ketamine, nitrous oxide, local anesthetics and NSAIDs. Some of these drugs have peripheral sites of activity which contribute to their analgesic efficacy and/or to their side effects, e.g. inflammatory mediators such as bradykinin and the prostaglandins, which are produced in response to tissue damage, activate or sensitize peripheral receptors in the body that respond to noxious stimuli. The NSAIDs act by decreasing the production of some inflammatory mediators in the periphery (*q.v.*) thereby enhancing their significant centrally mediated analgesic activity.

Local anesthetic drugs have both peripheral and central analgesic activity. Peripherally, they block conduction of impulses from the nociceptors along sensory fibers; centrally, their analgesic activity is attributed to antagonism of specific sodium channels involved in central sensitization of nociceptive transmission. Thus such drugs, when used in an appropriate manner, are highly effective.

The **opioids** produce their effects by activation of one or more specific receptors, the μ (mu), κ (kappa) and δ (delta) receptors. Thus they mimic the action of endogenous ligands such as the endorphins, dynorphins and enkephalins. The opioid drugs are probably best classified according to their relative activity at each receptor. They act as pure agonists or pure antagonists, or may fall into the spectrum between and be termed partial antagonists. In addition, a drug may be a partial agonist at one receptor and an antagonist at another. Activation of one, two or all of the opioid receptors produces analgesia. Other pharmacologic effects consequent to opioid receptor activation either centrally or in the periphery may vary considerably according to the particular receptor activated.

Opioids are indicated for the treatment of **moderate to severe pain**. The undesirable side effects of increased locomotor activity and respiratory depression appear to occur less frequently when the drugs are given to horses experiencing pain. Respiratory depression in horses, unlike that seen in humans, is not a major side effect when the drugs are used at clinically recommended doses. It is notable that administration of opioids by extradural (epidural) injection achieves highly effective spinally mediated analgesia while avoiding the systemic side effects described above.

Horses in pain respond to opioids with a decrease in locomotor activity as relief is obtained, however **increased motor activity** occasionally occurs, particularly after repeat administration to control severe pain. This behavioral disturbance can be controlled with a low dose (0.03–0.05 mg/kg IM or IV) of acepromazine or, alternatively, the effect reversed with an opioid antagonist such as **naloxone**, although analgesia will then also be abolished.

Decreased gut motility is a potential side effect of opioid administration, the consequences of which may be relevant depending on the individual animal and its pathology; however, the depression of gut motility associated with opioid administration should be considered in the context of the depressant effect of unrelieved pain and altered behavior and feeding patterns on gastrointestinal motility.

Individual drugs (for recommended doses, see Table 4.6)

Morphine is a controlled drug and is classified as a pure agonist with a high affinity for μ receptors. It produces analgesia in the horse that is relatively **slow in onset** and lasts for up to 4 h, depending on the severity of pain and the dose administered (0.05–0.1 mg/kg, IV). Respiratory depression and gastrointestinal depression are not considered significant at clinically recommended dose rates in conscious horses, although locomotor stimulation can occur at higher doses. Cardiovascular side effects are minimal. Morphine can be given IM, IV or by extradural injection.

Methadone (controlled drug) has been used widely in combination with a tranquilizer drug to produce chemical restraint in the standing horse, and is frequently administered in some countries. In humans, methadone is roughly equipotent with morphine but has a longer duration of action, and in dogs it appears to be a very effective analgesic. It can be administered IM, IV or by extradural injection at doses of 0.05–0.1 mg/kg.

In addition to its pharmacologic properties as an opioid drug, **pethidine** (controlled drug) has anticholinergic activity and consequently is an effective gastrointestinal spasmolytic. It has a selective role in the horse. The short duration of action and lack of potency limit its use as a postoperative analgesic. However, it may be beneficial for short-term analgesia (approximately 1 h) either to allow movement of a horse, where a rapid onset of effect is required, or for the relief of spasmodic abdominal pain. It is best given by the IM route (2 mg/kg). Effective extradural analgesia has also been described

Table 4.6 Drugs and drug doses commonly used for extradural analgesia

Drug	Doses	Onset of action	Duration of analgesia	Side effects (associated with systemic absorption)
Lidocaine	0.22–0.35 mg/kg	5–15 min	60–90 min	Ataxia/recumbency at high doses
Ropivacaine	0.08 mg/kg	5–15 min	2.5–4 h	Questionable quality of analgesia
Xylazine	0.17–0.35 mg/kg	10–30 min	2.5–4 h	Perineal edema, sweating, ataxia
Detomidine	30–60 μg/kg	10–15 min	2–3 h	Sedation, ataxia
Morphine	0.1–0.15 mg/kg	Slow; 4–8 h	8–18 h	Sedation, ataxia
Pethidine	0.8 mg/kg	5–15 min	4–5 h	Mild sedation and ataxia
Ketamine	0.5–2 mg/kg	5–15 min	30–90 min	Sedation, mild ataxia
Ketamine/morphine	1 mg/kg and 0.1 mg/kg	Poorly defined; slow, up to 4 h	12–18 h	Sedation, mild ataxia
Ketamine/xylazine	1 mg/kg and 0.5 mg/kg	5–15 min	>2 h	Mild sedation, bradycardia
Tramadol	1 mg/kg	30 min	8–12 h	

As a standard, drugs are administered in an injection volume of 4–8 mL for a 500 kg horse to provide analgesia appropriate for perineal surgery. The higher end of the volume range should be used to provide analgesia suitable for hindlimb surgery. If local anesthetic is used, a total injection volume of, 10 mL to adult (500 kg) horses is recommended to avoid paresis/paralysis of motor supply to the hindlimbs. Where analgesic drugs (without addition of local anesthetic agents) are used, a volume of 10–20 mL can be used in adult horses (500 kg) to facilitate cranial migration of the solution.

using pethidine (0.6–0.8 mg/kg). Intravenous administration in conscious horses can precipitate excitement and collapse associated with systemic histamine release and severe hypotension. This is of particular significance in anesthetized animals.

Butorphanol is a partial agonist that is licensed in the UK for use in the horse. Experimental and clinical evidence suggest that it is more effective in the management of mild to moderate visceral pain than in the treatment of somatic pain and other types of severe pain. It is administered IV at doses of 0.03–0.1 mg/kg. When injected at a dose of 0.1 mg/kg, it may precipitate an increase in locomotor activity, observable as "compulsive walking". Butorphanol is frequently combined with a sedative such as **detomidine** (*q.v.*) for standing sedation. It is not a controlled drug and, unlike morphine, pethidine and methadone, is consequently not subject to such strict controls regarding its purchase, storage and use.

Fentanyl patches for transdermal analgesic administration have been described for treatment of both postsurgical pain and other refractory pain conditions including severe laminitis. Fentanyl is a potent opioid agonist that has been used parenterally in other species, and its use in transdermal patches has been described in dogs and cats. There are as yet no published studies documenting the pharmacokinetic profile and analgesic efficacy of these potentially useful transdermal patches in the horse, and at this stage their use is not recommended in the horse.

None of the other opioid partial agonists is licensed for use in the horse. **Buprenorphine** and **nalbuphine** have been used in neuroleptanalgesic combinations for standing chemical restraint, but their efficacy as analgesics in this species is unknown. **Pentazocine** has been used to treat visceral pain in the horse but can produce excitement and is best avoided.

α_2-Adrenoceptor agonists provide profound analgesia for both visceral and somatic pain. Xylazine, detomidine and romifidine are licensed as sedatives/analgesics for use in the horse and are among the most effective and potent analgesics available. Medetomidine is currently not licensed in horses, but has been investigated as a potentially useful analgesic agent intraoperatively. At high (sedative) dose rates, these drugs have numerous side effects and cause marked disturbance in **cardiovascular function**—hypertension, hypotension, bradycardia, decreased cardiac output—and a more significant reduction in gut motility than that recorded with opioid agonists. In addition, they are **contraindicated** in the latter stages of pregnancy due to potential stimulatory effects on uterine smooth muscle. Recent evidence suggests that these drugs may be effective analgesic agents at low doses associated with markedly reduced side effects and minimal sedation. They can be administered IM or IV and appear to be effective when administered epidurally to provide perioperative analgesia for surgery of the vagina, tail and vulva, although significant systemic absorption (particularly of medetomidine) occurs so that systemic side effects must be anticipated following extradural injection.

Xylazine is less potent and shorter acting than either detomidine or romifidine and, when used IV at doses from 0.5 to 1.1 mg/kg, will induce profound analgesia (with significant sedation at the higher end of the dose range). While xylazine can be very useful for the **transport** of horses in severe pain, or prior to surgery, **ataxia** may be undesirable. Extradural administration of

xylazine (0.17–0.25 mg/kg in 10 mL 0.9% NaCl) has been reported to produce prolonged perineal analgesia for at least 2.5 h.

The potency of **detomidine** allows its use in small volumes by IM injection, an important factor in severely distressed animals. Detomidine (10–20 μg/kg) provides effective analgesia with marked sedation at 20 μg/kg. It has been effectively administered by both extradural injection (60 μg/kg) and extradural infusion for prolonged perineal analgesia in horses. **Medetomidine** (7 μg/kg bolus/3.5 μg/kg/h infusion) has recently been described as a potential sedative and analgesic agent in the horse. The analgesic efficacy of **romifidine** has not been detailed but as an α_2-adrenoceptor agonist is likely to have analgesic properties.

Ketamine has analgesic properties in animals and humans. It is most often used in the horse after xylazine or detomidine or romifidine administration to induce general anesthesia. However, its excitatory effects on the CNS limit its use and it should never be administered alone. It may be injected IV (50–100 mg for a 450 kg horse) to provide intraoperative analgesia and has few cardiovascular or respiratory side effects at these low doses in halothane-anesthetized horses. Its use by infusion has also been described in horses anesthetized with either halothane or the IV anesthetic agent propofol. Research in species other than the horse has shown that ketamine administered at significantly lower, non-sedative doses (0.2–0.5 mg/kg, infusions of 0.5–1.0 mg/kg/h) produces effective analgesia without undesirable behavioral side effects.

Ketamine has also been administered by extradural injection (0.5–2 mg/kg) to produce effective **perineal analgesia**; however, some side effects may occur at the higher dose due to systemic absorption of the drug.

Nitrous oxide (N_2O) is an anesthetic gas used as an adjunct to general anesthesia because of its analgesic properties. The analgesic properties have been attributed to stimulation of endogenous opioid release, and α_{2A}-receptor agonism. The limited potency of N_2O in horses necessitates the use of a 40–50% mixture in the inspired gas, therefore increasing the risk of hypoxemia in the recumbent horse. Hypoxia may also occur at the end of anesthesia if the animal is suddenly allowed to breathe air without allowing time to eliminate N_2O from the body. In addition, N_2O can diffuse readily into air-containing gas spaces such as the intestine, displacing nitrogen, thereby increasing the volume of these spaces and possibly inducing abdominal bloat. Despite these disadvantages it is used by some veterinary surgeons, but should only be considered where facilities for monitoring oxygen saturation or arterial oxygen tension are available. It is useful in foals to hasten induction with volatile anesthetic agents.

Local anesthetics

Lidocaine is a short-acting (approximately 1 h) local anesthetic drug, frequently used in horses to provide analgesia for suturing wounds. **Mepivacaine** is intermediate in its duration of action (approximately 1.5–2 h), produces little tissue reaction and is widely used to block specific nerve trunks in the diagnosis of lameness. **Bupivacaine** is long-acting (up to 6 h) and, although not licensed for use in the horse, has obvious potential as a long-acting analgesic to provide intraoperative and postoperative analgesia for surgery of the lower limbs and head. It is more cardiotoxic than lidocaine in humans and dogs, but

its use in horses is not well documented. Ropivacaine, the dextrorotatory isomer of bupivacaine, is not licensed in horses but is associated with a lower degree of cardiotoxicity than bupivacaine and greater selectivity for C-nociceptor fibers, combined with a prolonged duration of action.

There are numerous routes of administration of local anesthetic agents. In addition to **local infiltration** and **splash blocks** of surgical sites, **intra-articular** (IA) injection of local anesthetics provides analgesia during articular surgery. **Epidural injection** with a local anesthetic will provide analgesia of the tail, perineum, rectum and vagina, but care must be taken to avoid overdosage and therefore hindlimb incoordination and ataxia. Local anesthetic preparations of the above named compounds without preservative are marketed for epidural use (*q.v.*). Reported doses of local anesthetics used for effective extradural perineal analgesia with an acceptable degree of hindlimb ataxia are 0.35 mg/kg lidocaine (60–90 min of analgesia), 0.06 mg/kg hyperbaric bupivacaine, and 0.1 mg/kg 0.5% ropivacaine.

Recently, **lidocaine** has been administered by **controlled-rate infusion** (2 mg/kg very slow bolus followed by 50 μg/kg/min IV infusion) to provide effective intraoperative analgesia. Intravenous infusion of lidocaine is believed to produce analgesia through central antagonism of specific sodium channels involved in central sensitization of nociceptive transmission. During colic surgery, it is postulated that IV lidocaine infusion will also produce useful prokinetic effects. Given the potential for cardiotoxicity, it is imperative that cardiovascular performance is closely monitored during lidocaine infusion.

For the use of **non-steroidal anti-inflammatory** drugs as analgesics, see below (*q.v.*).

CLINICAL PAIN AND CHOICE OF ANALGESIC DRUG

Analgesia may be required in horses to control acute or chronic **pain**, or acute exacerbations of chronic conditions. The acute pain associated with colic (*q.v.*) can be particularly difficult to control effectively while chronically painful conditions (e.g. navicular disease) can present long-term therapeutic problems due to drug toxicity. The acutely laminitic pony (*q.v.*) presents as an urgent case with a potential long-term need for analgesics.

Colic

Horses suffering from colic (*q.v.*) may vary widely in their behavior depending on the precipitating cause of their abdominal pain. Mild to moderate pain may respond well to a NSAID such as **flunixin** (1 mg/kg IV), although the implications of using such a long-acting drug make an accurate clinical diagnosis a prerequisite.

Butorphanol (0.05–0.1 mg/kg IV) may produce reasonable but relatively short-lived (2 h) analgesia in these animals. **Pethidine** (2 mg/kg IM) is particularly useful in horses with spasmodic colic due to its antispasmodic action, however its effects, while rapid in onset, are short lived (30–60 min). **Morphine** has a slow onset time and so for a rapid, reliable effect it is recommended that either **xylazine** (0.5–1 mg/kg) or **detomidine** (10–20 μg/kg) be used, although the cardiovascular effects of these agents must be borne in mind.

Should IV injection prove difficult due to **handling problems**, detomidine (20–30 μg/kg) can be administered IM in a small volume. Both drugs have the advantage of being relatively short acting (xylazine 30–45 min, detomidine 45–90 min) and so the horse's condition can be reassessed frequently. The sedative action of these drugs may be useful when animals have to be transported to a surgical center, provided doses at the low end of the quoted range are used. High doses cause ataxia.

Acute laminitis

The provision of analgesia to horses and ponies suffering from acute, subacute or chronic laminitis (*q.v.*) is vital and yet there is much controversy over the best choice of drugs. The optimal approach is provision of multimodal analgesia combined with **therapeutic farriery** and non-pharmacologic strategies (rest, careful nutrition, cryotherapy, hosing the feet, deep bedding).

Complete pain relief can be provided by the use of **nerve blocks** (*q.v.*) with a long-acting drug such as **bupivacaine**. However, many equine clinicians consider the complete abolition of pain to be contraindicated, as movement may aggravate the mechanical separation of laminae within the hoof. Parenteral therapy with a NSAID such as **flunixin** appears to afford a good degree of relief lasting up to 12 h. Parenteral therapy can be continued for 2–3 days until the acute phase has subsided, the animal then being maintained on an oral NSAID. Care should be taken to avoid toxicity and the manufacturer's maximum recommended duration of therapy with an NSAID should not be exceeded.

The use of other parenteral analgesics, such as the **opioids**, has not been well documented. The prolonged duration of action of methadone (relative to other opioids) may make it a useful agent in the acute condition, although caution with dosing should be exercised in case of inducing locomotor stimulation. **Fentanyl patches** have recently been described as potentially useful for medium-term therapy for acute/subacute patients. α_2-Adrenoceptor agonists, which may cause peripheral vasoconstriction, would be detrimental to these animals and in addition would necessitate frequent administration. Vasoactive drugs (acepromazine, isoxsuprine) may indirectly reduce pain but their success remains controversial.

Trauma

Following trauma, individual horses may display variable behavior patterns. An animal displaying **violent behavior** may need to be sedated rapidly to avoid injury to itself and to its handlers. **Xylazine** (0.5 mg/kg, IV), **detomidine** (10 μg/kg IV; 20 μg/kg IM) or romifidine (0.07–0.1 mg/kg, IV; 0.2 mg/kg IM) is useful in providing both sedation and analgesia while the extent and severity of the trauma are assessed. The cardiovascular effects of these drugs must be borne in mind, particularly where hemorrhage has occurred. Combinations of α_2-agonists and opioids enhance the degree of analgesia and chemical restraint. Useful combinations include **romifidine** (0.07–0.1 mg/kg, IV) with **morphine** (0.12–0.15 mg/kg, IV) or **detomidine** (10 μg/kg, IV) and **butorphanol** (0.02–0.05 mg/kg IV).

If the horse is quiet, an opioid alone may be sufficient to permit close examination or transport of the animal, although doses of these drugs should be carefully chosen in order to avoid stimulating locomotor activity. **Regional anesthesia** (e.g. nerve blocks around the head and limbs, or epidural block) (*q.v.*) may be helpful in permitting examination and care of a wound or traumatized area. The choice of local anesthetic will depend on the desired duration of action.

PERIOPERATIVE ANALGESIA

Preoperative use of analgesic drugs

Routine preemptive and multimodal administration of several types of analgesic drugs (NSAIDs, opioids, α_2-agonists, local anesthetics, ketamine, nitrous oxide) through various routes of administration (systemic, extradural, local infiltration, intra-articular administration) is recommended in horses suffering from painful conditions (e.g. fractures).

Prior to induction of anesthesia, combination of an opioid analgesic drug with a sedative or tranquilizer will enhance the degree of sedation obtained, thus facilitating induction of anesthesia and reducing anesthetic requirements intraoperatively. **Butorphanol** (0.05 mg/kg IV), **methadone** (0.05–0.1 mg/kg IV) or **morphine** (0.05 mg/kg IV) may be incorporated with the premedicant.

Intraoperative use of analgesic drugs

Judicious use of analgesic drugs **intraoperatively** provides easier control of depth of anesthesia in all species. However, reluctance is often experienced with the application of this concept in horses. Clinical experience with opioids used intraoperatively in the horse suggests that, at the doses recommended, cardiovascular effects and respiratory effects are minimal and there is no effect on the quality of recovery.

Morphine may be administered perioperatively at 0.12–0.15 mg/kg (IV). **Pethidine** may be injected IM (1–2 mg/kg) just after induction of anesthesia (not IV) and has a rapid onset of action (within 10 min), although the clinical effect may last only 1–1.5 h. The analgesic effect of opioids given intraoperatively in horses has proved difficult to quantify since they do not appear significantly to reduce the dose of inhalational agent required to maintain anesthesia.

Ketamine has been used in low doses (0.1–0.5 mg/kg IV) to provide intraoperative analgesia in horses anesthetized with **halothane** (*q.v.*). It has little effect on cardiorespiratory parameters at these doses and rapidly reduces responses to surgical stimuli. The total dose used intraoperatively should remain less than 1 mg/kg, and ketamine should not be used within 30 min of the end of anesthesia to avoid potential excitatory effects during the recovery period.

Local nerve blocks (*q.v.*) are very useful in providing intraoperative analgesia in the horse. Blocks such as the high palmar nerve block, for surgery below the fetlock, reduce the requirement for deep planes of anesthesia and, if **bupivacaine** is used, provide analgesia during the recovery period. Loss of

any motor function appears to be clinically unimportant in influencing the recovery. Intra-articular injection of lidocaine (2 mg/kg) or bupivacaine (1 mg/kg) also provides highly effective analgesia for arthroscopic and other articular procedures.

Injection of lidocaine (20 mL, 2% solution) into the testes or spermatic cord (avoiding the spermatic artery and vein) improves the quality of anesthesia for castration (*q.v.*), as does SC infiltration of lidocaine around the incision site, reducing the requirement for incremental doses of IV anesthetic agents.

EXTRADURAL ANALGESIA (See Table 4.6)

Caudal epidural anesthesia is a relatively simple technique that can be used to facilitate surgery and analgesia of the tail, perineum, rectum, vulva, vagina, urethra and bladder. The technique is best performed in the standing horse.

Many analgesic agents have been effectively administered by **extradural injection** including lidocaine, bupivacaine, ropivacaine, morphine, methadone, pethidine, ketamine, detomidine, xylazine, medetomidine and tramadol. A combination of agents administered extradurally achieves synergistic long-lasting analgesia but may enhance the likelihood of ataxia and recumbency.

The volume of extradural injection depends on body weight and the desired degree of **cranial spread**. A total injection volume of 4–8 mL has been described as adequate for **perineal analgesia** in a 500 kg horse, while 10–15 mL is indicated for further cranial spread, but with greater risk of hindlimb ataxia.

Extradural catheterization (through the caudal extradural space or occasionally through the lumbosacral space into the sacral extradural space) facilitates prolonged highly effective analgesia. Commercial kits for extradural catheterization are widely available; it is recommended that a 17/18 G 7.5 cm **Tuohy needle** be used rather than a spinal needle for greater ease of successful catheterization, followed by insertion of a 19–20 G extradural catheter, advanced usually 2–4 cm (no more than 30 cm) from the cranial tip to achieve effective analgesia. **Strict asepsis** is mandatory.

Potential side effects of extradural catheterization include **sedation** associated with significant systemic absorption of drugs (particularly likely with highly lipophilic drugs such as medetomidine and butorphanol); recumbency associated with relative drug overdose; cardiovascular effects associated with systemic absorption of significant doses of α_2-agonists; localized sweating and neurotoxicity (not reported clinically). However, risks of these side effects are relatively low and the significant benefits of optimal analgesia associated with extradural analgesia warrant its consideration as a routine means of analgesia provision.

POSTOPERATIVE ANALGESIA

Postoperatively, the same principles of multimodal analgesia apply. An additional dose of an opioid and NSAID drug may be given at the end of surgery to enhance immediate postoperative analgesia with minimal effects on recovery.

It is vital to remember that horses suffering **severe postsurgical pain** are likely to have recoveries of poor quality if their pain is not attenuated. Low doses of **xylazine** (0.1–0.2 mg/kg), **detomidine** (5–8 μg/kg) or medetomidine

(3 μg/kg) may be used IV or IM at the end of surgery to provide short-term analgesia and sedation during the recovery period.

Of the NSAIDs available for use in the horse, **flunixin** (1 mg/kg IV) and **carprofen** (0.7 mg/kg IV) are useful to control **acute postoperative pain,** although information on their use in this situation is scanty. Unlike many of the other analgesics, they have no observable effects on the CNS and therefore should not adversely affect the recovery period. The efficacy of these drugs as intraoperative analgesics has yet to be quantified. NSAIDs have potential nephrotoxic effects, which could be exacerbated in hypotensive or hypovolemic anesthetized horses, and care should be taken to ensure good hydration.

The local anesthetics are also useful in the postoperative period, but specific nerve blocks must be done before the end of anesthesia.

NON-STEROIDAL ANTI-INFLAMMATORY DRUGS

INTRODUCTION

Microbiologic, chemical or physical injury to tissues causes either necrosis or an inflammatory response. The latter may be defined as the response of the living microcirculation and its contents to injury.

The initial phase of acute inflammation is characterized by the **cardinal signs** of heat, redness, pain, swelling and loss of function; the underlying microcirculatory changes comprise arteriolar vasodilatation, increased microvascular permeability (resulting in local edema) and the extravascular accumulation of leukocytes. These changes are **protective** in that they normally lead to isolation and destruction of the injurious stimulus and, in the resolution phase of acute inflammation, to restoration of normal tissue structure and function. If the stimulus persists, however, the inflammation becomes chronic and tissue destruction and fibrous tissue formation ensue.

These changes are attributable to the release from storage sites or the de novo synthesis of a wide range of chemical mediators and modulators of the inflammatory response. The complexity of the response is reflected in the large numbers of **mediators** involved, their diverse actions and interactions (one mediator modulating, enhancing or suppressing the actions of another), and the fact that each produces only some of the features of the inflammatory reaction. Mediators may be released from resident tissue cells, from infiltrating leukocytes and other blood cells, e.g. platelets, or from precursors in the plasma. A simplified account of the identity and roles of inflammatory mediators is presented in Table 4.7.

Anti-inflammatory drugs are used extensively to **suppress** the pain, erythema, edema and tissue destruction of acute and chronic inflammatory conditions. In general, available drugs at clinical dose rates suppress but do not abolish components of the inflammatory reaction, thereby providing clinical benefit. Their mode of action is often only partially understood, even in the case of well-known and extensively used agents such as corticosteroids and NSAIDs. However, it is believed that all anti-inflammatory drugs act by preventing the release, blocking the synthesis or inhibiting the actions of inflammatory mediators and modulators.

Table 4.7 Mediators and modulators of inflammation

Mediator/modulator	Inflammatory properties
Histamine	A basic amine released from mast cells; produces vasodilatation, increased permeability of small venules and pain
Bradykinin and tachykinins	Small peptides synthesized de novo increase small venule permeability and cause pain
Eicosanoids (prostaglandins [PGs], leukotrienes [LTs], monohydroxyeicosatetraenoic acids [HETES] and lipoxins)	Polyunsaturated fatty acids derived from cell membrane phospholipid by activation of phospholipase A_2. (a) PGE_2: prolonged arteriolar vasodilatation and potentiation of increased vascular permeability and pain induced by other mediators; usually the predominant prostanoid in equine acute inflammatory exudates; possibly chemoattractant for equine leukocytes (b) PGI_2: similar properties to PGE_2 with a shorter duration of action; also inhibits platelet aggregation (c) LTB_4: chemoattractant for polymorphonuclear leukocytes; increases permeability of small venules (weak) (d) LTC_4, LTD_4: increase microvascular permeability; may be important mediators in allergic airways disease, causing bronchoconstriction, bronchial hyperresponsiveness and increased mucus secretion (e) 5-, 12- and 15-HETE: cause vasodilation (weak) and leukocyte migration (f) Lipoxins: stimulate polymorphonuclear leukocytes to generate superoxide radicals and release lysosomal enzymes, also anti-inflammatory actions
Platelet-activating factor (PAF)	Analogue of phosphatidylcholine, derived from cell membrane phospholipid, causing vasodilatation, increased vascular permeability and chemotaxis of polymorphonuclear and mononuclear leukocytes, platelet and neutrophil activation, bronchoconstriction and bronchial hyperresponsiveness
Complement system	Derived from precursor proteins in plasma. Several components (e.g. C3a, C5a) possess pro-inflammatory properties, e.g. vasodilatation, increased vascular permeability, leukocyte chemotaxis and mast cell degranulation
Nitric oxide	Derived from endothelium, macrophages: potent vasodilator, potentially implicated in several components of acute inflammation
Cytokines (e.g. interleukins (IL), tissue necrosis factor [TNFα])	Many mediators possessing either pro- or anti-inflammatory properties released by leukocytes; pro-inflammatory cytokines possess chemotactic activity, mitogenic and pyretic properties; stimulate production of collagenase, stromelysin and PGE_2 by synovial cells, chondrocytes and dermal fibroblasts (IL-1); involved in arthritides and the pyretic response to infection
Chemokines (e.g. CXCL8, CCL2, CCLS, CCL11)	A super family comprising many mediators with pro-inflammatory or homeostatic properties, controlling the selective recruitment of leukocytes.

ANTI-INFLAMMATORY DRUG CLASSIFICATION

Given the complexity of inflammatory processes, with the involvement of many mediators and the synergistic and antagonistic interactions between them, it is not surprising that those anti-inflammatory drugs with selective activity against a single mediator (e.g. antihistamines) possess only limited clinical efficacy.

Table 4.8 Classification of anti-inflammatory and anti-arthritic drugs

Class	Examples
1. H_1 receptor antagonists	Chlorphenamine, clemastine, cyproheptadine
2. Glucocorticoids	Prednisolone, dexamethasone, betamethasone, triamcinolone
3. Non-steroidal anti-inflammatory drugs (NSAIDs)	Aspirin, phenylbutazone, flunixin, ketoprofen, carprofen, vedaprofen, nimesulide, meloxicam, eltenac, dipyrone, isopyrin
4. 5-lipoxygenase inhibitors	Zileuton
5. Cysteinyl leukotriene receptor antagonists	Montelukast, zafirlukast
6. Dual cyclo-oxygenase/5-lipoxygenase inhibitors	Tepoxalin
7. Platelet-activating factor (PAF) receptor antagonists	Bepafant, lexipafant
8. Phosphodiesterase inhibitors	Theophylline, roflumilast, cilomilast
9. Disease-modifying agents	Penicillamine, levamisole, gold salts
10. Cytotoxic immunosuppressants	Chlorambucil, azathioprine, ciclosporin
11. Free radical scavengers	Copper, orgotein, some NSAIDs
12. Chondroprotective agents	Polysulfated glycosaminoglycan (PSGAG), pentosan polysulfate, hyaluronic acid, possibly some NSAIDs

Table 4.9 Structural classification of NSAIDs

Carboxylic acids		Enolic acids		Sulfonamide derivatives
Subgroup	**Examples**	**Subgroup**	**Examples**	**Examples**
Salicylates	Acetylsalicylic acid Sodium salicylate	Pyrazolones	Phenylbutazone Dipyrone Isopyrin Oxyphenbutazone	Nimesulide
Quinolines	Cinchophen	Oxicams	Meloxicam Piroxicam	
2-Aryl-propionic acids	Carprofen Ibuprofen Ketoprofen Vedaprofen Naproxen			
Anthranilic acids	Flunixin Meclofenamic acid Tolfenamic acid			
Indolines	Indometacin Eltenac Tepoxalin			

Table 4.8 presents a classification of drugs that either possess anti-inflammatory properties or have been used to treat various joint diseases. It is not comprehensive. Many of these agents are used infrequently or not at all in equine medicine (groups 1, 4, 5, 6, 7, 10). This account will therefore deal principally with drugs in groups 3 (NSAIDs), 8 and 11. Group 2 agents (corticosteroids) are dealt with elsewhere (*q.v.*).

Non-steroidal anti-inflammatory drugs are weak organic acids that can be subdivided into three main groups on the basis of chemical structure, carboxylic (R—COOH) and enolic (R—COH) acids and sulfonamides. Further subdivisions, also on the basis of chemical structure, can be made (Table 4.9). This classification is of limited value to the extent that it does not signify major differences in pharmacologic activity, as most NSAIDs have the same spectrum of therapeutic actions and side effects, regardless of grouping. There are, however, major pharmacokinetic differences and some pharmacodynamic differences between individual drugs.

PHARMACOLOGIC ACTIONS OF NSAIDs

All NSAIDs inhibit **cyclo-oxygenase (COX)**, an enzyme that converts the 20-carbon unsaturated fatty acid, arachidonic acid, to the cyclic endoperoxide prostaglandins (PG), PGG_2 and PGH_2. Further enzyme action leads to the formation of several **eicosanoids**, some of which, like PGE_2, are important inflammatory mediators or modulators. Thus, PGE_2 synergizes with mediators such as histamine, bradykinin and platelet-activating factor (PAF) to enhance their pain- and edema-inducing effects. However, recent evidence indicates that COX generates other prostaglandins with anti-inflammatory properties in the resolution phase of acute inflammation.

Inhibition of COX is believed to be the principal mechanism of action of NSAIDs. However, anti-inflammatory and analgesic potency does not always parallel potency as COX inhibitors; **carprofen,** for example, produces only moderate inhibition of this enzyme in the horse and dog at clinical dose rates and may act partially through other mechanisms. In vitro studies on chondrocytes and cartilage explants in both the horse and dog have shown that carprofen stimulates the synthesis and reduces the breakdown of the high molecular weight cartilage matrix molecules, **proteoglycans**. Carprofen also inhibits activation of the transcription factor NFκB and suppresses release of the cytokine, IL-6. It is unclear whether these actions, demonstrated in vitro, contribute to the therapeutic effects of carprofen in vivo.

Moreover, additional actions of NSAIDs on other enzymes in the arachidonic acid pathway (and on unrelated enzymes) have been described. Thus, **phenylbutazone** inhibits a more distal enzyme, endoperoxide isomerase, and scavenges free radicals, and some fenamic acid NSAIDs inhibit some **actions** of prostaglandins as well as blocking their synthesis. Higher than therapeutic dose levels, and even clinical dose rates of some NSAIDs, may also inhibit 5-lipoxygenase (5-LO) to suppress the synthesis of **leukotrienes** and related compounds. **Tepoxalin** has been introduced into canine medicine on the basis of its dual inhibition of COX and 5-LO.

Recognition that COX exists in at least two and possibly three **isoforms** (COX-1, COX-2 and COX-3) has stimulated major additional interest. COX-1

is a constitutive enzyme, responsible for **housekeeping functions** including blood clotting and protective actions in the GIT and kidney. It may also contribute to the synthesis of prostaglandins at sites of inflammation. COX-2, like COX-1, is constitutive in some tissues, including the kidney and CNS, but it is primarily an **inducible enzyme** formed at sites of tissue damage and it is responsible for most or all of the eicosanoids generated by such damage.

Commencing in 1990, with the discovery of the separate COX-2 and COX-1 isoforms, there has been an intensive search for novel NSAIDs that **selectively inhibit COX-2**. Recent years have witnessed the introduction of several such agents in the "coxib" group, e.g. rofecoxib (now withdrawn), celecoxib, valdecoxib, etoricoxib, into human medicine. The coxibs have moderate to high selectivity for COX-2 inhibition and they have been shown to have similar efficacy but lower toxicity than classical NSAIDs, the majority of which are now recognized to be non-selective COX inhibitors. Two drugs of this class, **deracoxib** and **firocoxib** have been introduced into canine medicine but no coxib has yet been licensed for equine use. The discovery in dog brain of a splice variant of COX-1, COX-3, has added another dimension. It is possible that paracetamol and some of the older drugs used in equine medicine, such as dipyrone and isopyrin, are partially selective for COX-3, and this might explain the relatively high GIT tolerance of paracetamol.

On the basis of limited evidence the following tentative conclusions concerning NSAID selectivity for COX isoforms in the horse may be drawn: phenylbutazone, flunixin, and ketoprofen are non-selective; carprofen and meloxicam are non-selective or possibly slightly preferential for COX-2; and vedaprofen may be COX-1 selective. To what extent such differences in pharmacologic actions at the molecular level contribute to the clinical efficacy and toxicity of NSAIDs is unclear.

Most NSAIDs possess three classes of clinical action at tissue and whole animal levels; a **local anti-inflammatory** and **analgesic** action and **central antipyretic** and **analgesic** effects (Table 4.10). Differences between drugs have been reported for the three types of activity. Thus, **phenylbutazone** is effective as a **peripheral anti-inflammatory agent** but may be a weak central analgesic, whereas other agents in the same subgroup, isopyrin and dipyrone, are effective analgesics but relatively weak anti-inflammatory agents. These differences may be explained by differential activity against COX isoenzymes, as indicated above.

Differences in COX structure may also explain species differences in plasma concentrations of NSAIDs required for efficacy. For example, plasma phenylbutazone concentrations required in humans for the treatment of inflammatory joint diseases are of the order of 100–150 μg/mL, while therapeutic concentrations in the horse are in the range of 10–20 μg/mL. Concentrations regarded as therapeutic in man are lethal to the horse. Similarly, much *higher* plasma concentrations of phenylbutazone in the cow produce much *smaller* effects at both molecular and clinical levels than in the horse, indicating a major difference in potency between these two species.

As well as the anti-inflammatory, analgesic and antipyretic actions of NSAIDs, other properties have been identified and these provide the basis for further therapeutic uses. Thus, their **anti-endotoxemic** and **antithrombotic** actions are well recognized (*q.v.*).

Table 4.10 Pharmacologic actions, therapeutic uses and toxic effects of NSAIDs

Organ/system	
Pharmacologic actions and therapeutic uses	
CNS	Antipyretic: reduction of body temperature in fever but not in normothermic animals Analgesic; relief of pain but activity generally weaker than morphine-like drugs
Peripheral sites	Anti-inflammatory (antiedemic) Analgesic Antithrombotic Anti-endotoxemic
Toxic effects	
Gastrointestinal tract	Irritation and potentially ulcerogenic; possibly leading to blood or plasma loss (enteropathy) and melena
Kidney	Nephropathy: tubular nephritis, renal papillary necrosis or acute renal failure
Liver	Cholestatic and parenchymal toxicity
Blood and cardiovascular system	Small vein phlebopathy; various blood cell dyscrasias including aplastic and hemolytic anemias and agranulocytosis; methemoglobinemia, hypoprothrombinemia and prolongation of bleeding time
Fetus	Possible embryopathic, teratogenic effects if administered during period of organogenesis; delayed gestation at term
Skin	Urticaria, erythema
CNS	Stimulation, muscle tremor, convulsions (at high dose rates)

SIDE EFFECTS AND TOXICITY OF NSAIDs

Eicosanoids produced from the COX arm of the arachidonic acid cascade play important roles in a number of physiologic processes. It is therefore not surprising that a wide range of side effects have been described (see Table 4.10). These may be common and are normally dose related (e.g. effects on the GIT) or they may be idiosyncratic, arising only rarely and not necessarily related to administered dose (e.g. aplastic anemia in human subjects). Other side effects may become apparent only in the presence of predisposing factors; for example, clinical dose rates of most NSAIDs are not normally renotoxic but in the presence of **hypotension** or **hypovolemia**, intrarenal release of the vasodilator prostaglandins PGE_2 and PGI_2 maintains renal blood flow and glomerular filtration rate (renal autoregulation). In these circumstances, blockade of prostaglandin synthesis by NSAIDs can lead to **renal vasoconstriction** and **acute renotoxicity**.

In the horse, phenylbutazone and flunixin, probably acting through the latter mechanism, can produce **renal papillary necrosis** at clinical dose rates when animals are deprived of water, but not in adequately hydrated animals. High doses of NSAIDs may cause **tubular nephritis.** The fluid retention and edema reported with some NSAIDs in humans seems to be uncommon in animals.

To varying degrees, all NSAIDs produce **GIT irritation** and **ulceration** and, in the horse, this has been well described for phenylbutazone, leading to a **plasma protein-losing enteropathy** and, with high doses, hemoconcentration, hypovolemic shock and death. The horse may be particularly susceptible to this action of **phenylbutazone**, as doses only moderately in excess of

recommended dose rates are **ulcerogenic** and lesions can potentially occur throughout the GIT after IV as well as oral dosing.

Intravenous administration of NSAIDs leads to exposure of the GIT mucosa to the drug through its blood supply; with oral dosing exposure may arise in the same way and also through the presence of drug in the lumen of the GIT. The likely cause of toxicity is inhibition of synthesis of the vasodilator local hormone, **prostacyclin** (PGI_2), leading to ischemia and hypoxia and, in the stomach, inhibition of gastroprotection by loss of the action of PGE_2 to decrease parietal cell hydrogen ion and to enhance mucus and bicarbonate ion secretion. Experimentally, administration of both PGE_2 and **misoprostol,** a stable analogue of PGE_2, protects against the ulcerogenic action of NSAIDs.

Other means of reducing NSAID toxicity have been sought. Slow-release and enteric-coated formulations have been developed and water-soluble forms of aspirin (e.g. the lysine salt) are available but these are rarely used in equine medicine. Also of potential interest regarding efficacy–toxicity ratios is the introduction of both coxibs and **tepoxalin**—this drug interestingly being selective for COX-1 rather than COX-2—into human and canine medicine. The nitroso NSAIDs or CINODs (cyclo-oxygenase inhibiting nitric oxide donors) are also of potential interest; these are derivatives of classical NSAIDs, such as aspirin, indometacin and phenylbutazone, which are non-selective for COX isoforms, that are converted in vivo to the parent compounds and nitric oxide. The latter, either through a local vasodilator action or through inhibition of leukocyte attachment to vascular endothelium, seems to be mucosa protective, leading to improved efficacy–toxicity ratios. No drugs of these classes (coxibs, dual inhibitors and CINODs) are yet available for equine use.

Laboratory animal studies have indicated that a wide range of factors, including species, sex, age, nutritional status and extent of biliary secretion may influence **NSAID ulcerogenicity**, but whether they apply in the horse is unknown. Some studies in the horse have suggested that pony breeds may be more susceptible to GIT damage from phenylbutazone than larger breeds, but this has not been substantiated in other equine studies. Laboratory animal and canine studies suggest that **carprofen**, which produces only moderate COX inhibition in the horse, is much less ulcerogenic than most other NSAIDs and this seems to apply also to the horse, as it has a wider margin of safety than many other NSAIDs in this species. However, dose–effect relationships of NSAIDs for the ulcerogenic action have not been established in the horse; only phenylbutazone has been studied extensively.

Many studies over the last 25 yr have reported on the **toxicity** of **phenylbutazone** in the horse. Side effects include anorexia, depression, colic, hypoproteinemia, diarrhea, melena, GIT erosions and ulcers, weight loss, ventral abdominal edema, petechial hemorrhages of mucous membranes, renal papillary necrosis and hepatotoxicity. Such effects, possibly leading to death, may occur with doses in excess of 8.8 mg/kg/day. It is therefore most important to keep the **daily maintenance dose** of this drug at 4.4 mg/kg or less.

Both cholestatic and parenchymal hepatotoxicity have been described in horses receiving phenylbutazone and the latter effect seems to be **dose related**. As most NSAIDs are extensively metabolized in the liver, drug-induced damage to this organ can potentially lead to a vicious cycle of cumulation and

further toxicity. **Blood dyscrasias** have also been reported in horses receiving high doses of phenylbutazone but such changes, as far as is known, are uncommon with clinical dose rates. Clinical dose rates of flunixin and meclofenamate, administered over several days, reduce plasma protein concentration by 15–20% and this may indicate toxicity to the GIT mucosal cells and/or the kidney and/or the liver.

High doses of NSAIDs inhibit platelet aggregation through inhibition of synthesis of the pro-aggregatory eicosanoid, **thromboxane (TX) A_2**, and this may be associated with internal or external hemorrhage through **impaired clotting mechanisms** (*q.v.*). This is particularly likely with **aspirin**, as this drug, alone amongst NSAIDs, inhibits COX-1 **irreversibly** and hence for the lifespan of platelets. This can be advantageous if an anti-aggregatory action is required, as platelets can be targeted by low doses of aspirin while minimizing side effects on other tissues.

In summary, most NSAIDs currently licensed for the horse are non-selective COX inhibitors, or even selective for COX-1. The efficacy–toxicity ratios are low (carprofen seems to be the main exception), and adherence to recommended dose rates is important if side effects are to be minimized.

PHARMACOKINETICS AND ADMINISTRATION OF NSAIDs

Route of administration

The usual route of administration of NSAIDs is oral, but several drugs are available as solutions for IV dosing (phenylbutazone, dipyrone, isopyrin, flunixin). Some of these are used as concentrated solutions (as high as 20%) which are alkaline (sodium salts) and therefore very irritant to tissues when injected **perivascularly**. Flunixin, which is used as the meglumine salt, has been administered IM to horses. Absorption is very rapid and this drug is less irritant than some other NSAIDs, although IM dosing is not recommended in the product literature.

Acid–base conditions

The pH of fluid in the GIT is usually more acid than plasma (pH 7.35–7.40) and in the equine stomach pH may range from 1.5 to 6.5; **pH usually increases after feeding**. Acid gastric pH **promotes the absorption** of NSAIDs by the mechanism of ion trapping because, as weak organic acids, these drugs are less ionized than in plasma and therefore well absorbed. However, in the horse the stomach is small and this limits absorption from this site. Other factors also influence absorption. Low solubility in acidic conditions, of aspirin for example, can cause precipitation in the stomach, which slows absorption and may increase local irritation.

Feed and formulation effects

Diet may be very important in horses, as some NSAIDs **bind to hay** and other feeds (e.g. pony nuts) of high fiber/cellulose content. This has been demonstrated for phenylbutazone, meclofenamate and flunixin, the degree of binding decreasing in that order (99% for phenylbutazone and 70% for flunixin). This

may explain the **considerable delays** and marked inter-animal variations in phenylbutazone absorption that have been reported after oral dosing in horses, with the time to maximal concentrations in plasma delayed for as long as 18 h after administration to animals with free access to feed.

Restricted access to feed reduces, but does not abolish, the delay in absorption of phenylbutazone. Access to feed also delays absorption of orally administered flunixin in horses, but the effect is less pronounced than with phenylbutazone and peak concentrations in plasma are achieved more rapidly with the former drug in circumstances of both free and restricted access to feed. With both drugs, multiple peaks in the plasma concentration time profile occur when horses have free access to feed at the time of dosing. Binding to hay, and subsequent release of the drug by fermentative digestion in the large intestine of the horse, has been proposed as a basis both for the absorption profile and the ulcerogenic effect of phenylbutazone in the distal regions of the gut.

When racemic (rac)-ketoprofen (a 50:50 mixture of the two enantiomers) was formulated in an oil-based product the bioavailability of both enantiomers was <5%, both in the presence and absence of feed, whereas administration of the drug in hard gelatin capsules gave a bioavailability of 50%. An episodic absorption pattern occurs with phenylbutazone (even when administered orally after withholding feed) when the drug is formulated in an oil-based paste.

In spite of these factors, absorption of NSAIDs is generally good, bioavailability of most drugs exceeding 60%, irrespective of feeding schedules. Veterinarians providing advice to owners on the use of NSAIDs in relation to competitive equine sports should, however, be aware of the **delayed and variable absorption patterns** of these drugs. Many national and international racing and eventing authorities have banned the use of these drugs but in some cases drugs are permitted provided plasma concentrations do not exceed certain limits (*q.v.*).

Elimination half-life

Marked inter-drug and inter-species differences in the elimination half-life of NSAIDs have been reported. Selected examples are presented in Table 4.11. Significant differences can also occur with the two enantiomers of a single compound. This may be especially important when the drug product is licensed as the racemic mixture of the two enantiomers (as is the case for **carprofen**, **ketoprofen** and **vedaprofen**), as the enantiomers have major differences in potency, the *S*(+) being more active than the *R*(−) enantiomer in laboratory animal and in vitro studies. Potency ratios (COX-1–COX-2) may be 20:1 or higher.

In the horse, the *S*(+) enantiomer of ketoprofen is cleared more slowly from plasma than the *R*(−) enantiomer, while the opposite applies to carprofen and vedaprofen. In spite of the greater persistence in plasma of the (presumed) less active enantiomer of the latter two compounds, the racemic mixtures have been shown to possess analgesic activity.

Species and breed differences in pharmacokinetics

It is important to recognize that marked **species differences** in NSAID pharmacokinetics exist. Some examples are presented in Table 4.11. In view of

Table 4.11 Elimination half-life ($t_{1/2\beta}$) of NSAIDs (h)

	Horse	Cow	Dog
Aspirin	0.2	–	–
Salicylate	1–3[1]	0.5	9
Flunixin	2	8	4
Naproxen	5	–	35–74[2]
Meclofenamic acid	1	–	–
Tolfenamic acid	1	–	–
Phenylbutazone	5–8[3]	37–60	3–6[3]
Meloxicam	3	13	12–36

[1] *1 h following administration of salicylate; 3 h following administration of aspirin.*
[2] *Breed dependent, longer in mongrels than beagles.*
[3] *Possibly dose dependent, increasing with administered dose.*

these differences, pharmacokinetic data generated in one species can **never be transposed** to another.

Related to the phenomenon of species differences in half-life is the observation of **breed differences**. This has been reported for **naproxen**, the half-life in beagles being approximately half that in mongrel dogs (see Table 4.11), but whether similar differences for this or other NSAIDs occur in different breeds of horse is not known.

Metabolite activity

The activity of most NSAIDs is attributable solely or primarily to the parent compounds, but in other cases active metabolites are formed. **Aspirin**, for example, is rapidly de-acetylated to **salicylate** and the half-life of aspirin in the horse is ⩽10 min. Most of the activity of aspirin (except for the drug's antithrombotic action) is therefore due to **salicylate**. Salicylate elimination half-life was also found to be short in the horse following sodium salicylate administration (1 h) but was longer (3 h) after aspirin administration.

Another example of active metabolite formation is **oxyphenbutazone**, which is formed by hydroxylation of phenylbutazone. In laboratory animal studies, this compound has a similar potency to **phenylbutazone**. If this were applicable to the horse also, oxyphenbutazone would account for 20–25% of the pharmacologic activity of administered phenylbutazone.

Drug dosage

Dose-dependent pharmacokinetics, believed to be attributable to saturation of hepatic metabolizing enzymes, have been demonstrated, or proposed, for certain NSAIDs in some species, and can present difficulties in establishing dosing schedules that are effective and also safe. The relatively **narrow safety margin** of phenylbutazone in the horse may be due, in part, to increased half-life when doses are raised only moderately in excess of those recommended. This drug can normally be used safely over prolonged periods in most horses, provided doses are not increased above recommended levels.

Drug interactions

At least two types of **pharmacokinetic interaction** between NSAIDs are known (and many similar examples would no doubt be revealed by further investigations). When the pyrazolone NSAIDs **isopyrin** and **phenylbutazone** are administered in combination to the horse, the half-life for both drugs is **longer** than when they are administered separately. Administered dosage and duration of treatment with this drug combination product should be carefully controlled, as the metabolic interaction ensures that the drugs will be more than additive in clinical use and this may increase **toxicity** as well as enhancing efficacy.

Reduced plasma clearance of **phenylbutazone** has also been demonstrated in horses receiving **oxyphenbutazone, cimetidine** and **chloramphenicol**. The two latter drugs inhibit hepatic mixed function oxidase and therefore suppress or prevent the ring and side chain hydroxylation that normally occurs.

Protein binding

Almost all NSAIDs (aspirin/salicylate is exceptional) are **highly bound to plasma protein** (98% or greater) and this not only reduces urinary excretion and extravascular drug penetration, but also provides a theoretical basis for interaction with other protein-bound drugs of the same or differing classes.

Competition for protein binding sites can raise plasma concentrations of the free, and therefore active, drug. In practice, such interactions are unlikely. An often-quoted example is the use in combination of **phenylbutazone** and **warfarin** in the treatment of navicular disease (*q.v.*). Both drugs are highly bound to plasma protein, and displacement of warfarin by competition with phenylbutazone could lead to high "free" (and active) concentrations of warfarin in plasma, leading to **fatal hemorrhage**. In fact, available evidence suggests that the interaction between these drugs is due to inhibition of warfarin metabolism and not to plasma protein binding competition.

Age

In general, biotransformation is less efficient in young animals (<4 wk of age), and aged animals may also metabolize NSAIDs less effectively than young adults. Limited data in the horse indicate that plasma drug concentrations are higher in old than in young adult ponies following both IV and oral dosing with phenylbutazone. Reduced dosage and/or longer dosing intervals are therefore advisable in both old and very young horses.

Summary of pharmacokinetics

It is clear that many factors may influence NSAID pharmacokinetics and these should be borne in mind with clinical usage, because in some circumstances efficacy or safety may be compromised. Even when basic pharmacokinetic data are available, however, they cannot be used alone to set dosage schedules. This is partly because different plasma concentrations are likely to be needed for different therapeutic (analgesic, anti-inflammatory, antipyretic,

anti-endotoxemic, antithrombotic) responses, and partly because activity is commonly longer for NSAIDs than might be predicted from plasma clearance. It has been shown that phenylbutazone, flunixin, carprofen and vedaprofen (and potentially other NSAIDs highly bound to plasma protein) penetrate readily into, and are slowly cleared from, **inflammatory exudate**.

PHARMACOKINETIC–PHARMACODYNAMIC MODELLING OF NSAIDs

Pharmacokinetic–pharmacodynamic (PK–PD) modelling provides a means of deriving useful data on the action–effect–response relationships of NSAIDs. The principal *action* is inhibition of COX; the *effect* is to reduce the formation of pro-inflammatory prostaglandins; and the *response* is analgesia, antipyresis, etc.

At either or both inflammatory mediator (i.e. effect) and response levels, PK-PD modelling of NSAIDs, including phenylbutazone, flunixin, ketoprofen, vedaprofen and meloxicam, has provided numerical values for key pharmacodynamic parameters, expressing efficacy, potency and sensitivity of NSAID effects and responses. The data on effect have yielded useful insights into mechanism of action, while data on response have provided a major advance in the design of dosage schedules. For example, it is of interest that the **potency** of flunixin is approximately 40 times greater for prostaglandin inhibition than for clinical analgesic response, implying that a very high level of mediator inhibition (possibly 95% or greater) is required to achieve clinical responses. PK–PD modelling has further shown that, in an equine model of joint inflammation, the efficacy of flunixin in suppressing lameness is greater than that of phenylbutazone.

THERAPEUTIC USES OF NSAIDs

Analgesia and anti-inflammatory effects

Suppression of the pain associated with tissue damage is the major use for NSAIDs in equine medicine, including the acute inflammation associated with **traumatic injury**. Major indications of NSAIDs as analgesics also include all forms of **joint disease** and **pre-** or **postoperative** use.

The hyperalgesia-inducing mediator PGE_2 is present in detectable concentrations in approximately half of all **synovial fluid** samples harvested from horses with several forms of joint disease (the only exception when PGE_2 is not detectable being cases of **osteochondrosis dissecans** [*q.v.*]).

The relief of signs of **lameness** by NSAIDs is probably explained therefore by inhibition of synthesis of PGE_2 and related compounds. NSAIDs may be administered IV at the commencement of therapy, while maintenance is usually provided by oral administration of powder (admixed with feed) or paste formulations.

In relation to **surgery**, NSAIDs are key drugs as analgesics, to control postoperative pain for all procedures and especially for the severe pain associated with orthopedic procedures. In addition, their potential anti-edematous action may prevent the swelling that can lead to wound breakdown.

The use of NSAIDs in the therapy of joint diseases (the arthritides) (*q.v.*) is based on their analgesic action. The common routes of administration are IV

for initiation of therapy and orally for maintenance. Occasionally, intra-articular (IA) injection has been used, although most parenteral NSAIDs are too irritant for this route to be used.

There is no convincing evidence to suggest that NSAIDs are "disease modifying", i.e. they do not retard the **underlying pathologic process** of cartilage erosion. Indeed, there is some experimental evidence (the clinical significance of which is unclear) to indicate that some, but not all NSAIDs can **accelerate** the rate of cartilage loss, possibly by inhibiting the synthesis of new cartilage matrix. This has been shown both in tissue culture and in vivo for **salicylate**, but the action is not shared by all NSAIDs and a few, such as **carprofen**, have the opposite action, i.e. they enhance the synthesis of glycosaminoglycan molecules by chondrocytes and cartilage explants in tissue culture in the horse and dog. Also, in the horse, phenylbutazone has been shown to produce a small increase in proteoglycan synthesis in vitro but it reduces cartilage mass in vivo.

Laboratory animal studies have shown that NSAIDs can either retard or prevent fracture healing. This is an important consideration, but its relevance to clinical equine use remains to be determined. In view of these concerns, NSAIDs should not be withheld from animals in pain but they should be used judiciously.

Intravenous administration of solutions of NSAIDs, usually **dipyrone** (metamizole), **flunixin** or **phenylbutazone**, provides rapidly effective analgesia in equine patients with **spasmodic colic** (*q.v.*) and other sources of pain. However, the clinician must remain aware that the suppression of clinical signs by high-efficacy drugs such as flunixin may obscure diagnosis and mask progress of the condition.

Edema

Laboratory animal studies have shown that NSAIDs reduce edematous swelling and can decrease leukocyte infiltration into inflammatory sites. However, high doses are usually required for both effects and it is not clear whether clinically recommended doses of all NSAIDs currently in equine use reduce the swelling associated, for example, with surgery, although such claims have been made. Experimentally, suppression of edema in the horse has been demonstrated for carprofen.

Endotoxemia

NSAIDs such as flunixin and carprofen are used routinely in horses with endotoxemia. **Endotoxic shock** arises when the lipopolysaccharide (endotoxin) component of Gram-negative bacteria gains access to the circulation in cases of **colic** (*q.v.*).

Some of the life-threatening effects of endotoxin on cardiovascular and respiratory systems and some of the metabolic and gastrointestinal changes in the horse are suppressed or abolished by pre-treatment with NSAIDs in experimental circumstances. This presumably reflects the role of eicosanoids (such as PGE_2, PGI_2 and TXA_2) in mediating some of these changes. Treatment with NSAIDs, therefore, represents a rational approach to therapy for endotoxemia. However, their effectiveness in **established shock** (*q.v.*) is likely to be

significantly less than that provided by pre-treatment in experimental animals. It should also be noted that those effects of endotoxemia mediated by eicosanoids are likely to be due to both COX isoforms, so that the classical, non-selective NSAIDs should be more efficacious than the newer COX-2 selective drugs.

Fever

In fever, **endogenous pyrogens** such as interleukin-1 and other cytokines (*q.v.*) release PGE_2, which acts on the anterior hypothalamus to reset the thermoregulatory center. Inhibition of PGE_2 synthesis explains the antipyretic action of NSAIDs in infections associated with fever. Lowering of body temperature provides clinical relief but NSAIDs may sometimes **prolong** the course of viral diseases, since the production of interferons is enhanced when body temperature is raised. NSAIDs are not widely used in horses for their antipyretic action.

Antithrombotic actions

Aspirin irreversibly inhibits platelet COX-1, this action forming the basis for a further use—not shared by other NSAIDs at clinically recommended dose rates—**inhibition of thrombus formation**. The full potential uses of the antithrombotic action of aspirin in equine medicine have yet to be determined but some diseases of unknown etiology, involving thromboembolic and/or vasoconstrictor components, might benefit from the use of low dose aspirin. These diseases include disseminated intravascular coagulation, laminitis and navicular disease (*q.v.*).

CHONDROPROTECTIVE AGENTS

Compounds with unknown and possibly multifactorial mechanisms of action and various tissue extracts that may retard cartilage breakdown and promote new cartilage synthesis have been administered as chondroprotective (disease modifying) agents in veterinary medicine. Two compounds with established activity in vitro are **polysulfated glycosaminoglycan (PSGAG)** and **pentosan polysulfate** (*q.v.*). The latter is administered by intra-articular (IA) or IM injection in the therapy of traumatic and degenerative joint disease (*q.v.*) (but not in septic arthritis) in the horse.

PSGAG is a polymer of approximate MW 10 000 Da. It is extracted from bovine tracheal tissue and, structurally, it is based on repeating units of hexosamine and hexuronic acid. Chemically, it is a sulfated molecule similar to heparin and the aggregated proteoglycan molecules that form cartilage matrix. **PSGAG binds to cartilage**, exhibiting especial affinity for osteoarthritic cartilage, leading to retardation of cartilage breakdown. Additionally, the synthesis of new matrix is enhanced. In contrast to steroids and NSAIDs, which provide only relief of signs in inflammatory conditions, PSGAG therapy may attenuate the degeneration of cartilage.

Various **pharmacologic actions** of PSGAG have been described, including inhibition of the clotting and complement cascades, inhibition of lipopolysaccharide-induced PGE_2 synthesis, reduced superoxide radical generation, delayed dedifferentiation of cultured chondrocytes, increased synthesis and decreased breakdown of hyaluronic acid, protection of chondrocytes from steroid-induced toxicity and inhibition of many lysosomal and non-lysosomal enzymes such as cathepsins, collagenase and metalloproteinases. Thus, at concentrations achievable in equine joints following IA injection, therapeutic doses of PSGAG inhibit stromelysin, an enzyme that breaks down cartilage matrix. This is the probable basis for the drug's therapeutic effects.

The side effects of chondroprotective agents seem to be minor; however in doses above the therapeutic range they inhibit clotting through their heparin-like actions. In addition, transient synovial effusion and arthralgia have been reported following IA administration of PSGAG in the horse. Aggravation of inflammation may therefore occur in the presence of synovitis, so that PSGAG is used primarily in subjects in which synovitis is slight or absent. Experimentally, PSGAG has been shown to facilitate the growth of a sub-infective dose of *Staphylococcus aureus* in equine carpal joints. Chondroprotective agents should not therefore be administered by the IA route in the presence of joint sepsis (*q.v.*), and some clinicians concomitantly administer an **aminoglycoside antibiotic** such as gentamicin when PSGAG is injected IA into non-infected joints.

Hyaluronic acid is a high molecular weight mucopolysaccharide. It is a normal constituent of connective tissue matrix and synovial fluid, produced by type B synoviocytes and chondrocytes. It accounts for the high viscosity of synovial fluid. In joint injury, the viscosity of synovial fluid decreases as the hyaluronic acid content falls, and depolymerization occurs. In healthy articular cartilage, hyaluronic acid is linked to the aggregated proteoglycan molecules to form the matrix. In the early stages of arthritis (*q.v.*), cartilage degradation occurs with the loss of proteoglycans and hyaluronate; only later is collagen depleted.

Intra-articular and IV administration of sodium hyaluronate have been used in **joint disease** therapy. The mode of action is unknown, but **binding to cartilage proteoglycans** may slow down processes of cartilage degradation and increased synovial fluid viscosity may also be protective. Hyaluronate possesses additional properties, however. It inhibits PGE_2 synthesis, suppresses leukocyte migration, reduces phagocyte activity and decreases the permeability of synovial membranes. Good clinical responses have been claimed following IA injection of sodium hyaluronate. Efficacy seems to be greatest in the presence of **joint inflammation**. Dosing may be repeated at weekly intervals until a satisfactory response is obtained, or no response occurs. It has also been used as supportive therapy in subjects with infective arthritis and tenosynovitis (*q.v.*).

In recent years there has been a marked rise in the use of a range of compounds classified as nutraceuticals. They include glucosamine and chondroitin (*q.v.*) and they provide the **building blocks** for the synthesis of cartilage matrix. The bioavailability of these compounds is likely to be acceptable, although further studies are required. Their effects in controlled clinical trials have yielded some positive results.

CORTICOSTEROIDS

GENERAL PROPERTIES OF CORTICOSTEROIDS

The principal steroid hormones secreted by the adrenal cortex (corticosteroids) comprise two classes, **mineralocorticoids** (e.g. aldosterone) and **glucocorticoids** (e.g. cortisol and hydrocortisone).

The physiologic effects of the mineralocorticoids are exerted on water and electrolyte balance in the kidney (*q.v.*) and parts of the gastrointestinal tract, at which sites aldosterone promotes sodium retention and potassium extrusion. Glucocorticoids affect carbohydrate, lipid and protein metabolism and thus all body tissues. The division is not absolute, however, as some glucocorticoids possess weak mineralocorticoid activity and vice versa.

Both endogenous and synthetic glucocorticoids possess anti-inflammatory properties, and the glucocorticoid hormone cortisol is used, usually in creams for topical application, as an anti-inflammatory agent for general skin conditions involving irritation (*q.v.*) but excluding those associated with microbial infection. Most synthetic steroids possess greater glucocorticoid and reduced mineralocorticoid potency relative to cortisol, so that side effects on electrolyte balance (sodium retention and edema) can be avoided or minimized. Relative potencies of several corticosteroids (cortisol = 1) are presented in Table 4.12.

Anti-inflammatory activity parallels glucocorticoid potency, so that in clinical use equi-effective doses of synthetic glucocorticoids will generally produce the same degree of toxicity. It is important to recognize the very **diverse range** of actions of glucocorticoids, as these underlie the several side effects that can occur in medium- to long-term use, although the development of novel glucocorticoids that selectively inhibit the effects of pro-inflammatory transcription factors may result in fewer unwanted side effects. Topical application of conventional steroids may however be associated with thinning of the skin and there may be increased risk of local infection. These actions are summarized in Box 4.1, and the circumstances in which steroids are either contraindicated or must be used with special care are listed in Box 4.2.

Table 4.12 Relative potencies of corticosteroids (cortisol = 1) and biologic half-life values in the horse

Compound	Mineralocorticoid potency	Glucocorticoid and anti-inflammatory potency	Biologic half-life (h)
Cortisol	1	1	8–12
Aldosterone	800	0.2	–
Deoxycorticosterone	40	0	–
Prednisolone	0.8	5	12–36
Prednisone[1]	0.6	4	12–36
Methylprednisolone	0	5	12–36
Triamcinolone	0	5	24–48
Dexamethasone	0	30	36–54
Betamethasone	0	25	36–54
Flumetasone	0	100	36–54

[1] *Inactive, converted in vivo to prednisolone.*

Box 4.1 Corticosteroids: Pharmacologic actions and side effects in the horse

1. Increased storage of glucose as glycogen in liver but decreased uptake and utilization in other tissues, with increased gluconeogenesis leading to hyperglycemia
2. Decreased protein synthesis, increased protein catabolism leading to muscle weakness and wasting (myopathy) and delayed wound healing
3. Increased lipolysis and, at high dose rates, redistribution of body fat
4. Initial polyphagia, polyuria and polydipsia
5. Mineralocorticoid effects with some drugs (hypokalemia, metabolic alkalosis)
6. Decreased absorption from gastrointestinal tract (GIT) of calcium, increased renal excretion of calcium leading to osteoporosis
7. Thinning of skin
8. Normally little effect on GIT integrity but ulceration occurs in subjects with spinal cord trauma
9. Hepatomegaly
10. Depression of cell-mediated immunity, suppression of antibody production leading to increased susceptibility to infection
11. Hematologic effects: neutrophilia, eosinophilia, lymphopenia
12. Steroid-induced arthropathy possible with intra-articular injection of depot formulations
13. Hypoplasia and ultimately atrophy of adrenal zona fasciculata of the adrenal cortex with reduced capacity to secrete cortisol; impairment of response to stress following withdrawal

Box 4.2 Corticosteroids: Contraindications or special care in use

1. Diabetes mellitus
2. Cardiovascular disease
3. Patients with renal insufficiency, disturbances of electrolyte balance, e.g. hypokalemia
4. Presence of infections, especially viral infections; antibacterial cover essential when used in animals with bacterial infections
5. Presence of corneal ulceration, glaucoma, cataracts
6. Late pregnancy—can induce parturition; early pregnancy—possibly teratogenic
7. Patients with compromised immune status
8. Care with joint disease, steroid arthropathy from inappropriate use of long-acting preparations

NB Cushingoid symptoms (muscle wasting, osteoporosis, redistribution of fat) can occur during treatment and problems deriving from adrenal hypoplasia during recovery.

CORTISOL SECRETION

Three mechanisms controlling the secretion of cortisol from the zona fasciculata of the adrenal cortex have been identified. All forms of **stress** increase the secretion of adrenocorticotropic hormone (ACTH) from the anterior pituitary and hence cortisol secretion from the adrenal cortex; increased plasma cortisol concentration reduces the secretion of corticotropin releasing factor from the hypothalamus and ACTH from the anterior pituitary leading to reduced cortisol secretion (a **negative feedback** system). There is also a **natural circadian rhythm** of ACTH and hence of cortisol secretion, with plasma concentrations peaking at 08.00 to 10.00 h (in humans, horse and dog) and in the late evening in nocturnal species like the cat.

Superimposed on circadian secretion is an **episodic pattern** of secretion of cortisol in the horse with 10–17 peaks occurring over 24 h. When exogenous steroids are administered, they mimic the action of endogenous cortisol on the negative feedback pathway and this hypothalamus–pituitary–adrenal (HPA) suppressant activity parallels glucocorticoid anti-inflammatory activity.

In the horse, plasma cortisol is suppressed for 24 h with the water-soluble prednisolone succinate, for 3–4 days with dexamethasone alcohol, and up to 21 days with prednisolone acetate. With long-term steroid therapy, the consequence is reduced cortisol secretion, hypoplasia and, potentially, atrophy of the cortex. Detailed equine studies are lacking but experience in the dog and human indicates that some degree of adrenal atrophy occurs after 1 wk of treatment. After 1 yr of therapy in humans, the **pituitary recovery** takes approximately 5 mo but adrenal responsiveness to ACTH recovers more slowly and may take 9–12 mo. When therapy is withdrawn, the adrenal suppressed animal is unable to mount the normal increase in cortisol secretion in response to stress and therefore is **vulnerable** to any stress situation.

Methods of minimizing **steroid-induced HPA suppression** should be considered. Administration of a short-acting steroid at the time of peak plasma cortisol concentration (early morning in the horse) gives the theoretical advantage that drug and endogenous steroid concentrations should decline together to provide a period of low circulating concentrations prior to administration of the next dose. It is also common to recommend administration of steroids on alternate days and, on terminating therapy after medium- to long-term treatment, dosage should be reduced gradually to increase the opportunity for adrenocortical regeneration.

ANTI-INFLAMMATORY ACTIONS OF GLUCOCORTICOIDS

Mechanisms of action

The mechanism of the anti-inflammatory action of steroids is not fully understood, but they do suppress all components and all forms of inflammation. Many studies have shown that glucocorticoids enter cells to combine with cytosolic receptors. The steroid–receptor complex is transported to the cell nucleus, where transduction leads to increased synthesis and release of polypeptides, the **lipocortins**, with anti-inflammatory properties.

One action of endogenous lipocortins is blockade of phospholipase A_2. This enzyme, when activated by all forms of tissue injury, acts on cell membrane

phospholipid to release the 20-carbon unsaturated fatty acid, arachidonic acid. Arachidonic acid may serve as a substrate for the enzymes COX (*q.v.*), which is inhibited by most aspirin-like drugs (NSAIDs), and lipoxygenases (LO) such as 5-LO, 12-LO and 15-LO (which are not inhibited by most NSAIDs). Steroids, by acting more proximally than NSAIDs in the arachidonic acid pathway, may inhibit the synthesis of a **wide range** of putative inflammatory mediators, including prostaglandins via the COX pathway and the leukotrienes LTB_4, LTC_4, LTD_4, LTE_4 and hydroxyeicosatetraenoic (HETE) compounds via inhibition of lipoxygenases.

This proposed mechanism of steroid action is widely accepted but experimental studies in the horse have shown that both clinical and higher dose rates of betamethasone and dexamethasone fail to inhibit the synthesis of 5-LO and COX derived eicosanoids, or do so only moderately and inconsistently. Glucocorticoids inhibit the synthesis of COX-2 at inflammatory sites, reducing prostaglandin synthesis by this additional mechanism. Glucocorticoids also inhibit induction of **nitric oxide synthase**, an enzyme that is expressed by macrophages and other cells after activation by some cytokines or by lipopolysaccharide. **Nitric oxide** is an endogenous vasodilator and may also be a mediator of tissue damage. Corticosteroids also inhibit activation of the transcription factor NFκB, an important cellular response following toll-like receptor activation.

Whatever the modes of action of corticosteroids, the nature and extent of their actions are clear. They are the anti-inflammatory agents par excellence, suppressing most, and probably all, components of acute and chronic inflammatory

Box 4.3 Glucocorticoids: Actions relating to anti-inflammatory properties

1. Decrease vasodilatation (due, in part, to a direct vasoconstrictor effect on small blood vessels)
2. Decrease fluid exudation (inhibit edema formation)
3. Decrease leukocyte accumulation at sites of inflammation (glucocorticoids also increase release of neutrophils and decrease release of mononuclear cells from bone marrow)
4. Decrease microbicidal activity of macrophages and reduce macrophage-induced tissue damage caused by release of enzymes and toxic oxygen metabolites (free radicals, e.g. hydroxyl radical)
5. Decrease fibroblast and chondrocyte activity (less collagen and glycosaminoglycans synthesized)
6. Inhibit osteoblast activity
7. Increase osteoclast activity (via decreased calcium absorption and the resulting increase in parathyroid hormone which activates osteoclasts)
8. Decrease circulating levels of complement components
9. Cause lympholysis in steroid-sensitive species, e.g. rabbit, rat, mouse
10. Decrease production of pro-inflammatory cytokines and chemokines
11. Decrease eicosanoid and PAF production (inhibition of phospholipase A_2)
12. Reduce histamine release from basophils
13. Suppress induction of nitric oxide synthase and COX-2

responses, including wound healing. Actions of steroids which have been established in laboratory animal studies and which may contribute to their anti-inflammatory actions are listed in Box 4.3, but their occurrence in the horse has not been conclusively demonstrated.

PHARMACOKINETICS AND ADMINISTRATION

There is a latent period of 1–5 h after administration before the occurrence of most corticosteroid-induced pharmacologic effects, and the actions then persist for longer than would be predicted from the plasma clearance and half-life. Thus, elimination half-lives of prednisolone and dexamethasone in the horse are relatively short following IV administration (100 and 53 min, respectively), while the biologic half-lives (the times for which single doses produce HPA suppression) (see Table 4.12) are approximately 24 and 48 h, respectively. The fact that plasma concentration and onset and duration of action are out of phase is explained by the **indirect** mechanism of steroid action.

Duration of action of steroids is also influenced by **route of administration**, the form in which drugs are used (parent compounds and water-soluble esters on the one hand and water-insoluble esters on the other) and product formulation (Box 4.4).

Box 4.4 Glucocorticoids: Formulations available for clinical use

1. Parent compound (steroid alcohol): tablets for oral administration, aqueous suspensions for IM injection
2. Solutions in mixture of water and organic solvents, e.g. propylene glycol (50%) solution for IV or IM injection
3. Water-soluble esters: aqueous solution for IV or IM injection:

   Succinate, Phosphate, *m*-Sulfobenzoate, Isonicotinate — Short acting (1–2 days)

4. Water or oil-based suspensions of lipid-soluble esters for IM injection: depot, slow release from IM injection site:

   Pivalate, Acetate, Propionate — Medium acting (2–14 days)

   Dipropionate, Acetonide, Adamantoate — Long acting (≥2 wk)

5. Mixture of water-soluble and water-insoluble esters (e.g. Na phosphate + dipropionate) for IM injection
6. Ointments, creams, aqueous drops for local application: esters with diphasic polarity (betamethasone-17 valerate) penetrate skin and retained locally
7. Dry powder for inhalation (e.g. beclometasone dipropionate and fluticasone dipropionate)

Water-soluble esters, or parent compounds solubilized with organic solvents, may be administered IV or IM, systemic absorption from the latter site being rapid. The insoluble esters are administered IM to provide a **depot** from which absorption occurs over several days or, in some instances, weeks. However, with such products, adrenal suppression and hence hypoplasia may be unavoidable. Moreover, the **control of steroid action** (both therapeutic and side effects), which can be achieved with shorter acting products administered once daily or on alternate days, is lost. Use of these should therefore generally be reserved for occasions when shorter acting products are unsuitable. In addition to ester solubility, and the use of some products containing fixed oils, which further prolong uptake, duration of action may be controlled by the use of aqueous suspensions of varying particle size.

As well as esters of variable aqueous solubility produced by substitution on carbon 18 of the basic steroid structure, other derivatives with esterification in the 17 position such as **betamethasone-17-valerate** and **beclometasone dipropionate**, which have diphasic polarity, have been used. These compounds are absorbed into, and bound in, the skin; they have low systemic availability and the risk of systemic side effects is therefore greatly reduced.

Although well absorbed orally, steroids are not generally administered to horses by this route; the usual routes for equine use are topical application to the skin and IV, IM and IA injection, although **inhaled steroids** are also used in patients with respiratory disease. The choice of agent depends on the clinician's personal preference. Daily or alternate day dosing with short-acting compounds is preferable but may be less practicable than depot therapy in conditions such as sweet itch (*q.v.*).

CLINICAL USES

Anti-inflammatory steroids are used to treat a wide range of both immune and non-immune inflammatory conditions. **Allergic conditions** (e.g. *Culicoides* hypersensitivity or "sweet itch"; recurrent airway obstruction) and **non-specific eczemas** respond well to therapy.

If animals cannot be removed from the source of antigenic challenge (biting flies of the genus *Culicoides*), **sweet itch** (*q.v.*) may represent one of the few indications for using **depot steroid therapy** with long-acting esters. As the condition is **seasonal**, such therapy can be applied intermittently. In mild cases, a single IM injection of **methylprednisolone acetate** early in the season may result in an animal having reduced signs for the remainder of the biting season. In more severe cases a second injection 3–4 wk later may be required.

Steroids may also be administered to break the itch–scratch or itch–rub cycles in equine **dermatoses** that can lead to self-excoriation. Local allergies also respond to therapy with steroids.

Steroids are commonly used to treat ear conditions (**otitis externa**) in small animals and **inflammatory conditions of the eye** (*q.v.*) in all species. The chronic use of steroids in the eye can cause sloughing of internal membranes and blockade of the canal of Schlemm, leading to reduced drainage, increased intraocular pressure and possibly glaucoma. Inflammatory responses in the eye and the resulting corneal opacity are effectively controlled by topically applied steroids, but these drugs are **contraindicated** if superficial corneal ulceration is present,

as they retard the initial phase of re-epithelialization. Viral infections in the eye have been converted to **fulminating forms** by the use of topical steroids.

In **acute anaphylaxis** (*q.v.*), the onset of action of steroids is too slow to be clinically useful. Steroids have been recommended for all forms of **shock** but the slow onset of action is again disadvantageous. Unfortunately, the very high doses (at least 10 times the anti-inflammatory dose) required in large animal species like the horse make such treatment prohibitively expensive for general use. Moreover, the efficacy of steroids is much less certain in established shock than when given before the onset of shock. In practice, steroids probably have no advantages over **flunixin** in horses with **endotoxic shock.**

In the presence of inflammation caused by **bacterial infection,** steroids should be administered only with appropriate **antibacterial agents.** Suppression of signs is commonly obtained in the early stages. However, steroid usage is controversial because of the **immunosuppression** (*q.v.*) produced by effective doses and hence possible exacerbation of disease.

Steroids should not be used in the presence of **viral infections**. In addition, tissue repair processes are impaired in the later stages of infection and this may be particularly important in parenchymatous tissues like the lung. If steroids are used, effective antibacterial therapy with a bactericidal agent should also be provided.

Steroids are used to treat disorders of the musculoskeletal system such as **traumatic arthritis** and **myositis, bursitis, tendonitis, eosinophilic myositis** and **osteoarthritis** (*q.v.*). Steroids may actually cause an **acute laminitis** (*q.v.*) by unknown mechanisms but possibly through potentiation of vasoconstrictors such as 5-HT and noradrenaline/norepinephrine in the circulation of the hoof. Most clinicians now consider steroids to be **contraindicated** in all forms of laminitis.

Joint disease

For the treatment of inflammation in **joint diseases**, IA injection of steroids, following the withdrawal of an **equal volume** of synovial fluid, is the most effective means of alleviating pain, inflammation and hence lameness.

Cases of **synovitis** and **capsulitis** (e.g. of the fetlock) (*q.v.*) and **acute pastern soreness** or **spavin** (*q.v.*) unaccompanied by bony changes usually respond to a single treatment with a long-acting ester. Administration by the IA route reduces, but does not abolish, the risk of systemic side effects, as rapid absorption can occur from some formulations. Thus combinations of soluble and insoluble esters or long-acting preparations alone, retained locally for several days or longer, have been used. With any IA injection, **aseptic technique** is essential as infection in joints has a poor prognosis and the **immunosuppressant actions** of steroids may exacerbate infection problems, although signs of infection will be masked for a few days by the anti-inflammatory actions.

Steroids suppress synovitis and capsulitis and alleviate stiffness and pain, and this permits **freer joint movement**. Exposure of treated animals to even moderate exercise regimens may exacerbate, through overuse, processes of joint degeneration. **Complete rest** is therefore generally advised following use of IA steroids. Moreover, steroids may interfere with natural repair processes. Laboratory studies have demonstrated steroid inhibition of chondrocyte

metabolism: high doses in vitro increase chondrocyte mortality, while lower doses suppress the synthesis and release from chondrocytes of proteoglycans and hyaluronic acid, both of which are important components of cartilage matrix. Such actions may explain the **steroid-induced arthropathy** (*q.v.*) that has been reported in vivo following IA dosing. However, this may also involve the presence of particulate matter (steroid suspensions) in the joint; experiments with equine chondrocytes and synovial cells have shown that "inert" particulate matter (bone and silica) can greatly increase the synthesis and release of the inflammatory mediator PGE_2. Steroids may also induce osteoporosis and osseous metaplasia (*q.v.*). The latter may be a reaction to the **vehicles** used for long-acting steroids.

A short-lived local inflammatory response, "**post-injection flare**", is occasionally seen following the injection of microcrystalline steroid suspension into joints, possibly through the "particulate" mechanism with formation of PGE_2 mentioned above. However, the greater concern is with the **reduction** in cartilage strength and thickness with longer term use.

The debate on IA steroid usage centers on the undoubted benefits provided by their anti-inflammatory (and analgesic) actions on the one hand and the depressant effects on **chondrocyte metabolism** on the other. In the early stages of osteoarthritis, chondrocyte metabolism is increased and the catabolism of existing cartilage and synthesis of new cartilage are both increased. The inhibitory effects of steroids on enzymes responsible for the synthesis of new collagen and cartilage matrix may be regarded as deleterious, while their action in inhibiting cartilage-degrading enzymes is presumably beneficial. Given the present state of knowledge it would seem wise to advocate the cautious use of IA steroids, restricting the size of administered dose and number of injections and **avoiding exercise routines** following treatment.

Three types of joint disease in which IA steroids are wholly **contraindicated** are septic arthritis (*q.v.*) (although they have been administered to suppress persisting inflammation once infections have been completely cleared), osteochondrosis dissecans (OCD) (*q.v.*) as increased cartilage flap formation and the stripping of cartilage from bone have been described, and when bony changes are seen radiographically. Intra-articular fractures and luxations (*q.v.*) should be treated by surgery and rest rather than steroid therapy.

Respiratory conditions

A number of non-allergic and allergic respiratory conditions, such as mixed infection pneumonias in calves and **recurrent airway obstruction** (RAO) (*q.v.*) in horses, may be treated with steroids. However, in RAO, bronchodilator therapy with β_2-agonists such as **clenbuterol** is preferred for treatment of acute episodes, and steroid use is more common in moderate or severe cases.

TOXICOLOGY

GENERAL CONSIDERATIONS

Horses in many countries are kept as individuals or in small groups rather than in large free-ranging herds. Even in small groups they are often treated

as individuals with relatively close attention, for example in relation to feeding, rather than as extensively ranched animals. As the horse is herbivorous and a grazer, most epidemiologic investigations of equine toxicoses focus on food and forage, although other routes of exposure cannot be ignored. The **history** of a toxicosis (numbers of animals affected, feeding practices, farm procedures, etc.) is often the first indicator pointing to the possibility of poisoning. **Availability** of a poison and access to it are prerequisites for a toxicosis to occur; in the majority of cases either ingestion or skin contact has to precede toxicosis. Careful observation at the farm or stable and interrogation of handlers helps to confirm the toxicosis and aids in identifying causes.

A **thorough clinical examination** is essential for successful diagnosis and treatment. Many poisons do not cause pathognomonic signs or lesions. However, **aggregated** signs or syndromes may assist in identifying the likely cause. A careful and methodical post mortem examination may also be required.

Local knowledge of plants or agrochemical usage may be helpful. Knowing when feed was introduced to the horse or the horse was introduced to the food source, such as to a field with plants, can aid in defining causes and sources. A timeline of the course of the disease will help in tracking the nature of the disease. The progress of a disease and morbidity can help to differentiate between spread of an infectious disease and development of toxic disease.

Clinical pathology is often of great help in assisting the clinical assessment. The laboratory diagnosis can further guide the clinician with regard to sampling and interpretation of results, particularly when the cases encountered are sporadic and even idiosyncratic. Further assistance can be sought from referral centers, veterinary investigation laboratories and poison information centers, although the latter two sources cater mainly for agricultural and companion small animals, respectively.

It is important to have a good working knowledge of toxicology and to be sufficiently cognizant of potential toxic compounds encountered in order to recognize particular toxicoses and to provide the necessary conditions for the successful conclusion of treatment. For many toxicants and plant toxicoses there are **no specific antidotes**. In such cases **decontamination treatment** is employed together with symptomatic and supportive therapeutic measures.

Decontamination treatment involves **removing the source** of the poison (or the animal from the source as in changing the pasture) followed by clearing of the gastrointestinal tract with **liquid paraffin** (light mineral oil) at 2–4 L per 500 kg as a laxative. For many toxicants, **activated charcoal** at 2–5 g per kg made into **a sludge** with up to 4 L of water, can be placed in the stomach for 20–30 min **prior to the laxative** in order to adsorb the toxicant before it is expelled by the laxative. In the case of **skin exposure**, decontamination will include cleansing of the skin.

Symptomatic treatment involves treating the presenting signs in order to ameliorate the toxicosis, whether or not there is an antidote. Supportive therapy includes **fluid and electrolyte therapy** and **pain management**. Hastening renal excretion with administration of fluids and diuretics will be beneficial in the treatment of some toxicants and their metabolites.

Finally, it is necessary to bear in mind the possibility of insurance and medico-legal ramifications as well as the need to handle the case and any samples collected in a reliable manner.

Pharmaceuticals and nutraceuticals are not covered in this text, although cases of iatrogenic origin from overdosing, from side effects, from residues or through adverse reactions have been reported. **Herbal medicines** may also cause poisoning and these are often used without full knowledge of their pharmacologic and toxicologic effects.

FEED-RELATED TOXICOSES

Short feed, concentrates

Apart from accidental mixing of feed, toxicoses that occur through ingestion of horse feedstuffs are uncommon. **Mycotoxins** (*q.v.*) produced in food substrates by fungi during storage are more likely to cause problems in ruminants, poultry or pigs, in part because horses are less likely to be given large amounts of poor quality meal. In many countries, mycotoxicoses are considered very rare. **Aflatoxicosis** (*q.v.*), with its widespread effects including liver damage and hemorrhage, is uncommon to rare in horses, as is mycotoxicosis resulting from **trichothecenes** (*q.v.*).

An interesting mycotoxicosis in horses in some parts of the world is **leukoencephalomalacia (LEM)** (*q.v.*), resulting from maize contaminated with *Fusarium moniliforme* or *F. tricinctum*. CNS damage leads to horses exhibiting head pressing, facial paralysis, aimless walking, goose-stepping gait, circling, blindness, swaying backwards and rapid death after onset of signs. Since the neurologic signs are permanent, recovery is unlikely. Another occasionally encountered mycotoxin is slaframine or "**slobber factor**," a piperidine alkaloid giving parasympathomimetic effects, notably salivation. The source is clover infected with *Rhizoctonia legumicola.* The animal recovers a few days after removal of the offending infected hay.

Ionophores can be highly toxic to horses. Such poisoning has been reported worldwide but is uncommon in those countries where there is limited extent of usage. However, accidental cases can occur when ionophores are mistakenly added to horse rations. Acute cases, or chronic cases with acute manifestations (including sudden death following cardiac damage) do occur. Signs in acute cases include inappetance (more specifically refusal of the concentrate feed), neuromuscular weakness, ataxia, tremors and recumbency, and cardiothoracic signs of tachycardia, dyspnea and hyperpnea. Terminally there may be seizures. In chronic cases there may be circulatory disorders with pitting edema and exercise intolerance. The cardiac signs correlate with streaking in the myocardium, although renal and hepatic lesions are also likely to be present in the carcass at post mortem examination. There being no specific antidote, treatment consists of decontamination therapy (*q.v.*), supportive treatment and rest because of the cardiac damage.

Plant-related

Introduction

Most domesticated animals avoid toxic plants, and horses are no exception. However, change of circumstances (overgrazing, change of land management,

relocation) can lead to an increase in poisoning cases. The following listing is intended to highlight the prominent features of poisoning by the more important plants with a tabular summary of those that are less important (Table 4.13).

Table 4.13 Plants with potential to poison horses

Plant	Toxic principle	Main system(s) affected	Other signs	Comment
Black walnut (*Juglans nigra*) English walnut (*J. regia*)	—	Locomotor	Laminitis, colic possible	Laminitis from bedding on shavings with black walnut shavings, unknown from English walnut
Blue-green algae (*Microcystis* spp.)	Microcystin	Liver, skin	Photosensitization, jaundice, tremors, ataxia	—
Box (*Buxus sempervirens*)	Buxine and other alkaloids	GIT; CNS	Gastroenteritis, colic Death from respiratory failure	Rare poisoning
Giant hogweed (*Heracleum mantegazzianum*)	—	Mouth	Stomatitis, hypersalivation	Irritant plant at site of contact
Hawthorn (*Crataegus* spp.)	Cyanogenic glycoside		Sudden deaths, respiratory signs	Common hedge plant
Hellebores (*Helleborus* spp.)	Helleborein	CNS; CVS	Tremors, colic, diarrhea, polyuria	Rare in horses in UK
Holly (*Ilex* spp.)	—	GIT	—	Very rare poisoning
Horseradish (*Armoracia rusticana*)	Sinigrin	GIT	Gastrointestinal irritancy, colic	Obnoxious plant, so rarely eaten
Horse chestnut (*Aesculus* spp.)	Aesculin	GIT	Peculiar gait	Not a problem in Britain but reported in USA
Horsetails (*Equisetum* spp.)	Thiaminase	CNS	Progressive CNS signs, incoordination to seizures, recumbency and death	Treat with thiamine and purgatives Remove source and feed grain
Ivy (*Hedera helix*)	—	GIT	Irritancy	Rare
Laburnum (*Laburnum anagyroides*)	Cytisine, anagyrine	CNS	Excitement, incoordination, sweating, convulsions, death	Highly poisonous tree; horses the most susceptible species
Mercury (*Mercurialis* spp.)	Mercurialine	GIT	Jaundice, salivation, diarrhea, weakness, lethargy, hematuria and coma	Rare since plant is unpleasant to eat

(*Continued*)

Table 4.13 (*Continued*)

Plant	Toxic principle	Main system(s) affected	Other signs	Comment
Monkshood (*Aconitum napellus*)	Aconitine	Respiratory, CNS	GIT irritancy, salivation, colic, weakness, paralysis, death from cardiac or respiratory failure (asphyxiation, aspiration)	Rare woodland plant (so rarer poisonings)
Oleander (*Nerium oleander*)	Various cardenolides such as oleandroside	CVS	Colic, melena, diarrhea, cardiac arrhythmias, sudden death	Surprisingly, has been suspected in UK although it is a tropical and subtropical plant
Privet (*Ligustrum vulgare*)	Ligustrine	GIT; renal	Gastroenteritis, colic, incoordination, renal damage	Rare
Rhododendron	Grayanotoxin (andromedo-toxin)	GIT	Colic, salivation, variously diarrhea or constipation, staggering, tremors, collapse	Horses with access to gardens or woodland
Robinia, black locust (*Robinia pseudoacacia*)	Robin, robitin	GIT, CVS, locomotor	Salivation, colic, diarrhea, anorexia, paralysis, laminitis Tachycardia Excitement and seizures	Common municipal tree so potential is present Bark is also toxic
Sweet clover, melilot (*Melilotus* spp.)	Coumarins in hay/silage	Blood	Hemorrhages	Poisoning in horses is unlikely, especially given that horses are generally fed higher quality, unspoiled hay
Umbellifers Poison hemlock (*Conium maculatum*)	Coniine, coniceine	CNS, ANS	Mydriasis, weakness, staggering, respiratory arrest	Uncommon poisonings Nicotine-like and curare-like action
Water hemlock, cowbane (*Cicuta virosa*)	Cicutol, cicutotoxin	CNS	Violently toxic plant Mydriasis, colic, violent convulsions	Yellow juice in root contains the toxin Walnut-sized piece of root will kill a horse
Water dropworts (*Oenanthe* spp.)	Oenanthotoxin	CNS	Sudden deaths, salivation, mydriasis, convulsions	Multiple roots, "dead men's fingers"
White bryony (*Bryony dioca*)	Various	GIT; respiratory	Purgation, dyspnea, sweating, polyuria	Rare poisoning Hedge plant
Wild mustards, charlock (*Sinapis* spp.)	Irritant oils, e.g. allyl isothiocyanate at seed stage	GIT	Gastroenteritis including diarrhea, hypersalivation	Rare in horses

ANS, autonomic nervous system; CNS, central nervous system; CVS, cardiovascular system; GIT, gastrointestinal tract.

Yew (Taxus baccata)

The yew, or ground hemlock, is a common plant in many countries, often found in hedges and gardens away from anticipated animal access. Yew is **palatable** and is green when other forage is scarce in autumn/fall through to spring; however, a common source of the plant for horses is clippings. There are a number of toxic principles in the plant but the result of ingestion is often sudden death due to taxine. Traces of yew leaves or twigs may be found in the mouth or stomach at post mortem examination. Signs that have been reported include cold extremities, incoordination, a rapid weak pulse, collapse and excitability. In horses that do not succumb, there may be pyrexia or hypothermia, tremors, muscle fasciculations, dyspnea, bradycardia, colic and diarrhea.

As with many plant poisonings there is no specific antidote, but decontamination therapy (*q.v.*) followed by symptomatic treatment (including **atropine** for the autonomic signs) and supportive therapy should be instigated as soon as possible, since **yew toxicosis can be rapid**.

Bracken (Pteridium aquilinum)

Bracken is widespread in many countries, particularly on marginal land. The source of poisoning can be dried fronds contaminating straw bedding or, in the spring, the more succulent young "fiddleneck" appearing before vigorous grass growth. The plant causes several syndromes in animals: the affected horse shows signs of **thiamine deficiency** through the action of a thiaminase. Horsetails (*Equisetum* spp.) also contain a thiaminase.

Thiamine deficiency results in "**bracken staggers**" with incoordination and tremors increasing in severity as the toxicosis progresses to recumbency, convulsions and death; in chronic cases there is anorexia and weight loss. If the horse is encountered before recumbency occurs, then administration of **thiamine** at 0.25–1.25 mg/kg, b.i.d. for 7–10 days on a reducing dose basis, should be carried out IM or by slow IV injection.

Oak (Quercus *spp.*)

Several species of oak tree can affect horses, but cases of poisoning are rare. The toxic principle is from the tannin family of chemicals. Precise characterization of the toxins has not been determined. **Acorns** are the main source of toxicity in Britain, although leaves can be toxic; cases associated with leaves have been reported in the USA. Acorns may be more abundant in some years than others, with hot dry summers increasing the yield.

Clinical signs of acorn poisoning include colic, constipation and melena, pale mucous membranes, buccal ulceration, bradycardia, dark-colored urine, hypothermia, weakness and staggering. Renal and hepatic damage occurs with renal nephrosis and perirenal edema. Treatment consists of decontamination therapy (*q.v.*) (mineral oil or saline) and supportive treatment, particularly with IV fluids to maintain urine flow in view of the possible uremia.

Ragwort (Senecio jacobea)

Ragwort is notorious as a poisonous plant that affects horses. The toxic principles are pyrrolizidine alkaloids. Other plants of the same genus also contain pyrrolizidine alkaloids and must also be suspect. Unrelated plants containing

pyrrolizidine alkaloids include comfrey (*Symphytum officinale*) and hound's tongue (*Cynoglossum officinale*). Crotalaria (*Crotalaria* spp.) occur in warmer climatic zones.

Pyrrolizidine (*q.v.*) alkaloid metabolites, reactive pyrroles, bind to DNA and affect cell division, resulting in megalocytosis and cell necrosis, bile duct hyperplasia, portal fibrosis and **irreversible perivenous and IV fibrosis in the liver**; in chronic stages the liver can attempt recovery with nodules of regenerative tissue between the fibrotic areas.

Signs reported include colic, pallor, jaundice, constipation or diarrhea, wasting and deranged behavior resulting from hepatic encephalopathy; the common terms "hepatic cripples", "sleepy staggers" and "walkabout disease" summarize the conditions most frequently seen. One problem with these plants is the **lag time** between consumption and the appearance of clinical signs; the animal showing signs may not even be in the same locale as the plants or the hay at ingestion time. Owing to the lag time to onset of clinical signs, the disease is often in its **advanced stages** by the time of presentation to the clinician and treatment is therefore unlikely to be of benefit. Symptomatic and supportive treatment should be used, including sedation and fluid therapy. Control of the disease is best accomplished by **control of the plant**.

Nightshades (Solanum dulcamara, S. niger, Atropa belladonna)

Nightshades are widely distributed in many countries but heavy stands of the plants are usually encountered only infrequently. **Deadly nightshade** (*Atropa belladonna*) prefers chalky soils but the solanaceous nightshades can be found in light woodland and in disturbed soils, neither of which are prime horse grazing locations so that poisoning is uncommon. Additionally, the plants are not particularly palatable so are not preferentially eaten by horses, but **careless disposal of weed waste** can provide a source of the plant, leading to toxicosis.

The toxic principles, which include **atropine** from deadly nightshade, produce inhibitory actions on the parasympathetic branch of the autonomic nervous system, effects ranging from colic and diarrhea or constipation, tachycardia, mydriasis, and dry mouth to CNS effects of depression, weakness, incoordination, convulsions and recumbency. Solanine, a glycoalkaloid, is a **GIT irritant**, resulting in salivation and diarrhea (the latter sign is supposed to be prognostically favorable). It can cause hemolysis and acts on the CNS to produce excitement followed by depression, recumbency and coma. Cardiac arrest may occur.

Symptomatic and supportive therapy is indicated, particularly **demulcents** and possibly **atropine** for the salivation caused by solanine. **Plant control** is the best prevention.

Buttercups (Ranunculus *spp.*)

Buttercups occur widely in pastures and contain ranunculin, which hydrolyzes to the irritant protoanemonin. Protoanemonin is a **vesicant** and can cause blistering around the muzzle of horses grazing infested pasture. Severe cases can be painful with salivation, stomatitis and weakness, incoordination and diarrhea with dark feces due to a hemorrhagic gastroenteritis. Severe cases may involve colic and convulsions.

Demulcents are best used for the GIT irritation, with **emollients** being applied to the skin and supportive therapy used for severe cases.

Clovers (Trifolium *spp.*)

Red clover can become infected with *Rhizoctonia* spp., a fungus that produces "**slobber factor**" (*q.v.*), a parasympathomimetic alkaloid, which in turn causes profuse salivation.

Other syndromes can occur with clovers. "Dew poisoning" or "trifoliosis" is a **photosensitization** (*q.v.*) from which recovery occurs soon after removal from the pasture and sun. Lesions occur in fine weather, after a wet season, and appear on pale skin and around the muzzle. **Alsike clover** has been blamed for cases of hepatic failure and of CNS involvement. Alsike hay may allow more ingestion than pasture so changing the hay is necessary, but there is **no specific treatment**. Cyanide and nitrate poisoning are discussed below (*q.v.*), but can occur with heavy swards of clover.

Cyanide, nitrite, oxalate

In addition to the individual plants mentioned above, chemicals produced by plants in general can cause toxicoses in horses. These chemicals, to which ruminants are more susceptible than horses, are cyanide, nitrite and oxalate.

Cyanide poisoning usually arises from ingestion of plants containing cyanogenic glycosides. There are many potential cyanogenic plants, including grasses, from several plant families. Notable amongst these families is the Rosaceae, with cherry laurel and other plants in the same genus (*Prunus*). This family also includes some stone- and pip-containing fruits that are sources of cyanide.

The cyanogenic glycoside is converted to cyanide via nitrile under the influence of plant-derived β-glycosidases. The resulting effects include salivation, urination, defecation, convulsions, nystagmus, dyspnea and sudden death. Since the action of cyanide is to inhibit cellular respiration, a feature of this toxicosis is the dyspneic animal with red mucous membranes. A smell of **bitter almond** from hydrogen cyanide may indicate the presence of cyanide.

If treatment is feasible, there is a two-part antidote consisting of a single IV injection of **sodium nitrite** (10–20 mg/kg) to form methemoglobin and thence cyanmethemoglobin followed by IV **sodium thiosulfate** (500 mg/kg) to assist, with rhodanase, in converting the cyanide to thiocyanate; the thiosulfate is not as toxic as nitrite and can be repeated because conversion of the glycoside in the GIT is ongoing. Antidotal therapy should be augmented by decontamination therapy (*q.v.*) with activated charcoal and laxatives.

Nitrate poisoning usually results from conversion of nitrates in plants to nitrites under the influence of bacteria. Nitrites in turn convert ferrous hemoglobin to ferric methemoglobin. Nitrates are irritant and cause salivation and abdominal distress while methemoglobin toxicity (to which ruminants are more susceptible) results in dyspnea, cyanosis, bradycardia with weak pulse and death from hypoxia. Blood color changes to red–chocolate–brown, which causes darkening of organs. Treatment consists of the slow IV injection of 10 mg/kg of **4% methythioninium chloride solution** to convert the methemoglobin to hemoglobin via leukomethylene blue.

Oxalates occur in several plants of two families, the Chenopodiaceae (beets, goosefoot, fat hen) and the Polygonaceae (rhubarb, docks, sorrels), as well as being associated with some mycotoxicoses, ethylene glycol poisoning, and foliaceous houseplants such as dumb cane (*Dieffenbachia* spp.), Swiss cheese

plant (*Monstera deliciosa*) and philodendrons (*Philodendron* spp.). These latter plants are uncommon sources of poisoning in horses, as they are not very palatable, let alone accessible. Oxalates exist in different forms in plants.

Oxalate toxicity is linked to gastrointestinal irritancy, hypocalcemia and nephrotoxicity. There may be salivation, nasal discharge, weakness, tachypnea, collapse and death.

Treatment should be **symptomatic and supportive**, with **calcium administration** for the hypocalcemia as 100–500 mL of the 23% calcium borogluconate in an IV infusion together with fluids (**not bicarbonate**) for renal perfusion. The heart rate of the horse should be monitored during infusion. The animal may be refractory to treatment depending upon oxalate type.

Photosensitization

Primary photosensitization caused by ingestion of photodynamic chemicals can result from ingestion of buckwheat (*Fagopyrum* spp.), St. John's wort (*Hypericum perforatum*) and also some grasses.

Secondary (icterogenic) photosensitization (*q.v.*) occurs following liver damage and the consequent build-up of endogenous photodynamic substances. In cooler climates, some of the severe cases of photosensitization seen in sunnier parts of the world are not encountered but occasional cases may occur and require **symptomatic treatment** for the inflammatory skin lesions.

INDUSTRIAL AND AGROCHEMICAL TOXICOSES

Environmental toxicoses arising from industrial contamination or agrochemical treatment of the environment are not covered in full here in view of the vast number of chemicals used, but some of the possible agents are summarized in Table 4.14. Also presented in Table 4.14 are other chemicals, used as pesticides, which are occasionally encountered as causes of poisoning in animals.

Metals that can rarely cause poisoning include lead, arsenic, mercury, cadmium and zinc. Iron toxicity also occurs (*q.v.*) usually subsequent to overdosing with supplements.

Lead poisoning, which is decreasing in frequency, is more likely to be encountered in other species, but in the horse lead causes neurologic, hematologic and abdominal signs. The abdominal signs include colic, gastroenteritis and signs arising from liver and kidney damage. Neurologic signs may be peripheral, as in laryngeal hemiplegia (*q.v.*) and muscle fasciculations, or of central origin as with ataxia, depression and hyperesthesia. Chronically there may be weight loss and anemia. Associated hematologic changes are the presence of nucleated red blood cells and basophilic stippling.

Treatment of lead poisoning involves chelation therapy with **calcium disodium edetate** at 75 mg/kg/day in two doses as a slow IV infusion. Treatment should be given for 2–3 days, then stopped for 2–3 days, then repeated. Monitoring of blood and urine concentrations is recommended to determine that lead is being excreted. Therapy may have to be repeated if **blood lead** concentration increases >0.35 ppm.

Arsenic (*q.v.*) was once a widely used agrochemical but is less commonly encountered in recent times with modern systems of farming. Arsenic antidotes such as dimercaprol are unlikely to be readily available so **analgesic therapy**

Table 4.14 Potential toxicants in horses

Classification	Toxicant	Signs	Comments
Molluscicide	Metaldehyde	CNS excitation, tremors, later CNS depression	Has been reported in the UK in horses
Anticholinesterases	Organophosphate and carbamates	Autonomic signs, muscarinic predominating	Atropine antidote
Anticoagulants	Coumarin derivatives	Hemorrhagic syndrome	Inappropriate mix in feed Vitamin K_1 antidote
Metals/metalloids	Lead, arsenic, mercury, cadmium zinc	CNS, gastroenteritis, colic shock, renal, anemia Lead accumulates in bones Cadmium and zinc affect joints and bones Arsenic severe on GIT	Unlikely to cause poisoning in UK in horses Chelation with EDTA for lead and zinc Sodium thiosulfate for arsenic
Herbicides	Paraquat, diquat, glyphosate, phenoxyacetic acid derivatives	Various Paraquat targets lungs	Many types, no antidotes so symptomatic and supportive treatments needed
Caustics	Creosote	Caustic on mucosae, conjunctivae	Neutralize on mucosae with weak alkali; wash eye repeatedly

and decontamination therapy (*q.v.*) together with **oral thiosulfate** (to bind arsenic) and **IV fluid therapy** for shock should be instigated.

Mercury, cadmium and zinc toxicity is even more rare due to modern environmental legislation and with the decline in use of mercury medications, but environmental contamination can still occur occasionally from industrial sources such as mine tailings and smelting plants. If treatment is needed, **penicillamine** may help mercury chelation and thus hasten urinary excretion, but doses to be used are not established in horses. Decontamination and supportive therapy (*q.v.*) are needed. Similarly there are no antidotes for cadmium and zinc; supportive therapy is needed as with most toxicoses.

Pesticides

Pesticides range from insecticides, through molluscicides to rodenticides. Horses are unlikely to be placed where they ingest large quantities from individual baits, but, occasionally, an individual animal may acquire a significant dose because of faulty handling or misplacing of chemicals by farmers or pest control operators.

Many of the previous therapeutic roles of **organophosphate** (OP) and **organochloride** (OC) insecticides have been taken over by the synthetic pyrethroids, which are relatively safe. Large doses of pyrethroids are needed to reach toxic concentrations in the body and accumulation is less important than with the OPs and OCs.

Organophosphates and **carbamates** (including methiocarb) are agrochemicals with **anticholinesterase** actions. The inhibition of acetylcholinesterase is

caused by bonding with the anticholinesterase and results in cholinergic stimulation and cholinergic signs in the animal. Muscarinic cholinergic signs (on the GIT and heart) usually predominate but nicotinic cholinergic symptoms (such as muscle fasciculations) and adrenergic symptoms due to ganglion stimulation can occur and mask the muscarinic signs.

Major signs of OP/OC toxicity include tremors, profuse salivation, diarrhea and recumbency. Diagnosis can be difficult in view of the plethora of agents causing these signs and the wide range of possible signs. Diagnosis may be assisted by observing the **response to atropine**. A low (pre-anesthetic) dose of atropine (0.02 mg/kg IV) will probably not reverse the signs of anticholinesterase poisoning, so if atropinization occurs the signs may not be due to an anticholinesterase.

Definitive diagnosis involves laboratory identification of the insecticide and analysis of **blood acetylcholinesterase activity**. The latter test is less useful for the shorter-acting carbamates; samples need to be frozen and analyzed soon after collection.

Atropine (0.1–0.2 mg/kg: 25% given IV, the remainder SC or IM as needed) is used for the treatment of both organophosphate and carbamate poisoning in order to reverse the muscarinic signs. **Pralidoxime** (Protopam), an antidote for OP poisoning which acts by reversing OP binding to the enzyme, is unlikely to be available early enough in the treatment regimen, because the OPs act first reversibly but then irreversibly due to aging, or stabilization, of the bond with the enzyme. If pralidoxime is available it should be given IV at 20–40 mg/kg and repeated every 4–6 h.

Anticoagulants

Difenacoum is one of the more frequently encountered causes of **rodenticide poisoning** of horses in many countries; other anticoagulants of the same group also causing poisoning include **bromadiolone**, **warfarin**, **chlorophacinone**, **coumatetralyl** and **dicoumarin**.

The coumarin derivatives act to inhibit vitamin K-dependent clotting factors (*q.v.*) by inhibiting vitamin K epoxide reductase. Usually, in subacute to chronic cases there is a lag time before the clinical signs appear, while vitamin K stores become depleted. Clinical signs are a result of hemorrhage; individual signs depend upon the site of the hemorrhages.

Diagnosis is assisted by analysis of prothrombin times (*q.v.*) (early when factor VII, with a short half-life, is decreased) and whole blood clotting times (later when factors II, IX and X are decreased); ingesta and tissue analysis is also of use in making a diagnosis.

Vitamin K_1 (phytonadione) at a dose rate of 1 mg/kg/day SC is antidotal. With newer generation anticoagulants, treatment may need to be continued for days to weeks. Symptomatic treatment may also help and, rarely, blood transfusion (*q.v.*) may be appropriate.

Herbicides

Paraquat and **diquat,** two bipyridyl herbicides, occasionally cause poisoning in horses. Paraquat specifically targets receptors in the lungs and causes fibrosis.

The kidneys are affected by both compounds. With paraquat the horse becomes depressed, dyspneic and icteric, but apparent recoveries confuse the prognostic judgments in some cases. There is no effective treatment for advanced cases. Both compounds cause ulceration of mucous membranes, colic and diarrhea.

Glyphosate (Roundup™) is not very toxic in the horse, but can cause irritation to the eyes and skin following contact with treated herbage. Flushing of the eyes with **isotonic saline** followed by application of **artificial tears** as an emollient provides some relief, as do emollients for the skin.

The **phenoxyacetic acid** derivatives (including **2,4D**, **mecoprop**, **MCPA**, **MCPB**) are likewise not very toxic but can cause a spurt of plant growth that can lead to increase in nitrogenous compounds in the plants and also alter their palatability. Thus a horse may ingest the plant with the increased nitrate or cyanogenic compounds and be exposed to nitrite or cyanide (*q.v.*).

ZOOTOXICOSES

Snakebite

There are three main families of venomous snakes as shown in Table 4.15. Of these, only the Elapidae and Viperidae are important in the USA and Europe.

In the USA the **pit vipers** (*Crotalus* spp. and *Agkistrodon* spp.) of the subfamily Crotalinae are the source of most bites owing to the number of species and their distribution. Coral snakes of the Elapidae are less widespread in the USA. The only venomous snake likely to be encountered by a horse in Britain is the adder or European viper (*Vipera berus*). Its habitat is usually marginal land (moorland and scrub) rather than prime horse grazing.

The vipers, by their relatively docile behavior, leave themselves open to encroachment by an animal walking by or grazing. Often the viper lies by a track to await prey or to sun itself and, upon approach of a non-prey species "freezes", which either allows it to be trodden on or to think itself cornered. Otherwise most of these snakes are not overly aggressive at a distance. The viper that bites is usually defending itself rather than being aggressive. Nevertheless several bites may be made in one incident. Not all bites involve evenomation.

Bites to the horse are often on the face or the limb extremities and are not noticed until effects of the evenomation become apparent. Horses may be bitten on the limb extremities, but more usually **the head** is struck. Muzzle or

Table 4.15 The principal families of venomous snakes

Family	Subfamily	Example
Viperidae	Azemiopinae Viperinae (adders, vipers) Crotalinae (pit vipers)	Adder, viper, copperhead, cottonmouth water moccasin, rattlesnakes
Elapidae	Elapinae Hydrophinae Laticaudinae	Cobras, coral snakes, sea snakes, mambas, kraits, Australian death adder, tiger snakes, taipan, brown snakes
Colubridae	Colubrinae Aparallactinae Homalopsinae	Boomslang

facial bites may sometimes cause swelling that leads to a life-threatening **occlusion of the nares or trachea**.

The horse is susceptible to viper bites and the bitten horse should be kept in a calm, quiet environment to lessen cardiovascular effects. Preparation should be made for the horse to lie down. The effects of bites include hemorrhages and edema due to the cytotoxic and anticoagulant components of the venom. The cardiovascular effects include **hypotension** and **shock**, which should be treated with **fluid therapy**.

Actions to be taken include hygienic attention to the wounds with **antibiotic therapy** and symptomatic treatment including analgesics. **Tetanus antitoxin** should be administered as for wound treatment. **Antivenin**, while indicated, may not be practicable as it is expensive and should be given within 4 h of the bite. **Corticosteroids are contraindicated**. Observation is required for several days as complications to the wound may occur and the edema around the head may affect respiration. Adder bites are occasionally fatal.

Elapid bites (including coral snakes) tend to cause more local reaction and pain than crotalid or viper bites. There is potential for neurotoxicity including respiratory depression or respiratory paralysis but the small size of the snake and its low volume of venom make severe toxicosis unlikely in the horse.

Other zootoxins

While **insect bites and stings** do occur occasionally in horses, they are rarely of particular individual significance apart from an occasional allergic reaction. **Africanized bees** have entered the USA via South America and have a reputation for rapid-onset, sustained aggression compared with the European honeybee. In severe cases where the horse has disturbed a nest, symptomatic treatment with analgesics and possibly with epinephrine for treating any anaphylaxis, is usually all that is required.

Cantharidin—blister beetles (*Epicauta* spp.) (*q.v.*)—infest fields in the southern USA and may get into alfalfa hay. Contamination of fodder is unknown in hay of British origin but is of significance in alfalfa hay from parts of the USA. Countries importing such hay can request **beetle-free certified** hay. The cantharidin from the beetles irritates the GIT and also the urinary tract leading to colic, ulceration of the GIT with melena, and frequent urination with perineal pruritus. Death is possible. Decontamination therapy (*q.v.*) with activated charcoal and saline purgatives together with supportive fluid and electrolyte therapy may assist in the less severe cases.

Other arthropods such as the **black widow spider** and **recluse spiders** carry very toxic venoms but their habitat rarely coincides with that of the horse. The initial bite incident is often unnoticed. Antivenin is uneconomic; symptomatic and supportive treatment is needed.

DRUGS AND THE COMPETITION HORSE

INTRODUCTION

The horse is the pre-eminent competition animal: no other animal is involved in such a wide range of activities to test its strength and endurance, its control and conformation. With reputations and money at stake, these sports, which are

often underpinned by gambling, are susceptible to drug malpractice. Therefore, most regulatory bodies have devised strict **medication rules** that are designed to maintain integrity by promoting equine welfare and by discouraging the possibility of unfair competition. This presents the owner and veterinary surgeon with a serious dilemma when faced with an animal needing treatment with drugs close to the time of competition: what are the risks of contravening the rules; what is the **clearance time** (*q.v.*) for the intended drug; would it be wiser to withdraw from the contest; and where can advice be found?

Unfortunately, the answers to these questions are often not straightforward and the many autonomous bodies responsible for regulating equine competitions have produced differing proposals for maintaining the integrity of their sport. Philosophically, it is not difficult to accept the need to rule against the use of those drugs that have no legitimate place in equine sports medicine, or against drugs that are known to affect performance, or against drugs that are not licensed for veterinary use. The problems arise with those drugs that are quite properly contained in the veterinary armory, but whose effects on performance can only be speculated upon.

As it is not possible to find convincing information on the influence of drugs on performance, many authorities have ruled that the detection of a foreign substance or its metabolites in the body fluids of the horse is sufficient grounds for disqualification. Essentially, this is the position of the Fédération Equestre Internationale (FEI)*, and of the Jockey Clubs of Ireland, France and the UK (Box 4.5).

These authorities also recognize that positive medication tests can arise by accident from substances that contaminate food, from substances that occur in ordinary diets and from substances that are endogenous to the horse. In order to reduce the number of infringements arising from such accidental sources, the FEI and the Jockey Clubs have taken the logical step of introducing the concept of **threshold levels** (Table 4.16), although there are differences. For example, the FEI does not include arsenic in its list of threshold levels and has lower concentrations for salicylic acid in urine and plasma.

Other bodies have less exacting rules. Many racing jurisdictions in the USA, for example, allow certain therapeutic agents during competition, arguing that such permissive medication is acceptable because it merely restores the horse's normal performance capacity.

As shown in Box 4.5, and unlike the European Jockey Clubs, the FEI allows three drugs—cimetidine and ranitidine (H_2 receptor antagonists) and omeprazole (a proton pump inhibitor)—for the treatment of **gastric ulceration** (*q.v.*). The FEI, again unlike the major European racing jurisdictions, also permits the use of **altrenogest** for the control of estrus in competing animals. However, the three main conditions attached to its use are that it can be used only:

1. In mares
2. At the manufacturer's recommended dose rate, and
3. On completion and submission of the relevant FEI medication form (Form 2).

Under these conditions there is no apparent anabolic or performance enhancing effect.

* See www.horsesport.org

Box 4.5 Annex IV to the FEI Veterinary Regulations (2005)

PROHIBITED SUBSTANCES

Horses taking part in a competition must be healthy and compete on their inherent merits. The use of a Prohibited Substance might influence a horse's performance or mask an underlying health problem and could falsely affect the outcome of a competition. The list of Prohibited Substances has been compiled to include all categories of pharmacological action.

The following are prohibited substances:

- Substances capable at any time of acting on one or more of the following mammalian body systems:
  - the nervous system
  - the cardiovascular system
  - the respiratory system
  - the digestive system other than certain specified substances
  - for the oral treatment of gastric ulceration (see Note 1)
  - the urinary system
  - the reproductive system (see Note 2)
  - the musculoskeletal system
  - the skin (e.g. hypersensitizing agents)
  - the blood system
  - the immune system, other than those in licensed vaccines against infectious agents
  - the endocrine system
- Antipyretics, analgesics and anti-inflammatory substances
- Cytotoxic substances
- Endocrine secretions and their synthetic counterparts
- Masking agents.

A finding of a prohibited substance means a finding of the substance itself or a metabolite of the substance or an isomer of the substance or an isomer of a metabolite. The finding of any scientific indicator of administration or other exposure to a prohibited substance is also equivalent to the finding of the substance.

With the objective of helping riders, trainers and their veterinary advisers, the FEI may include in its rules examples of prohibited substances.

Note 1: Oral treatment by the histamine H_2-receptor antagonists ranitidine, cimetidine and the proton pump inhibitor omeprazole is permitted and will not necessitate the use of a medication form.

Note 2: Treatment of mares for estrus-related behavioral problems is permitted with the substance altrenogest (Regumate) under the following conditions:

1. It is permitted only for mares with an estrus-related behavioral problem.
2. The dose and duration of treatment must be in accordance with the manufacturers' recommendations.
3. A Medication Form 2 must be completed by a veterinarian and submitted to the Veterinary Delegate/Commission before the start of the event.

Notes 1 and 2 will be reviewed annually by the FEI.

Table 4.16 FEI list of thresholds (2005). Reproduced with permission of the Fédération Equestre Internationale (FEI)

Thresholds can be adopted only for:

- Substances endogenous to the horse
- Substances arising from plants traditionally grazed or harvested as equine feed
- Substances in equine feed arising from contamination during cultivation, processing or treatment, storage or transportation.

Thresholds shall be recommended by the Medication Advisory Group, after consultation with official analysts and veterinarians, and approved annually by the General Assembly.

Substances below the following thresholds are not actionable:

Available carbon dioxide	37 mmol per L in plasma
Dimethyl sulfoxide	15 μg per mL in urine or 1 μg per mL in plasma
Estranediol in male horses (other than geldings)	The mass of free and conjugated 5a-estrane-3b, 17a-diol to the mass of free and conjugated 5(10)-estrane-3b, 17a-diol in urine from male horses at a ratio of 1
Hydrocortisone	1 μg per mL in urine
Salicylic acid	625 μg per mL in urine or 5.4 μg per mL in plasma

A rule which demands that horses must be forensically clean has the benefit of being easy to apply but can result in an animal being disqualified when a trace of an improbable doping agent is detected by a particularly sensitive test. Rules that permit some form of medication make the problem of **clearance times** (*q.v.*) even more acute. Should the rule disqualify horses only if a sample contains a drug exceeding an arbitrary concentration, or should the rule attempt to reflect a level of drug below which there can be no pharmacologic effect? Should the rule simply allow any level of nominated drugs in competing animals, or should it specify that drugs must not be given within a certain time before competition? These are just some of the problems.

Policies designed to ensure compliance create further difficulties. Deterrence is better than detection. Therefore, a form of **sample selection** is required that is adequate to prevent malpractice and which makes economic sense. Furthermore, it can be seen that the law of diminishing returns can apply equally well in the world of forensic analysis: more does not necessarily mean better. In practice not every horse can be tested, nor may it be necessary to subject every sample to all available analyses. Strategic selection of both competitor and analysis can be undertaken in order to create a powerful protective influence in equine sports.

It is important to recognize that regulatory authorities have different approaches to doping and medication control and current rules should always be checked with the organization concerned.

PHARMACEUTICS AND PHARMACOKINETICS

Apart from selection and analytical processes, the factors that govern whether or not a drug administration produces a positive dope test are (1) drug entry into the body, (2) distribution and metabolism, and (3) elimination from the body.

Drug entry and distribution

Any drug that enters the body ultimately finds its way into the circulation, which distributes it to the tissues. The rate at which this occurs depends on

the formulation and dose frequency, the route and site of entry, the ability of the drug molecules to cross membranes and the rate of tissue perfusion. Once distributed, drug molecules are available to bind to specific or non-specific receptors, or become stored or modified prior to elimination.

It is useful to understand the processes that can lead to delayed drug absorption, since the IM, SC and PO administration routes can sometimes give **surprisingly long elimination times**. Such difficulties can often be avoided by giving drugs IV where possible. Other methods of administration may also result in significant concentrations of drugs or their metabolites in biologic samples.

Intramuscular administration

It has been shown experimentally with some drugs that, after IM injection, the rate and extent of absorption are greater from injection sites in the neck than from sites in the brisket or rump. This effect may be due to the extent of movement of muscles, the degree of spread of the injected drug within and between muscles, and blood supply and drainage. Drugs can also be excreted sporadically after IM injection. This may be caused by inadvertent injection into a poorly vascularized area like fatty tissue or intermuscular injection.

Subcutaneous administration

Absorption of drugs from SC sites is usually considered to be slower, and can also give rise to **considerable variability** between animals. Tissue cooling causes vasoconstriction, and this vascular effect can be exploited with local anesthetics that incorporate adrenaline in order to prolong their local action.

Sustained-release preparations

Suspensions, or oil-based formulations, or preparations of drugs with long ester side chains are used for depot therapy. **Procaine benzylpenicillin** is a salt containing one molecule of benzylpenicillin combined with one molecule of the **local anesthetic procaine**; this ensures prolonged absorption but involves a **high risk of infringing the rules** for up to 21 days after injection. Similarly, benzathine benzylpenicillin is a benzylpenicillin salt with very low solubility and even longer elimination time. Products containing benzathine benzylpenicillin are available in many countries but they have been banned from use in food-producing species in all EU countries.

In many countries, public health concerns have resulted in the removal of a veterinarian's right to prescribe **anabolic steroids** for horses, except for the treatment of certain fertility problems. These regulations have thus reduced the dangers of producing positive dope tests from sustained-release and implant preparations of anabolic steroids and testosterone. If their use is detected in a sample taken from a horse after competition, the person responsible for the administration would also be guilty of an offense.

Recent advances in **controlled release** from the injection site have resulted in drugs being incorporated into a biodegradable matrix, similar to oral slow-release anthelmintics available for ruminants. Other preparations involve the use of **pro-drugs** that are hydrolyzed or cleaved by enzymes to form active molecules.

Intra-articular administration

The belief that intra-articular (IA) injection limits drug effects to the joint, and that systemic side effects of the therapy are reduced, is not supported by experimental studies. For instance, after IA injection of an aqueous solution of a corticosteroid, it is possible to demonstrate rapid urinary excretion of the drug, accompanied by a marked reduction in circulating cortisol caused by the feedback process on the HPA axis (*q.v.*).

Inhalation therapy

Drug delivery by **nebulization** is becoming more widespread, especially for prevention or treatment of bronchospasm associated with airway disease. Corticosteroids, β-adrenergic agonists, antimuscarinics and sodium cromoglicate have all been recommended for inhalational administration.

It is the aim of this approach to deposit small amounts of drug at the sites where it is required without causing systemic side effects; nevertheless, rapid absorption does occur from the alveoli, resulting in demonstrable blood and urinary concentrations. At the same time, the nasal mucosa is similarly exposed to the administration. This route of entry, like the buccal route, can be very efficient and any drug thus absorbed is not exposed to the **first-pass hepatic metabolism** (*q.v.*) that may follow gastrointestinal absorption.

Absorption through the skin

The barrier to drug absorption provided by skin is not absolute: drugs can penetrate at rates determined by their lipid solubility. However, water-soluble molecules can also penetrate the underlying dermis if the epidermis has been damaged. Solvents such as **dimethyl sulfoxide (DMSO)**, which possess both high water and lipid solubility, can penetrate skin readily and carry drugs with them. These effects are accompanied by, and partly attributable to local tissue damage, despite the reputation of this agent as an anti-inflammatory agent.

Other apparently harmless skin preparations have given rise to detection of substances such as analgesics, corticosteroids, rubefacients and fly repellents.

Metabolism and elimination

Most drug metabolism is carried out by liver microsomes, although other tissues (kidney, lung, GIT) do contain important detoxifying enzyme systems. The most notable of these is the intestinal mucosa, which plays an important role in protecting the body from orally administered substances.

Usually, those drugs that are water soluble do not need to be metabolized in order to be eliminated and so do not persist in the body. The usual consequence of the metabolizing systems is to convert lipid-soluble drugs into more water-soluble molecules, which favors their excretion. These processes are complicated by the ability of drugs to undergo plasma protein binding or to become sequestrated in tissues. Adipose tissue in particular can act as an effective store for lipid-soluble drugs.

Phase I metabolism converts drugs into metabolites that are generally, but not always, inactive. **Phase II reactions** are conjugation reactions in which the drug

or metabolite is coupled via a hydroxy, carboxylic or amino group to a substrate. This produces molecules that are more readily excreted by virtue of their low lipid solubility; in the horse the main conjugates are glucuronides and sulfates.

Some orally administered drugs are metabolized in the intestinal wall or in the liver, and excretion occurs passively or by active secretion into the biliary system. In a few cases first-pass metabolism can almost completely eliminate the drug. Drugs that have undergone biliary secretion may be **reabsorbed** from the intestine to create an **enterohepatic recirculation**. The drug's persistence in the body can be **increased** by this mechanism. Furthermore, in the horse, the commensal cecal bacteria can contribute to this recirculation by hydrolyzing conjugates that have already been excreted via the bile, so allowing the liberated drug to be reabsorbed.

However, the main route for drug and drug metabolite excretion is in the **urine**. Small amounts of some drugs can be lost in expired air and others in external secretions like sweat and saliva, but these routes have limited forensic implications. The elimination of drugs in **hair** is of increasing interest as hair provides a stable environment for both drugs and their metabolites. Recent reports have identified and quantified many drugs in tail and mane hair, in one case (a potentiated sulfonamide) the trimethoprim and sulfonamide being detected three years after dosing.

In renal excretion those drugs that are not bound to plasma proteins are filtered at the glomerulus. Many drugs are weak acids or weak bases, and these may pass into the renal tubules by proximal tubule transport mechanisms. Drugs that are lipid soluble can diffuse across cell membranes from the renal tubules into peritubular capillaries, but such drugs can potentially diffuse also from capillaries into the tubular lumen. The amount of reabsorption of lipid-soluble acidic and basic drugs depends on **urinary pH**, so that the acidification of urine may have a **profound effect** on the rate of drug excretion. A horse that has undergone intense exercise often produces acidic urine, whereas the same horse can produce alkaline urine when out of training.

Other means of altering urinary acidity may also influence drug excretion. However, while urinary drug concentrations may change according to urine pH, the rate of decline of plasma levels is most commonly governed by drug metabolism.

Other biologic factors that create difficulties in predicting **clearance times** (*q.v.*) are the age and sex of the horse, and diurnal and seasonal variations; the use of urinary concentrations of drugs to indicate pharmacologic effects or times of drug administration is fraught with problems. Nevertheless, some good projections have been made (see below). Furthermore, although it is likely that plasma concentrations will be less variable, few drug trials have been conducted with sufficient numbers of horses in order to demonstrate a reliable distribution pattern.

CLEARANCE TIMES

The sources of pharmaceutic and pharmacokinetic variation described above unite to create the considerable uncertainty that surrounds clearance times and half-lives. **Half-life** is the time required for the drug remaining in the body to be reduced by 50% **after equilibrium distribution has been established**.

By knowing a drug's half-life, an estimate of clearance time can be made, for theoretically 99% of the drug will be cleared from the animal's body in seven half-lives.

However, quoting clearance times on the basis of this "99%" value may represent a problem where, through the use of sensitive technologies, detection of the excretion of the remaining 1% is possible. In providing advice to the practicing veterinarian, it may be more appropriate to attempt to establish "**detection times**". However, detection times are also dependent upon the sensitivity of the analytical technique used for their determination and are susceptible to changes in analytical technologies.

For many years within the competition horse industry, forensic laboratories applied **thin layer chromatography (TLC)** as the major screening procedure. This technique is still widely applied in North America but is now supported by the application of **enzyme-linked immunosorbent assays (ELISAs)**.

ELISAs provide a rapid, robust and sensitive approach to detect misuse of the more potent drugs. In forensic laboratories supporting the competition horse industry in Europe, Australia, Hong Kong, other major racing jurisdictions, and also to some extent in North America, there has been a move away from TLC to instrumental drug screening procedures, again supported by ELISAs. These **instrumental drug screening** procedures include gas chromatography (GC), high performance liquid chromatography (HPLC), gas chromatography-mass spectrometry (GC-MS) and liquid chromatography-mass spectrometry (LC-MS). For confirmatory analysis of the drug in the biologic fluid, where identification is required to satisfy legal criteria, mass spectrometric techniques are applied almost exclusively.

Thus, in determining detection periods based upon screening procedures, a wide range of techniques, varying markedly in their sensitivity capabilities, is available to the analytical scientist. Also, detection period data are usually available only for single doses of drugs administered to small numbers of animals. Veterinarians who use detection period data to offer advice on dosing schedules must therefore recognize the limitations of the approach.

The most comprehensive information on the approximate length of time that drugs can be detected in the blood and urine of horses is to be found in the *Race Track Division Schedule of Drugs* issued by Agriculture Canada. The charts produced in this document are the outcome of research into equine drug administrations, and although the analytical methods are not disclosed, they represent valuable guidance for veterinary surgeons involved in treating competition horses.

The Australian Equine Veterinary Association has also produced a booklet, *Detection of Therapeutic Substances in Racing Horses*, which provides detection times for a wide range of drugs based upon the analytical methodologies used in the four Australian racing laboratories. Similar guidelines are produced by the American Association of Equine Practitioners and published as *Guidelines for Drug Detection Times.*

More recently, the European Horserace Scientific Liaison Committee (EHSLC) has produced information on the detection times of a limited number of drugs (*Information for Veterinary Surgeons on Detection Periods of Named Drugs*). These data were generated through a collaboration of various racing laboratories within Europe with the detection times being determined using established

methods for confirmatory analysis for single drug administrations to small numbers of horses. The published detection times represent the longest time the drug was detected by this approach by any of the participating laboratories. For example, the Jockey Club in the United Kingdom has published times for which IM administered corticosteroids produce suppression of urinary cortisol, ranging from 30 h (dexamethasone sodium phosphate, 20 mg dose) to 830 h (triamcinolone acetonide, 30 mg dose). These figures are inevitably subject to inter-animal differences. For triamcinolone acetonide (30 mg) in two Thoroughbreds, times of urinary cortisol suppression were 700 and 830 h (a difference of more than 5 days). The FEI is undertaking similar studies.

For a number of years there has been concern within the competition horse industry regarding the increasing sensitivity of analytical techniques used for drug and medication control. This increasing sensitivity is necessary for the detection of potent illegitimate drugs but also allows more and more prohibited substances to be detected at very low levels. For some therapeutic substances this increase in the **sensitivity of analytical techniques** can allow for the control of **exposure** not associated to any effect. Also there is the realization that most drug infringements are not due to intentional malpractice, but to residues of therapeutic medication or caused by dietary or environmental contaminants. Thus, since the late 1990s, the EHSLC has been driving a major initiative to ensure that the control of substances commonly used for treating racehorses is both fair and effective. Primary factors for consideration in this are the welfare of the horse, the integrity of the horse racing industry and the harmonization of drug testing procedures in Europe.

Central to this initiative is the concept that approaches to controlling such substances should be based upon sound science and a rigorous analysis of pharmacologic and pharmacokinetic properties. To apply these principles, a pharmacokinetic/pharmacodynamic model has been developed by Toutain and Lassourd* to determine the **effective plasma concentration (EPC)** of therapeutic and commonly used drugs in racing. Risk assessment for individual drugs, taking into account their potential threat to the welfare of the horse and the integrity of the industry, then provides for the determination of irrelevant plasma and urinary concentrations (IPC and IUC, respectively). Following discussions at the International Conference of Racing Analysts and Veterinarians, Dubai (2004), it is hoped that this approach will provide the platform for the authorities to provide laboratories with recommended limits of detection for substances commonly used for treating competition horses.

At the outset of this initiative, a working group was formed to consider these various approaches and drive the practical aspects of the initiative. This working group comprised analysts, veterinarians and veterinary pharmacologists representing racing authorities in France, Germany, the UK, Ireland and Italy. It is clear that only through cooperation between the analyst, veterinary pharmacologist, veterinarian and regulatory bodies, and the pooling of expertise and resources on an international basis, can effective solutions be provided to address this challenge.

* Toutain, P.L., Lassourd, V. (2002) Pharmacokinetic/pharmacodynamic approach to assess irrelevant plasma or urine drug concentrations in post competition samples for drug control in the horse, *Equine Veterinary Journal* 34: 242–249.

Chapter 5

The skin

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Chapter contents

INTRODUCTION

Diseases of the skin are commonly encountered in equine practice and frequently present diagnostic and therapeutic problems. Many conditions do not have a pathognomonic clinical presentation, with diseases of different etiology having a similar appearance. A **logical and systematic approach** to the investigation of dermatologic disorders is essential in order to reach a definitive diagnosis and initiate appropriate therapy. Failure to do so results in the use of remedies on an empirical basis, which all too often wastes time, money and the owner's patience, as well as having **welfare implications** for the patient.

A thorough history is required and it may be helpful to use a **customized dermatology questionnaire** to assist in this respect. After completing a general examination and detailed dermatologic examination, appropriate samples should be taken for laboratory examination. In many cases this will include collection of surface debris by brushing or scraping, for identification of ectoparasites or for fungal culture; surface adhesive tape strips are useful for collection of surface ectoparasites and identification of microorganisms by cytologic evaluation. Other samples might include bacterial swabs and skin biopsy.

Skin biopsy is essential to differentiate between the many causes of **papular and nodular lesions**. Multiple biopsies should be taken and the use of disposable biopsy punches facilitates this, with the patient sedated and use of local anesthetic. Larger nodules, masses and ulcerated lesions may require the use of excisional biopsy. Correct choice of biopsy site is important in gaining

the most helpful diagnostic information, and no surgical preparation should be performed, apart from clipping, in order to preserve surface pathology. **Full thickness skin** should be removed, excess blood blotted away and the tissue placed on stiff paper or card to prevent distortion during fixation. A complete history and clinical details must be supplied to enable the pathologist to give an informed interpretation of the pathologic features observed in the tissues examined.

Biopsy should not be viewed as a last resort in the investigation of skin disease and should be performed within 3–4 wk of lesions appearing if a definitive diagnosis has not been made already. Early diagnosis allows early introduction of the most appropriate therapy and accurate prognostication for the owner of the horse.

PARASITIC SKIN DISEASES

MANGE

Sarcoptic mange

Etiology

Sarcoptic mange is a now rare disease of horses, notifiable in the UK and in many other countries, caused by the mite *Sarcoptes scabei*. The disease has been eradicated from the USA and currently is not specifically listed in the US Department of Agriculture list of Reportable Diseases and Conditions, although any confirmed or strongly suspected case should be brought to the attention of State or Federal veterinarians. Current opinion is that the various mites found on different hosts, although phenotypically different and adapted for a particular host, are genotypically identical. **Cross-infestation** among animals and humans is not uncommon.

The female sarcoptic mite lays 40–50 eggs in epidermal burrows tunneled into the skin. These hatch and, after passing through larval and nymphal stages, reach maturity within 2–3 wk.

Infestation is usually transmitted by **direct contact** between animals, but may also be transmitted on **fomites** such as riders' clothing, stable blankets, harness, etc. In temperate regions and under conditions of poor hygiene, mites and eggs may survive away from the host in grease and debris within buildings, vehicles or on tack and grooming equipment for 1–4 wk.

Clinical signs and diagnosis

Initial infestation is asymptomatic, but within 2–4 wk there is evidence of **papule formation** and scaling accompanied by a **very severe pruritus** in sites of infestation, leading to rubbing, biting and the production of self-inflicted skin damage. Lesions spread rapidly, finally involving all areas of the body. The skin becomes increasingly thickened and corrugated with marked hair loss. Rest and feeding patterns are severely disrupted, leading to serious generalized debility, weight loss, weakness and even death.

Infestation is suspected in animals showing the typical history and clinical picture, and particularly when **humans in contact** present with a papular rash

over the exposed areas of the body. Diagnosis may be confirmed by microscopic examination of scale and debris obtained by scraping affected areas, although mites may be difficult to find. Serologic tests for other sarcoptic mange antibody titers in other species may be adaptable for horses.

Treatment and prevention

A **very strict code of hygiene** must be enforced. All infested animals and those suspected of infestation must be isolated; their blankets, harness, grooming material and living accommodation should also be isolated. Animal attendants must change clothing and wash thoroughly before tending other animals.

Ivermectin has been shown to be effective in the treatment of sarcoptic mange. Infested animals may also be treated using lime sulfur, bromociclen, lindane or organophosphorus preparations, where available, used as a dip, spray or wash at 7–10-day intervals on at least three occasions. These preparations may also be used when necessary for treatment of infested buildings, vehicles and equipment after prior cleaning. In advanced cases or when scaling and skin thickening is excessive, it may be necessary to treat over a much longer period of time.

It is essential that infested animals be kept on a high plane of nutrition. Secondary infections such as by *Dermatophilus congolensis* may require concurrent treatment.

In areas where sarcoptic mange is still endemic, all newly acquired horses must be carefully examined and preventive measures taken where deemed necessary.

Psoroptic mange

Etiology

Psoroptic mange mites are **non-burrowing**, living on the skin surface and feeding by puncturing the epidermis, which causes serous exudation, inflammation and scab formation accompanied by irritation. The female mite lays eggs in the surface debris that hatch within 2–3 days and develop to maturity within 11–14 days. Mite activity, and the development of lesions, is greatest during autumn and winter and is probably associated with periods of **higher humidity**. Transmission is by direct or indirect contact.

Several species of psoroptic mite are reported to infest the horse: *Psoroptes equi*, *P. natalensis*, *P. ovis* and *P. cuniculi*. *Psoroptes* mites show little host specificity and appear to be **genetically homogenous** and it is probably best not to assign specific clinical manifestations to any individual species.

Clinical signs and diagnosis

Clinical signs and pruritus associated with infestation vary from asymptomatic to localized ear disease to truncal dermatitis, predominantly involving the **dorsal midline**. Scaling, papules, hair loss and skin thickening are seen, similar to lesions associated with sarcoptic mange, although irritation is usually less severe. Mild cases may present with mane and tail **seborrhea** (*q.v.*). **Psoroptic otoacariasis** may cause severe scaling, irritation and

exudation leading to ear twitching, rubbing, head shaking and a lop-eared appearance.

Diagnosis requires the microscopic examination of material obtained from the **underside of scab specimens** and the surface of underlying skin.

Treatment and control

Ivermectin is very effective in the treatment of psoroptic otoacariasis and dermatitis; two doses of 200 μg/kg PO given 14 days apart are recommended. Treatment of psoroptic otoacariasis may be restricted to the use of topical ectoparasiticides to the head, upper neck and ear canals, but as the mites can survive in the coat for several weeks treatment may have to be prolonged. The owner should be advised to check the **ears** routinely for evidence of recurrence. Attention should be paid to the **cleaning and disinfection** of grooming utensils and harness, which frequently play an important role in transmission of infestation.

Chorioptic mange

Etiology

Chorioptic mange is caused by the surface-living mange mite *Chorioptes equi*, which is a phenotypic variant of *C. bovis.* Mites feed on cutaneous scale and debris without either tunneling or puncturing the epidermis. Their presence may, however, induce **localized inflammation**, irritation and hyperkeratotic changes.

Mite eggs are laid and subsequently develop in **skin debris** with the life cycle being completed within 14 days. Reproductive activity is markedly influenced by microclimatic factors, being greatest under conditions of high humidity. Survival time away from the horse is relatively short, but mites and mite eggs can survive on debris within buildings, bedding and on grooming equipment for several weeks, depending on temperature, humidity and hygiene.

Clinical signs and diagnosis

Chorioptes mites have a predilection to infest the skin of the legs from **below the knee and the hock**. Infestation may also occur on the tail and ventral trunk, and occasionally generalized lesions occur. Draft horses and cobs with feathered limbs are predominantly affected. **Pruritus** is very variable, from intense to absent.

Skin lesions may show a marked **seasonal variation**. Characteristic regionalized scaling lesions accompanied by marked irritation, stamping and rubbing are noted during the autumn/fall, winter and early spring, but apparently resolve spontaneously during the late spring and early summer, with a corresponding reduction in mite numbers, only to recur again the following autumn. The skin becomes **grossly thickened** and may become **secondarily infected** with bacterial or yeast organisms.

Chorioptic mange may be suspected on clinical examination and can be confirmed by microscopic examination of scale and debris obtained from active lesions.

Treatment and control

Selenium sulfide shampoo, systemic **ivermectin** and **fipronil spray** have all been shown to be effective in the treatment of chorioptic mange. Flumethrin is licensed for bovine chorioptic mange.

The legs of heavily feathered animals should be **clipped out** and the legs thoroughly washed and skin debris removed to facilitate topical application. Treatment may need to be repeated over a prolonged period before complete resolution occurs in chronic infestation. **In-contact animals** should be treated, since asymptomatic infection may occur.

Transmission often occurs following contact with infested bedding or grooming equipment and it is essential that contact with infested bedding is eliminated and that all grooming equipment is segregated and routinely sterilized.

Demodectic (follicular) mange

Etiology

Two species, *Demodex caballi* (long-bodied, affecting eyelids and muzzle) and *D. equi* (short-bodied, found on the trunk), have been described in the horse. The mites live and complete their life cycle within the **pilosebaceous apparatus**, only spending a relatively short period on the skin surface at any one time. Many animals carry the mite within their skin without any evidence of skin disease or damage. The factors influencing mite activity and numbers in the horse are poorly understood, but inflammation, debility and immune status may all be of importance. Demodicosis has been reported in association with **chronic glucocorticoid therapy**.

Clinical signs and diagnosis

Demodex mites are a not infrequent finding during routine microscopic examination of skin material. On rare occasions, local massive increases in mite numbers may occur and lead to the production of either:

1. A patchy, non-pruritic, scaling reaction accompanied by hair loss and, on occasions, increased pigmentation. Lesions are most frequently noted over the face, neck and/or shoulders; often these lesions appear to be a sequel to insect bites and many resolve spontaneously in time.
2. Multiple, nodular, follicular cysts, which are non-painful and vary in size from a pinhead to a small pea.

Diagnosis may be confirmed either by finding large numbers of mites on microscopic examination of scale or substantiating the presence of mites in the caseous material obtained from opened follicular cysts or in skin biopsies.

Treatment and control

Scaly lesions may be treated topically with **lime sulfur** in oil, **rotenone** in spirit, or **benzyl benzoate**. Amitraz is contraindicated in horses. Nodular lesions are refractory to all treatments, such lesions persisting for many years and causing little discomfort or serious hair loss.

It is important to investigate and eliminate any factors that may have caused local inflammation, or localized or generalized debility.

FORAGE AND OTHER MITE INFESTATIONS

Etiology

Free-living members of the suborder Astigmata, which occur in livestock bedding and stored foods, are often known as **forage mites**. Certain species, including *Tyrophagus* spp., *Glycyphagus* spp. and *Pyemotes* spp., may produce cutaneous disease by inoculation or deposition of irritant or pharmacologically active substances into the skin or by induction of hypersensitivity reactions.

Many species of larval Trombiculidae (**harvest mites**, red bugs or chiggers) are capable of producing skin lesions and irritation in the horse. These include *Trombicula* (formerly *Eutrombicula*) *alfreddugesi*, *T.* (formerly *Neotrombicula*) *autumnalis*, *T.* (formerly *Eutrombicula*) *splendens*, and *T.* (formerly *Eutrombicula*) *sarcina*. The larvae are active for 4–6 wk in the year in late summer and early autumn/fall. Once they have obtained a meal of lymph and disintegrated skin cells they progress to free-living nymphal and adult stages, and the problem is therefore limited.

Clinical signs and diagnosis

The **cutaneous responses** associated with forage mite infestation in the horse are extremely variable and depend on the particular mite, its mode of infestation and the reactivity of the host. Lesions may present as areas of multiple, pinpoint crusted papules; patchy, irritant scaling; papular urticaria or urticarial plaques. Lesions associated with infestations contracted at pasture most frequently involve the heels, legs, brisket, ventral and lateral chest and abdomen, face and lips.

Harvest mites produce variable numbers of **asymmetrical patches** of small, focal weeping lesions over areas of predilection. In early lesions harvest mite larvae may be recognized by their orange/red appearance. Confirmation of diagnosis in older lesions is difficult as larvae feed and vacate their host within a few days.

Horses at pasture can also pick up other pathogenic forage mites. The lesions they produce may be similar to those of harvest mites or may present as localized irritant scaling, papular urticaria or urticarial plaques.

In stabled and yarded horses the distribution of cutaneous lesions associated with forage mite infestation will vary according to the source of that infestation. Infestations associated with **food troughs** and hay nets frequently only involve the face, neck and brisket, while those associated with **bedding** frequently only involve the lower parts of the body.

Mites such as *Trombicula* and *Pyemotes* species, which produce a mainly irritant response rather than an allergic response, induce skin changes on **all in-contact animals and humans**. Other forage mites, such as some *Tyrophagus* species, only produce changes in individual animals. Lesions due to forage mite infestation must be differentiated from papular urticarial reactions caused by biting insects in temperate summers or throughout the year in subtropical and tropical climates. Similar cutaneous responses may be encountered in association with parasitic mites of birds, fleas and bed bugs in housed animals.

Survival of forage mites on the horse is variable. Many vacate their host after feeding but some species, such as *Pyemotes*, often remain in the coat for a much longer period, particularly if the host has a thick coat or heavily feathered legs. In such cases microscopic examination of **coat brushings** or surface adhesive tape strips may confirm diagnosis. In the majority of cases such an approach is unrewarding and steps must be taken to identify the source of infestation and extract the mites from it for microscopic examination. Identification of forage mites is extremely time consuming. There are over 60 000 known species of mite, of which only a relatively small number have so far been confirmed as being capable of causing skin disease in the horse and other animals.

Treatment and control

Infested animals at pasture should be **moved immediately**, either onto another pasture or into a yard or stable. **Palliative treatment** may be required, either as topical steroid or short-acting systemic steroid. **Fipronil spray** has been demonstrated to be effective against trombiculid mites. In the case of harvest mite infestation, animals may usually be returned to the original pasture after 8 wk but, as infestation is likely to remain from year to year, animals should be **removed from the pasture** at the same time the following years. Populations of other forage mites in vegetation tend to show transitory fluctuations related to growth of herbage and microclimatic factors and it is usually safe to return animals to the original pasture after a break of 2 mo.

Survival and multiplication of forage mites within stored hay, straw and cereals is dependent on the microclimatic conditions within bales, stacks or stores. Many are capable of undergoing **massive increase in numbers** when in store over winter and when humidity and temperature are favorable. Frequently such massive increases in number will be confined to one small group of bales within a stack. Infested material must be removed and replaced by material from a different source. If this is done, then the chance of recurrence of symptoms is low. If the infestation is in the bedding then this may be replaced with shavings or the animals turned out to grass.

PEDICULOSIS

Etiology

Two species of **lice** may infest horses and other Equidae: *Haematopinus asini*, a sucking louse, which feeds on blood obtained by puncturing the skin; and *Damalinia equi*, which survives by feeding on scale and skin debris.

Lice are **host specific** and can only survive for a few days, even under optimal conditions of high humidity and cool temperatures, away from their host. The life cycle is completed on the host. The female louse produces eggs that are firmly cemented onto hair shafts. After hatching, larvae undergo three molts and reach maturity within 3 wk.

Louse activity is subject to **seasonal variation** with numbers being greatest during the autumn/fall, winter and early spring.

Clinical signs and diagnosis

The symptoms and cutaneous changes associated with louse infestation in the horse show marked individual variation unrelated to parasite numbers. Many

animals with a comparatively heavy louse burden present with minimal skin changes and irritation, while other animals with very low levels of infestation present with severe pruritus, patchy alopecia, erythema and excoriation.

Louse infestation is common in the horse and should always be suspected in cases of skin irritation. Isolation of lice can be difficult when numbers are low, as adult lice are relatively small and, being either pale pink or gray, merge easily into the coat. A long and careful search of the coat under strong light is often essential to find the parasite. On some occasions its presence is more easily recognized by the identification of eggs or egg cases firmly attached to hairs on the trunk and neck, or the base of the mane and tail.

Treatment and control

Louse infestation may be treated effectively by the use of either dusting powders or washes containing **pyrethrins or synthetic pyrethroids**. Selenium sulfide shampoo and other insecticidal shampoos may also be effective. All dressings should be applied at 7–10-day intervals on **at least three** occasions. **Fipronil spray** has also been shown to be curative. Systemic ivermectin is likely to be effective against sucking, although not necessarily the chewing, lice. Particular attention should be paid to **stable hygiene** as infestation can be transmitted on blankets, rugs and grooming equipment. All animals should be routinely checked for the presence of lice and any infested or potential carrier animal treated accordingly.

FLY-RELATED DERMATOSES

Fly bites and fly worry

Lesions resulting from the bites of tabanids (*Tabanus*, *Haematopota* and *Chrysops* spp.), stable flies (*Stomoxys calcitrans*), and black flies (*Simulium* spp.) are **crusted papules**, which fade within a few days. Mosquito bites result in papules without crusts and also fade in a few hours to days. Considerable "worry" can result from large numbers of biting insects, and large swarms of black flies can kill cattle and horses.

Hypersensitivity reactions to these insects have been postulated but not demonstrated. Face flies (*Musca autumnalis*), head flies (*Hydrotaea irritans*), and house flies (*Musca domestica*) do not bite but feed on moist secretions in wounds or near mucocutaneous junctions.

Diagnosis of the problem is by **fly identification**. Fly bites should be distinguished from other types of cutaneous nodules such as early dermatophytosis, urticaria, equine eosinophilic (collagenolytic) granuloma and sarcoids (*q.v.*).

Treatment and prevention

Most bites, unless very numerous, do not require treatment, but significant "**fly worry**" should be alleviated. Successful control of the insects involves treatment or elimination of the **breeding grounds** for the insect involved. This is not always possible due to environmental considerations.

Control of stable flies and house flies requires regular removal of manure so that the larvae have nowhere to develop. Regular treatment of the affected

animals with insecticidal agents and repellents, particularly pyrethrins and pyrethroids, and stabling during the feeding times of those insects may be useful.

Myiasis

Etiology

Primary myiasis due to **screwworm infestation** of healthy tissue of wounds, dermatitis lesions, ulcerated neoplasms or granulomas, and mucocutaneous junctions occurs in the Americas (Central and South primarily), Africa and Asia. The genera *Cochliomyia* and *Chrysomyia* are involved. The adult fly deposits eggs in the moist areas. When the larvae hatch, they burrow into the healthy subcutaneous tissue causing liquefaction and enlargement of the lesion. They drop out in 3–6 days to pupate.

Secondary myiasis (blowfly strike) is not common in horses but may occur. The genera involved are *Lucilia*, *Calliphora*, *Phormia*, and *Cordylobia*. These flies lay their eggs in decomposing tissue of wounds and macerated skin lesions as well as in carcasses. Larvae feed on the decomposing matter and secrete enzymes, causing wound enlargement.

Clinical signs and diagnosis

Lesions are similar in primary and secondary myiasis. They are **painful and odoriferous** with exudation. The animal may become septicemic and die.

Diagnosis is by **larval identification**. Larvae should be preserved in 70% alcohol for shipment to a laboratory. It is necessary to differentiate cases occurring in simple wounds from those cases where tumors or granulomas are secondarily invaded.

Treatment and prevention

Treatment includes debridement and cleansing of lesions, use of topical insecticides, systemic antibiotics for septicemic states, and other symptomatic therapy. The avoidance of surgical procedures during the fly season and prompt wound care with bandaging and application of topical insecticides will prevent myiasis.

Hypodermiasis (warbles)

Etiology

Warbles are caused by heel flies, the larval stages of *Hypoderma bovis* and *H. lineatum*, in many countries in the Northern hemisphere, and sometimes *H. silenus* in parts of Europe and Asia. These are primary parasites of ruminants and horses are only sporadically affected.

Warble flies are similar in appearance to bumblebees and fasten their eggs to hairs on the legs and ventrum. After a few days, the larvae hatch and burrow through the skin, migrating through the body via the connective tissues. *H. lineatum* migrates through the submucosa of the esophagus and *H. bovis* migrates in the epidural fat of the spinal canal. Eventually, the larvae migrate to the subcutaneous tissues of the dorsal back where they become

encysted and form breathing pores. After about 2 mo and two molts, they emerge through the hole and fall to the ground to pupate. Warbles do not usually develop properly in the horse, failing to complete their life cycle. Horses kept near cattle are at the greatest risk of developing these cysts.

Clinical signs and diagnosis

Cattle can have large numbers of nodules while the horse, an aberrant host, seldom has more than one or two nodules, usually located on the dorsal back or withers. Lesions of hypodermiasis are easily distinguished from other nodules (dermoid cysts, eosinophilic granulomas, neoplasms) by the presence of the breathing pore. Identification of the larva removed from the cyst is confirmatory.

Treatment and prevention

The best treatment for horses is **careful surgical removal** of the intact larva. Care must be taken to avoid crushing the larva during surgery because leakage of its internal contents can cause an anaphylactic reaction in the horse.

Control of the warble in the primary or other hosts is important. Ivermectin is an effective larvicide for the control of warbles in cattle and its use in horses for regular intestinal parasite control probably prevents many cases from developing. Prior to the availability of ivermectin, organophosphate insecticides were used to control cattle warbles.

HELMINTH-ASSOCIATED DERMATOSES

Habronemiasis

Etiology

A **hypersensitivity reaction** to the migrating nematode larvae of the equine stomach worms *Habronema majus*, *H. muscae* and *Draschia megastoma* is believed to be the cause of habronemiasis, also called "**summer sores**", seen in North America, Australia, Africa and northern Asia.

Both the stable fly and house fly deposit their own larvae in manure. The larvae then ingest the early stomach worm larvae and in this way serve as intermediate hosts in the life cycle. The adult flies deposit stomach worm larvae wherever they feed, such as in mucocutaneous junctions, in wounds, and other moist areas. Larvae that are ingested by the horse when deposited on or near the mouth and lips complete the life cycle in becoming adults in the stomach. Larvae are able to penetrate damaged or chronically moistened skin to reach the dermal and subcutaneous tissues where they eventually die.

Clinical signs and diagnosis

Few horses with stomach worms will develop the characteristic ulcerative and proliferative, seasonal lesions that may be responsive to glucocorticoid treatment alone. The problem tends to recur in the same animals year after year. The classic lesions are poorly healing wounds, which develop a granulomatous appearance and discharge a small amount of exudate. Lesions also develop around mucocutaneous junctions. Some are crater-like ulcers with

raised margins and can become quite large and extensive. Small hard granules resulting from calcification of larvae are frequently present.

Lesions of **cutaneous habronemiasis** should be distinguished from other bacterial and fungal granulomas, exuberant granulation tissue, and neoplasms (*q.v.*).

Histopathologic examination of **biopsies** is diagnostic, revealing nodular to diffuse eosinophilic dermatitis with mast cells and foci of coagulation necrosis surrounded by palisading granuloma formation. Larvae are found within the necrotic foci in some sections. Rarely, larvae may be identified on microscopic examination of scrapings from the lesions.

Treatment and prevention

Ivermectin, organophosphates and/or glucocorticoids are the most commonly used systemic treatments. One to three treatments with **ivermectin** (200 μg/kg) at 10-day intervals is usually curative but reinfection may occur if control of flies and stomach worms is not instituted. Systemic organophosphate treatment has variable success and is not without risks. **Glucocorticoids** as the sole therapeutic agent are very successful, lending credence to the hypersensitivity theory. Prednisolone or prednisone at 1 mg/kg orally for 7–14 days is recommended. Adjunctive therapy such as surgical reduction of the lesion, good wound care, and use of topical, glucocorticoid-containing ointments may be employed, as the case requires. Ocular inflammation due to habronemiasis should be controlled prior to antiparasitic treatment.

Regular deworming with **ivermectin** eliminates the adult *H. muscae* from the stomach. Stringent sanitation practices prevent flies from breeding in infected manure and carrying the larvae to susceptible horses. Additionally, good wound care and topical fly control is of particular importance for susceptible horses.

Onchocerciasis

Etiology

Cutaneous onchocerciasis in the horse is thought to be caused by a hypersensitivity reaction to the **microfilariae** of *Onchocerca cervicalis* in the dermis. It occurs in many countries of the world. The adult filariid resides in **fibrous nodules** within the **ligamentum nuchae** and produces microfilariae that migrate via the connective tissues to the dermis, especially of the ventrum, neck and face, as well as ocular tissues. Microfilariae in the dermis are ingested by feeding *Culicoides* spp., which serve as intermediate hosts for *Onchocerca cervicalis*.

Clinical signs and diagnosis

Cutaneous onchocerciasis is a **non-seasonal**, variably- to non-pruritic affliction of mature horses. It is characterized by patches of alopecia, scaling, crusting, erythema, ulceration, exudation, and leukoderma on the face, neck, chest and ventrum. Ocular lesions may also be present, including leukoderma of the temporal bulbar conjunctiva.

The major differential diagnosis for cutaneous onchocerciasis includes *Culicoides* hypersensitivity (*q.v.*) and horn fly dermatitis (*q.v.*). Other diseases

to consider include dermatophytosis, pemphigus foliaceus, eosinophilic dermatosis (*q.v.*) and other systemic infectious or immune-mediated dermatoses (*q.v.*).

Diagnosis is based on typical clinical signs, cutaneous biopsy samples revealing dermal inflammatory infiltrates surrounding microfilariae, and a favorable response to treatment with ivermectin. Since many horses carry the *O. cervicalis* microfilaria in the dermis, the presence of microfilariae without the surrounding dermal inflammatory infiltrates is not diagnostic.

Treatment and prevention

The treatment of choice is **ivermectin** at 200 μg/kg PO to kill the microfilariae. If not simultaneously treated with anti-inflammatory doses of **glucocorticoids**, some of these horses will experience exacerbation of clinical signs resulting in ventral edema and increased inflammation during the first few days post administration. The hypersensitivity reaction is especially strong against dead and dying microfilariae and such exacerbations are more common and more severe when levamisole is used as a microfilaricide. Neurologic side effects are also seen with levamisole use. Improvement after ivermectin treatment takes 2–8 wk and is maximal if biting flies are well controlled.

Since ivermectin does not kill the adult worm in the ligamentum nuchae, treatment usually has to be **repeated** at regular intervals (2–12 mo) to prevent recurrence of clinical signs. Residual alopecia, leukoderma and scarring are likely to occur in severely affected regions. Ocular inflammation due to onchocerciasis should be controlled before treatment and monitored for several days afterwards. Regular use of ivermectin for parasite control may prevent this disease.

Parafilariasis

Etiology

Parafilariasis is caused by *Parafilaria multipapillosa*; adult worms live, coiled within nodules, in the subcutis and connective tissues. The nodules discharge a **hemorrhagic exudate** containing eggs and larvae, which are picked up by various flies, acting as vectors or intermediate hosts.

Clinical signs and diagnosis

The condition has been reported in Eastern Europe and the UK and is characterized by non-pruritic, non-painful nodules affecting the neck, shoulders and trunk in the spring and summer. The lesions become hemorrhagic, crust and heal, with spontaneous regression in the autumn and winter.

Larvae (approximately 0.2 mm long) and embryonated eggs are found in smears of exudate, together with large numbers of eosinophils.

Treatment and prevention

Although the condition resolves, many cases show seasonal recurrence for several years. **Avermectins**, which are effective against bovine parafilariasis, should be effective in horses.

Oxyuriasis

Etiology

The pinworm *Oxyuris equi* (*q.v.*) is a common parasite of the **large bowel** of horses. The female worm lays her eggs on the perineal skin around the anus of infested horses. Eggs fall to the ground and infection occurs by ingestion. The ovipositing behavior of the females, and possibly the substance that cements the eggs to the skin, may cause varying degrees of irritation and pruritus to the host.

Clinical signs and diagnosis

Most infected horses show no clinical signs, but horses experiencing irritation rub at the tail base, causing damage to hairs, hair loss and excoriation. They may also be restless and irritable.

Diagnosis is by identification of characteristic operculate eggs, collected from the perineum by application of clear adhesive tape.

Treatment and prevention

Routine worming is indicated.

Strongyloidosis

The small intestinal parasite *Strongyloides westeri* (*q.v.*) is acquired by ingestion or percutaneous penetration of larvae. Cutaneous larva migrans is characterized by varying degrees of dermatitis, involving eosinophilic infiltration and necrotic tracts. The damage caused by the larvae may predispose to ulcerative lymphangitis.

Pelodera dermatitis

Etiology

Larval stages of the free-living nematode *Pelodera strongyloides* can invade the skin of domestic animals kept in moist, dirty, unhygienic environments.

Clinical signs and diagnosis

Lesions consisting of papules, pustules, ulcers, crusts, alopecia, scale and erythema may occur on contact areas, usually with moderate pruritus.

Larvae approximately 600 μm long can be identified in deep skin scrapings, and adult and larval nematodes may also be found in bedding and soil. Biopsies reveal numerous eosinophils, folliculitis, furunculosis and nematode segments within follicles and dermal pyogranulomas.

Treatment and prevention

The lesions are self-limiting once exposure to the contaminated environment is prevented, although topical insecticides may hasten resolution. Contaminated bedding should be removed and destroyed. Symptomatic treatment with medicated shampoos to remove crusts and debris may be helpful; treatment of secondary infection may be indicated and glucocorticoids may be required if pruritus is severe.

PROTOZOAL SKIN DISEASES

BESNOITIOSIS

Etiology

Besnoitiosis is an extremely rare dermatosis of Equidae that is caused by protozoans in the genus *Besnoitia*. It is found primarily in southwestern Europe and Africa, but has been diagnosed in burros in the USA. The major carrier of this parasite is not known, but it may be transmitted orally by fecal contamination of feedstuffs, by biting insects or by injection of contaminated blood.

Clinical signs and diagnosis

Early lesions consist of papules, tufted in haired areas, raised in glabrous areas. Focal leukoderma may be present. In severe cases the condition is characterized by alopecia, thickening, scaling and lichenification. The skin of the limbs, ventrum, perineum and genital regions may be affected and nodules may be found in the nasopharyngeal regions, eyelids and sclera.

More common causes of nodular and seborrheic skin conditions should be considered before making a diagnosis of besnoitiosis. Diagnosis is made by identification of parasitic cysts containing bradyzoites within skin biopsy specimens.

Treatment and prevention

There is no specific treatment for besnoitiosis. Bathing with medicated shampoos and antibiotics for cases with secondary infection may be beneficial. Oral potentiated sulfonamides were reported to be effective in a miniature donkey.

BACTERIAL SKIN DISEASES

Equine skin is **highly resistant** to invasion by bacteria. When bacterial skin infection does become established, host defenses are commonly impaired. Pyoderma may be superficial or deep depending on the level of skin affected.

SUPERFICIAL PYODERMAS

Superficial pyodermas are bacterial infections that involve the epidermis and extend into intact hair follicles. They frequently coexist with deep pyodermas and include staphylococcal folliculitis (*q.v.*) and dermatophilosis (*q.v.*).

Dermatophilosis

Etiology

Dermatophilus congolensis, a Gram-positive, non-acid-fast, filamentous, microaerophilic actinomycete, is the causative agent. The disease occurs worldwide, but is especially prevalent in tropical countries. In temperate areas the condition is commonly seen during or following periods of **prolonged rainfall**. Certain predisposing factors, for example moisture and cutaneous trauma,

are necessary for infection to become established. The infective agents are zoospores that are highly resistant to desiccation and may remain dormant in crusts for many months until adequate wetting enables reactivation. The organism is **transmissible by insects** for up to 24 h after contact with infected lesions.

Clinical signs and diagnosis

Clinical signs are extremely variable, but lesions are frequently found in one of two sites: dorsal midline and flanks; or distal limbs, especially fetlocks. The muzzle and eyes may also be affected. Non-pigmented areas are particularly susceptible. In Hong Kong, a generalized form of the disease has been reported in horses washed after racing.

The primary lesion is a **follicular papule** but, as this is felt more easily than seen, it may often be missed. Lesions may vary according to the age and general condition of the horse, the environment in which it is kept and the length of hair coat. Lesions are often highly exudative resulting in crust formation. In horses with a long winter coat, groups of hairs may matt together producing the so-called "**paint-brush**" **effect**. In short-haired horses, lesions are smaller and occur as multifocal papules covered with crusts or scale. Maceration in moist areas of the body may lead to loss of crust and the characteristic appearance may be absent in these regions. Animals are rarely pruritic but may show pronounced discomfort or pain that may render them unable or reluctant to work. Severely affected horses may show depression, lethargy, weight loss, fever and lymphadenopathy.

Dermatophilosis is an important differential diagnosis of grease heel, a condition of the fetlock causing erythema, exudation, alopecia and crust formation (*q.v.*). Differential diagnosis also includes dermatophytosis, staphylococcal folliculitis and pemphigus foliaceus (*q.v.*). Definitive diagnosis is based on history and clinical examination supported by the results of laboratory techniques. **Impression smears** taken from the undersurface of crusts or from the underlying skin surface may be stained with Gram or Giemsa and examined microscopically to show the characteristic branching hyphae made up of packets of coccoid cells. A portion of crust emulsified in saline or sterile water may release the motile zoospores, which can then be seen under high magnification (×250). Culture, skin biopsy and immunofluorescence techniques may also be employed. The organism requires microaerophilic conditions for laboratory culture and is easily overgrown by secondary invaders and contaminants; it can be difficult to isolate in chronic cases.

Treatment and prevention

If predisposing factors are eliminated, the infection will resolve spontaneously in many cases. The horse should be kept out of the rain and away from wet or muddy pastures. Clipping may be required, and **topical antibacterial agents** such as chlorhexidine, chloroxylenol, iodophors, lime sulfur (2–5%) or potash alum (1%) are recommended. As the crusts loosen, they should be removed and carefully disposed of, either by incineration or by immersing in a suitable disinfectant (e.g. 5% sodium hypochlorite or any of the above products) prior to removal from the premises. Systemic antibiotics are not normally necessary;

when they are indicated, potentiated sulfonamides and penicillins are frequently used and should be continued until lesions have resolved. No long-term immunity is acquired to this disease, and if crust removal is incomplete, the possibility of recurrence is quite high if environmental conditions are suitable.

Pastern folliculitis

Etiology

Coagulase-positive staphylococci are frequently isolated, *Staphylococcus aureus* or *S. hyicus* being commonly implicated. Streptococcal organisms may also be isolated.

Clinical signs and diagnosis

Pastern folliculitis is an **exudative dermatosis** affecting one or more limbs, principally around the caudal aspect of the pastern and fetlock regions. Erythema may accompany papules and pustules, which, if left untreated, may coalesce to form large areas of ulceration, suppuration and crusting. Systemic signs are usually absent.

Differential diagnosis includes chorioptic mange, dermatophytosis, dermatophilosis, horsepox, photosensitization and contact dermatitis (*q.v.*). Pustule contents may be used for smears and for bacterial culture and sensitivity. Skin biopsies for histopathology and for bacterial culture are often required.

Treatment and prevention

Affected areas should be clipped and washed daily with a **topical antibacterial** preparation. Sedation or even general anesthesia may be required. Topical antibacterial preparations containing **mupirocin** or **fusidic acid/sodium fusidate** may be useful. Systemic antibiotics are rarely indicated but may be required in severe or deep infections. Potentiated sulfonamides are commonly used, but resistant organisms may require treatment with drugs such as penicillin, cephalosporins, enrofloxacin, erythromycin and gentamicin. Antibiotic therapy should be continued for 7–10 days beyond resolution of infection and is typically required for 3 wk for superficial pyoderma. Minimizing exposure to moisture and irritant substances should help prevent this condition.

Truncal folliculitis

Etiology

Coagulase-positive staphylococci.

Clinical signs and diagnosis

Folliculitis is common in the horse. There is no age, breed or sex predilection, but most cases occur in spring or early summer when warmer environmental temperatures coincide with shedding, heavy riding and heavy work schedules.

Any part of the horse is susceptible, but the **saddle and girth** areas are most commonly affected. Poorly fitting tack and inadequate grooming are

predisposing factors. Initially, erect hairs may be seen over a follicular papule or pustule that may regress spontaneously or enlarge to form a crusty, exudative lesion. Lesions are rarely pruritic, but may be painful and render the horse unfit for work. The duration of the disease is commonly between 2 and 8 wk. The healing stage is characterized by progressive flattening of the lesion and a gradually expanding area of alopecia and scaling. Recurrence is common in some horses.

The differential diagnosis of folliculitis includes dermatophytosis, dermatophilosis, demodicosis and pemphigus foliaceus (*q.v.*). Samples of pus or exudate from intact pustules or nodules can be used for making impression smears and stained with Gram or Giemsa for light microscopic examination. Whenever possible, **bacterial culture** should be taken from intact pustules or nodules. Cultures taken from ulcerated lesions or exudative surfaces may yield misleading information. Skin biopsies for histopathology and bacterial culture are useful in deriving a definitive diagnosis.

Treatment and prevention

Mild cases may resolve spontaneously, particularly if the horse is rested or if predisposing factors are corrected. Daily washing with **topical antibacterial** agents such as chlorhexidine and iodophors is usually beneficial. In severe cases, systemic therapy may be needed. Selection of an appropriate antibiotic should be based on sensitivity testing, but in the horse procaine benzylpenicillin (22 000 IU/kg b.i.d. IM) given over 7–10 days is often effective.

Proper hygiene and management should avoid infection. In horses with recurrent infections, **antimicrobial shampoos** before and after work have been reported to be of benefit.

DEEP PYODERMAS

Deep pyodermas are serious bacterial infections that involve tissues deeper than the epidermis and hair follicle. Sinus tracts may appear at the skin surface allowing discharge of pus or serum. Treatment is often difficult and prolonged.

Furunculosis

Furunculosis refers to an inflammatory reaction that breaks through the hair follicle into the surrounding dermis. Folliculitis and furunculosis frequently coexist and may reflect different stages of the same inflammatory disease.

Etiology

Usually staphylococci; occasionally streptococci or *Actinomyces pyogenes*.

Clinical signs and diagnosis

Lesions may occur anywhere, but are most common in the **saddle area**. They consist of papules and pustules, which become exudative and crusted and sometimes coalesce to form large edematous nodules and plaques. Clinical examination alone may be insufficient to distinguish folliculitis from furunculosis. The condition is frequently painful and renders the horse unfit for work.

Differential diagnosis includes dermatophytosis, dermatophilosis, demodicosis and pemphigus foliaceus (*q.v.*). Definitive diagnosis requires microscopic examination of smears, fungal culture, skin scrapings and skin biopsies for histopathology and bacterial culture.

Treatment and prevention

Because weeks or months of antibacterial therapy may be required, in vitro sensitivity testing is recommended.

Cellulitis

Cellulitis literally means inflammation of the cells. It is a severe, deep, spreading suppurative infection involving the subcutaneous tissues of the skin. Lesions are poorly defined and affected horses are often febrile and distressed. Anaerobic bacteria may be involved and treatment with systemic antibiotics may need to be prolonged. The prognosis is guarded. See also vasculitis (*q.v.*).

Abscesses

Etiology

Frequently *Streptococcus equi, Corynebacterium pseudotuberculosis, Clostridium* spp. and staphylococci, also *Rhodococcus equi*.

Clinical signs and diagnosis

Abscesses are circumscribed, subcutaneous accumulations of pus, which may arise through bacterial contamination of skin wounds resulting from surgery, foreign bodies, ectoparasites or other forms of trauma.

Treatment and prevention

Surgical drainage and debridement, flushing or packing with topical antimicrobial agents. Systemic antibiotics based on sensitivity testing may be necessary but should not be given before the abscess matures or points. See also strangles (*q.v.*).

Ulcerative lymphangitis

Etiology

Usually *Corynebacterium pseudotuberculosis* (*q.v.*); other organisms including staphylococci, streptococci, *Rhodococcus equi, Pasteurella haemolytica, Fusobacterium necrophorum* and *Pseudomonas aeruginosa* are less frequently isolated. Mixed infections occur and the disease may arise from wound contamination when hygiene and management are poor. Transmission by direct contact or by insect vectors is possible.

Clinical signs and diagnosis

Painful, discharging nodules, unilateral or bilateral, may develop, usually on the distal hindlimbs. Horses are frequently **febrile** and the regional lymphatics may show enlargement, hardening and ulceration leading to lameness and

debility. An improvement may be seen after several weeks but new lesions continue to appear for months or even years. In rare cases, the condition may be fatal.

Differential diagnosis includes glanders, sporotrichosis, equine histoplasmosis, actinomycosis, nocardiosis and mycobacterial infections (*q.v.*). Definitive diagnosis is based on history, clinical signs, smears and skin biopsies for culture and histopathology.

Treatment and prevention

In early cases, surgical drainage, hydrotherapy, exercise and high doses of procaine benzylpenicillin (20 000–80 000 IU/kg b.i.d. IM) over a prolonged period may be adequate. In the later stages, the prognosis is always guarded. Autogenous bacterins have been used to treat this disease but they are of doubtful efficacy. Prevention is best achieved by good hygiene and management including early wound treatment and effective insect control.

Fistulous withers

Fistulous withers (*q.v.*) is an inflammatory condition of the **supraspinous bursa** and associated tissue.

Etiology

The etiology is uncertain and may be multifactorial, including *Brucella abortus* and other bacteria (*q.v.*) such as *Streptococcus zooepidemicus* and *Actinomyces bovis*, *Onchocerca cervicalis* and foreign bodies.

Clinical signs and diagnosis

A painful swelling around the withers may be closed (non-fistulated) or open (fistulated). Systemic illness and inflammation at other sites may be present. Radiography may reveal osteomyelitis, periostitis or fractured dorsal spines of thoracic vertebrae (*q.v.*) as well as calcification resulting from dead *Onchocerca cervicalis* worms. Contrast media can be used to determine the extent and direction of tracts in open lesions. Ultrasonography may help to show the extent of tissue damage.

Blood samples should be taken for routine hematology, biochemistry and serology. Neutrophilia and increased fibrinogen may be found. Serology may show a positive titer for *B. abortus*. In closed cases, tissue aspirates are useful for microbiologic culture and cytology, and deep tissue biopsies are indicated for culture and histopathologic examination.

Treatment and prevention

The mode of treatment depends on whether the lesion is open or closed. Closed lesions require treating with an appropriate antibiotic such as a potentiated sulfonamide (15–30 mg/kg b.i.d. PO) for a minimum of 3 wk. The use of non-steroidal anti-inflammatory drugs such as phenylbutazone and flunixin meglumine may be beneficial in reducing inflammation. Running water from a hose over the withers area twice a day or applying heat packs or ice packs

(20 min b.i.d.) will often help to reduce the inflammation. Open lesions may be washed with 0.5–1% povidone-iodine or 0.5% chlorhexidine solutions and also require long-term antibiotic therapy. Topical application of 10% clofazimine has also been used successfully in cases that were negative for *B. abortus*.

Cases that fail to respond to medical therapy may require **surgical excision** and drainage. Debridement of all affected tissues, dissection along drainage tracts and curettage of diseased dorsal spinous processes, or even subtotal osteotomy, are indicated. The surgery required is **radical and aggressive** and prolonged nursing care is needed. Repeat surgery is often required due to a high recurrence rate.

Complete rest from tacking up is essential. The prognosis is poor. The risk to humans from horses infected with *B. abortus* is believed to be small, but brucellosis in horses is covered by the Zoonosis Order of 1989 as a reportable disease in the UK, and is also notifiable in the USA.

Poll evil

Poll evil (*q.v.*) involves inflammation of a bursa between the nuchal ligament and the atlas or axis vertebrae leading to a **discharging lesion** in the poll area.

Etiology

Possible wound contamination by *Brucella* or *Actinomyces bovis*.

Treatment and prevention

Surgical drainage and antibiotics. See fistulous withers (*q.v.*).

ATYPICAL PYODERMAS

Bacterial granuloma (botryomycosis, bacterial pseudomycetoma)

Etiology

Coagulase-positive staphylococci are most commonly isolated. Mixed infections are possible. *Actinobacillus equuli* has also been isolated.

Clinical signs and diagnosis

Bacterial granuloma is frequently associated with wound contamination of **limbs or scrotum**. Lesions are non-pruritic, firm, poorly circumscribed, nodular growths often with draining tracts and ulceration. White or yellowish granules may be present in the purulent discharge.

Differential diagnosis includes other bacterial and fungal granulomas, habronemiasis, exuberant granulation tissue and neoplasia. Definitive diagnosis is based on history, clinical examination, skin biopsy and culture. Microscopic examination of Gram-stained tissue granules may reveal bacteria.

Treatment and prevention

Treatment consists of complete surgical excision and a prolonged course of systemic antibiotics based on in vitro sensitivity testing. Antibiotic therapy alone may be unrewarding due to inadequate penetration within the granuloma.

Actinomycosis

Etiology

Rare granulomas caused by *Nocardia* or *Actinomyces* spp., which may act as wound contaminants. Sometimes seen in **immunocompromised horses**, such as some Arab foals or horses with hyperadrenocorticism (*q.v.*).

Clinical signs and diagnosis

Lesions are variable and include abscesses, ulcers and draining tracts. The face and mammary glands are commonly affected. Diagnosis is confirmed by cytologic examination (sulfur granules), bacterial culture and biopsies for histopathology and special stains. Granules from lesions of actinomycosis should be cultured anaerobically.

Treatment and prevention

Surgical drainage and parenteral penicillin and streptomycin have been reported to be curative. Another reported case resolved after treatment with isoniazid (8 mg/kg PO daily), potentiated sulfonamides (30 mg/kg PO daily) and sodium iodide (66 ng/kg IV every 1–2 wk) for 12 wk.

Actinobacillosis

Etiology

Actinobacillosis (*q.v.*) is a rare, localized, granulomatous or suppurative condition of horses caused by *Actinobacillus lignieresii*. Prior damage to skin is necessary for infection to become established.

Clinical signs and diagnosis

Actinobacillus has been isolated from an **enlarged tongue** of a horse. Differential diagnosis includes other bacterial and fungal granulomatous diseases. Definitive diagnosis requires direct smears, culture and biopsy. Sulfur granules may be squashed on a glass slide and stained to show Gram-negative coccobacilli.

Treatment and prevention

Potentiated sulfonamide and oral iodide for 4 wk was successful in treating one case, and potentiated sulfonamide with rifampicin in another. In cattle, surgical excision and parenteral iodides are often successful.

Glanders

Etiology

Burkholderia mallei, a Gram-negative, facultative aerobic rod. Glanders (*q.v.*) is now rare or non-existent in many parts of the world although it does occur in Eastern Europe, India and parts of the Middle East.

Clinical signs and diagnosis
Acute and chronic forms occur with **nodules or ulcers** forming in the respiratory tract and skin. Distal limbs, including regional lymphatics, are often involved. Gram staining should demonstrate the organism.

Treatment and prevention
Euthanasia must be considered, as this can be a fatal zoonosis. The disease is notifiable in the EU and in the USA.

Cutaneous tuberculosis

Etiology
Mycobacterium avium, M. intracellulare.

Clinical signs and diagnosis
Hard, painful lumps with draining tracts on the abdomen and medial thighs.

Treatment and prevention
Treatment is rarely attempted due to the poor prognosis and public health risk associated with this disease. Strict hygiene procedures should be followed when handling horses suspected of having this condition.

Atypical mycobacterial infections

Etiology
Mycobacterium fortuitum, *M. chelonei*, *M. phlei*, *M. xenopi*, *M. smegmatis* are soil and water inhabitants that may act as wound contaminants.

Clinical signs and diagnosis
Painless nodules, sometimes ulcerated, may be seen typically on the legs. Diagnosis requires cytologic examination, culture and histopathology involving Ziehl–Neelsen staining to demonstrate the acid-fast organism.

Treatment and prevention
Surgical resection.

VIRAL SKIN DISEASES

PAPILLOMATOSIS

Etiology
Papillomatosis is caused by a DNA papovavirus; infection is by direct and indirect contact and requires **damaged skin**.

Clinical signs and diagnosis
Foals and yearlings are most commonly affected. There is no breed or sex predilection. Papillomas are usually found on the muzzle around the lips,

nostrils and eyes, but can also appear on the external genitalia or on the distal limbs. Lesions are often multiple and consist of raised, verrucose proliferations of epidermis. Spontaneous remission usually ensues within 6 mo and immunity is lifelong.

Diagnosis is based on history and clinical signs. Biopsy is not usually necessary. The main differential diagnosis is sarcoid (*q.v.*), which should always be considered when lesions do not resolve or when the age or site is atypical.

Treatment and prevention

Therapy is unnecessary owing to the self-limiting nature of the disease. Cryosurgery and topical agents such as podophyllin and dimethyl sulfoxide (DMSO) have been reported to be successful. There is no evidence that the administration of an autogenous wart vaccine is of any benefit in horses. Ensuring optimum hygiene and keeping down the density of foals and yearlings kept together may help prevent this condition.

AURAL PLAQUE (SQUAMOUS PAPILLOMA)

Etiology

A DNA papovavirus.

Clinical signs and diagnosis

Squamous papillomas principally affect the **inner surface of the pinna** and may be unilateral or bilateral. Other sites occasionally affected include the anus and the vulva. There is no age, breed or sex predisposition and the plaques do not resolve. Lesions start as small, smooth depigmented papules and progress to form larger, coalescing hyperkeratotic plaques. Pain and pruritus are not generally associated with this condition. There is no known treatment.

COITAL EXANTHEMA

Etiology

Equine herpesvirus 3 (*q.v.*). Coitus, insect vectors and fomites spread the disease.

Clinical signs and diagnosis

Affected areas include the penis and prepuce of males and the vulva and perineum of mares. The lips, mouth and nostrils may also be involved. The condition is characterized by papules, pustules and vesicles, which may crust over and ulcerate. Lesions may be painful although pruritus is not usually a feature. Normally there is complete healing within 14 days although focal areas of depigmentation may be a permanent sequel. Recurrence is common.

Differential diagnosis includes squamous cell carcinoma, bullous pemphigoid, horsepox and other genital infections (*q.v.*). Diagnosis is based on history, clinical examination, biopsy and virus isolation, preferably from vesicle contents.

Treatment and prevention

Rest from coitus for 4 wk. Topical creams or ointments may be beneficial. Mating with infected animals should be avoided.

HORSEPOX

Etiology

An unclassified poxvirus antigenically related to cowpox virus.

Clinical signs and diagnosis

Three clinical expressions have been described:

1. Oral lesions
2. Pastern and fetlock lesions
3. Vulval lesions.

Vesicles, umbilicated pustules and crusts are found on skin and mucosal surfaces. Mild pyrexia may be a feature. Lameness may accompany limb involvement.

Biopsy reveals ballooning degeneration of epidermal cells, intraepidermal microvesicles and intracytoplasmic inclusion bodies. A perivascular dermal inflammatory infiltrate is present with neutrophil invasion of the epidermis. Demonstration of poxvirus (*q.v.*) by electron microscopy and virus isolation confirm the diagnosis.

Treatment and prevention

Spontaneous recovery occurs within a few weeks. Infection confers long-term immunity.

VIRAL PAPULAR DERMATITIS

Etiology

An unclassified poxvirus, resembling cowpox and vaccinia viruses.

Clinical signs and diagnosis

Small asymptomatic papules progress to form crusty lesions within 7 days and an annular alopecia after about 14 days. Spontaneous remission usually occurs within 4–6 wk.

The differential diagnosis includes folliculitis, dermatophilosis, demodicosis and dermatophytosis. Definitive diagnosis requires viral culture. There is no specific treatment.

EQUINE MOLLUSCUM CONTAGIOSUM

Etiology

A molluscipox virus, with close DNA sequence homology to human molluscum contagiosum. Contagion between horses does not appear to occur and cases may represent an anthropozoonosis, with horses acquiring infection from humans.

Clinical signs and diagnosis

Lesions are found on the external genitalia, inguinal and axillary regions and on the muzzle. Early lesions appear as smooth, raised, waxy, whitish papules some 1–2 mm in diameter, which develop a central caseous plug. The histologic appearance is diagnostic, with epidermal hyperplasia and swelling of individual keratinocytes that contain large intracytoplasmic inclusions called molluscum bodies. These cells are exfoliated through a crater in the stratum corneum at the center of the lesion. There is no dermal reaction in most cases.

Treatment and prevention

No successful therapy is reported and animals may remain affected for months to years.

VESICULAR STOMATITIS

Etiology

A vesiculovirus of the Rhabdoviridae that is enzootic in the Americas. Vesicular stomatitis (*q.v.*) has a seasonal incidence and is believed to be transmitted by biting insects. The virus may infect horses, cattle, swine and humans.

Clinical signs

The condition is known as "sore nose" or "sore mouth" and is characterized by vesicles that progress to painful erosions of the muzzle and mouth, feet and occasionally udder or prepuce. The incubation period is 1–3 days.

Diagnosis

Biopsy reveals marked intra- and intercellular epidermal edema and spongiosis with microvesicle formation and necrosis. A superficial and deep perivascular dermal inflammatory reaction is seen with neutrophils predominating.

Treatment

Healing usually occurs within 2 wk, sometimes leaving depigmented areas. Hooves may be sloughed on rare occasions. Mortality is rare and no specific therapy is indicated.

EQUINE VIRAL ARTERITIS

Etiology

Formerly classified as a togavirus, equine arteritis virus (*q.v.*) is now classified as a member of the genus *Arterivirus*. The causative virus is transmitted by coitus and inhalation. The disease occurs in many parts of the world and is reportable in the UK and USA.

Clinical signs and diagnosis

Edema of the distal limbs, ventrum, prepuce and scrotum and periorbital areas may be seen, with less frequent involvement of the sternum, shoulder,

intermandibular space and udder. Rarely, papular to urticarial lesions are seen on the trunk.

Biopsies reveal a lymphocytic arteritis, with viral antigen demonstrable in affected vessels. Infected animals can be identified by serologic tests.

FUNGAL SKIN DISEASES

DERMATOPHYTOSIS ("RINGWORM")

Etiology

Superficial fungal infection of skin and hair in horses is caused by several species of dermatophytes, including *Trichophyton equinum*, *T. mentagrophytes*, *T. verrucosum*, *Microsporum gypseum*, and *M. canis*. *T. equinum* is by far the most common. Infection occurs by contact with viable spores from infected hair on **infected animals or people**, on contaminated fomites (especially tack and grooming equipment), and in contaminated soil. The incubation period is 1–4 wk.

Clinical signs and diagnosis

Young animals kept in damp, dirty conditions with overcrowding and poor nutrition are most susceptible to infection. Horses under the **stress of training** are also susceptible. Outbreaks are most common in autumn/fall, winter and early spring.

The lesions consist of **patchy alopecia**, **crusting and scaling** with varying degrees of **erythema**. Early lesions may appear urticarial. Some cases exhibit pruritus or pain. Generally, organisms that are less well adapted to the horse cause more inflamed lesions.

The differential diagnosis should include dermatophilosis, bacterial folliculitis, demodicosis, cutaneous onchocerciasis and some allergic or autoimmune conditions (*q.v.*). Preliminary diagnosis is based on history, clinical signs and positive microscopy (**ectothrix spores coating a hair shaft**). However, **fungal culture** with subsequent identification should follow for confirmation of the diagnosis and to establish the source of the infection in order to institute appropriate control measures.

Treatment and prevention

Most dermatophyte infections are **self-limiting** and regress in the individual animal in **2–3 mo**. Herd outbreaks may be prolonged as the fungus gradually spreads to the susceptible animals. In either case, the **zoonotic potential** of the disease cannot be ignored.

The goal of treatment is to prevent spread to other animals and humans. Topical therapy is aimed at elimination of **infected hairs** by clipping wide margins around lesions (when practical), followed by bathing in **chlorhexidine–miconazole shampoo**. Alternative topical therapies are washing with chlorhexidine or povidone-iodine shampoos and, finally, sponging on a **fungicidal dip** such as 100 ppm natamycin, 0.2% enilconazole, 3% captan, 3–5% lime sulfur, 2–3% chlorhexidine, 10% povidone-iodine or a 0.5% solution of

sodium hypochlorite. Published trials using systemic treatment with griseofulvin are flawed. Dosing according to the manufacturer's recommendations with **griseofulvin is of doubtful efficacy**.

Clipped hairs should be properly disposed of to prevent spread of infection. Bathing and dipping should be performed daily for the first week and then weekly thereafter until lesions have cleared. In a herd, affected horses should be **separated** from non-affected animals, which should be handled separately or before handling affected animals. All persons involved with the horses should be warned of the zoonotic potential and instructed in good hygienic practices. The expense of systemic therapy with griseofulvin is rarely warranted in the horse and systemic therapy does not eliminate the need for topical therapy.

Depending on the dermatophyte involved, **other animals** (cats, dogs, cattle) may require simultaneous treatment in order to eliminate the source of infection. Treatment of premises may be necessary such as fogging with enilconazole or spraying with 3% captan, 5% sodium hypochlorite, 5% lime sulfur, 3% cresol, benzalkonium chloride or other fungicidal agent. Stressful and unsanitary conditions should be corrected and horses in training should be rested until recovered. Fomites such as tack and brushes also require disinfection.

MALASSEZIA DERMATITIS

Etiology

A species of lipid-dependent monopolar budding yeast organism closely related to *Malassezia sympodialis* has been isolated from the skin of healthy horses. A non-lipid-dependent species has been isolated from a healthy horse and also in association with a facial dermatitis. Anecdotally, yeast organisms have been identified cytologically and also by culture, in association with intermammary dermatitis and scaling dermatoses elsewhere on the body.

Clinical signs and diagnosis

Pruritic, scaling and alopecic lesions affecting the face of a horse that had been on glucocorticoid therapy have been reported. The pruritus and the lesions resolved with antifungal therapy. Large numbers of yeast organisms have also been identified on cytologic preparations from crusting/scaling lesions on the trunk and distal limbs of horses (anecdotal), with variable pruritus and resolution with antifungal treatment.

Yeast overgrowth in the intermammary region of mares is associated with often copious greasy exudation, variable erythema and inflammation, sometimes with evidence of pruritus in the form of kicking, and rubbing.

Treatment and prevention

Topical antifungal shampoos such as **chlorhexidine–miconazole**, or chloroxylenol (with the antiseborrheic product salicylic acid and sodium thiosulfate), or miconazole shampoo are effective in securing resolution. Lotions or creams containing azole products may also be useful for cases of yeast-associated intermammary dermatitis. Normal grooming practice should involve keeping the intermammary area of mares clean, and the above shampoos would be suitable for this purpose on a prophylactic basis.

SAPROPHYTIC FUNGAL INFECTIONS

Three main syndromes, mycetoma, phaeohyphomycosis and sporotrichosis, can result from infection of cutaneous and subcutaneous tissues by fungal agents that are not primary pathogens but opportunistic invaders.

Eumycotic mycetoma

Etiology

Mycetoma is a **chronic subcutaneous** fungal (eumycotic) or bacterial (actinomycotic) infection characterized by tumefaction, draining tracts and tissue grains. Eumycotic mycetomas are caused by saprophytic fungi that gain tissue access by traumatic implantation. *Curvularia geniculata* (dark granules) and *Pseudoallescheria boydii* (light granules) are the most common fungal agents isolated.

Clinical signs and diagnosis

Nodules or masses with ulceration and drainage are the typical lesions. There may be single or multiple lesions. A history of wounding may be suggestive, but small wounds or punctures may be missed.

Actinomycotic mycetoma, other bacterial or fungal granulomas, neoplasia and cutaneous habronemiasis (*q.v.*) are the major differential diagnoses. Biopsy of the mass for histopathology and culturing from a sterile biopsy sample or grains, which contain the fungal elements, will yield the diagnosis. Identification of the cultured fungus is based on conidia morphology. Histopathology reveals a pyogranulomatous to granulomatous infiltrate surrounding tissue grains consisting of an amorphous matrix surrounding pigmented or non-pigmented fungal hyphae.

Treatment and prevention

Complete surgical excision of eumycotic mycetoma is the treatment of choice. Some of the newer antifungal agents, e.g. **ketoconazole**, may prove useful, although expensive, in some cases where surgical excision is impossible. Good wound care may prevent many cases.

Phaeohyphomycosis

Etiology

Phaeohyphomycosis is caused by darkly pigmented (dematiaceous) fungi that inhabit soil and vegetation and gain access to tissues via traumatic implantation. *Dreschlera spicifera* and *Hormodendrum* spp. have been isolated in lesions from horses.

Clinical signs and diagnosis

Lesions are typically single or multiple dermal nodules with normal overlying skin. Ulceration and drainage may be seen.

Cutaneous habronemiasis, other fungal or bacterial granulomas and neoplasia should be considered in the differential diagnosis (*q.v.*). Diagnosis is

made by biopsy and culture of tissue samples. Biopsies reveal **pyogranulomatous inflammation** surrounding pigmented, septate hyphae and round to oval yeast forms. Conidia produced by the cultured fungus are characteristic for the species.

Treatment and prevention

No single treatment mode is successful for all cases of phaeohyphomycosis. Where possible, surgical excision is the best therapy. Some of the fungi may respond to systemic antifungal agents such as amphotericin, ketoconazole or newer imidazole or triazole agents. Good wound care may prevent many cases.

Sporotrichosis

Etiology

Sporotrichosis is caused by the fungal agent *Sporothrix schenckii*. It is a dimorphic fungus that inhabits soil and vegetation and gains entrance by traumatic implantation.

Clinical signs and diagnosis

The **cutaneolymphatic form** of sporotrichosis is most common in horses. Firm, subcutaneous nodules develop along the lymphatics. The lymphatics may become hard and swollen, resulting in palpable linear cords. Nodules may ulcerate and drain small amounts of pus or blood-tinged fluid.

The differential diagnosis should include the bacterial and fungal causes of lymphangitis (glanders, equine histoplasmosis, ulcerative lymphangitis) and sterile nodular panniculitis (*q.v.*). Diagnosis is made by cytology, biopsy and culture. **Cytologic examination** of smears from exudate or touch preparations of biopsy specimens may reveal characteristic pleomorphic (round to cigar-shaped) budding organisms. Organisms may be difficult to find in cytologic preparations or in biopsy specimens. Culture of exudate and/or sterile tissue samples followed by identification is the most reliable means of diagnosis.

Treatment and prevention

Iodide therapy with sodium or potassium iodide or with the organic iodide, ethylenediamine dihydroiodide (EDDI), is the treatment of choice. Surgical removal of single lesions may be helpful. Sodium iodide is given IV as a 20% solution at a dose of 20–40 mg/kg s.i.d. for 2–5 days, and then PO in sweet feed or molasses once daily. Potassium iodide is given at a dose of 1–2 mg/kg PO once or twice daily for the first week and then at half that dose daily. EDDI is dosed and administered similarly. Regardless of the form, iodide therapy must be continued for a minimum of 4 wk after complete resolution of lesions. Toxic signs of iodism (scaling, alopecia, depression, fever, cough, excessive lacrimation, nasal discharge, anorexia and salivation) may occur. Iodides should not be used in **pregnant mares**.

Amphotericin has been used successfully in a few cases. The newer imidazole or triazole antifungal agents also may be useful, albeit expensive, alternatives to the iodides. Affected animals should be separated from healthy

animals to avoid accidental spread of the disease due to increased environmental contamination.

Zoonotic potential to persons handling infected horses should not be overlooked. Gloves and protective clothing should be worn when dealing with suspected or confirmed cases of sporotrichosis. Disinfectant agents should be used to scrub after handling.

DEEP/SYSTEMIC MYCOSES

The fungi that classically cause systemic mycoses in humans and animals, *Blastomyces dermatitidis*, *Coccidioides immitis*, *Cryptococcus neoformans* and *Histoplasma capsulatum*, are rarely causes of disease, especially cutaneous lesions, in horses. There are, however, three diseases that are appropriately considered under this category: zygomycosis, pythiosis and equine histoplasmosis. Zygomycosis and pythiosis were previously termed phycomycosis.

Zygomycosis

Etiology

Zygomycosis is the term applied to syndromes caused by infection with various environmental saprophytes in the class Zygomycetes. *Basidiobolus haptosporus* and *Conidiobolus coronatus* are the most common species causing equine infection.

Clinical signs and diagnosis

Lesions caused by *B. haptosporus* are **solitary, ulcerative granulomas**, which may become quite large and usually occur on the neck, chest and trunk. Pruritus is usually present. Elongated, gritty, whitish-yellow coral-like bodies known as leeches or "kunkers", which consist of fungal organisms and necrotic host tissue, are variably present but smaller than those seen in pythiosis. The ulcerative granulomas caused by *C. coronatus* are usually found on the external nares and nasal passages. They may be single or multiple and also may contain small kunkers. As the lesions enlarge, nasal discharge and/or dyspnea may occur. Systemic infection is rare.

The differential diagnosis includes exuberant granulation tissue, pythiosis, neoplasia, and other bacterial, fungal or parasitic granulomas (*q.v.*). The nasal form should be distinguished from amyloidosis (*q.v.*). Diagnosis is accomplished by biopsy and culturing. Broad, infrequently septate hyphae within the lesion are suggestive of zygomycosis but culturing is necessary to distinguish it from pythiosis. Tissue samples and/or kunkers are suitable for culturing. Identification is made by fungal morphology.

Treatment and prevention

Where possible, complete **surgical excision** is the treatment of choice. Systemic antifungal therapy is variably successful. Usually a combined approach with surgery, application of topical antifungal preparations to external lesions and systemic therapy is required. One successful topical agent

(**Brown's Phyco Fixer**) includes 7.5 g of ketoconazole and 4.8 g of rifampicin in 400 mL of DMSO and 100 mL of 0.2 M hydrochloric acid. Amphotericin is the systemic antifungal agent of choice, but results are variable and surgical treatment combined with topical therapy usually is still necessary.

Pythiosis

Etiology

Pythium insidiosum, formerly *Hyphomyces destruens*, is the etiologic agent of the condition called **pythiosis**. This condition is seen in swampy, tropical and subtropical locations and has been called "**Florida horse leeches**". The organism is not a true fungus and is classed in the kingdom Protista. It is a plant parasite that resides in stagnant water and releases motile zoospores that are attracted not only to plants but also to hair, especially of horses and some breeds of dogs. Skin wounds, if present, allow the zoospores to invade the subcutaneous tissues.

Clinical signs and diagnosis

The lesions appear similar to those of zygomycosis with granulomatous tumefaction, draining tracts, large kunkers and pruritus (*q.v.*). Rapid enlargement is characteristic. Lesions tend to occur where wounds are common, especially the lower limbs and also the ventral midline where lesions of horn fly dermatitis, *Culicoides* hypersensitivity or cutaneous onchocerciasis occur. The history may include a poor response to routine wound care. Systemic infection is rare.

The differential diagnosis is the same as for zygomycosis. Culture and identification of the organism from the kunkers or from tissue samples is the best method of diagnosis. Such cultures should be submitted to a laboratory experienced in the identification of *Pythium* spp. Biopsies reveal eosinophilic, granulomatous to pyogranulomatous inflammation containing broad, irregularly branching, infrequently septate hyphae. An immunohistochemical stain has been developed for diagnosis of pythiosis on formalin-fixed sections and is available in a few specialized laboratories.

Treatment and prevention

Treatment of pythiosis is similar to that for zygomycosis: **surgical excision** and application of **topical antifungal preparations**. Amphotericin is unlikely to be of benefit since the organism's cell wall does not contain ergosterol. Immunotherapy using preparations of *P. insidiosum* has been successful but is not free from side effects. Development of **sterile arthritis** has been reported. Early lesions respond more favorably to treatment. Very large lesions carry a poorer prognosis and may require multiple surgical excisions before they are controlled.

Restricting access to stagnant ponds and puddles and prevention of wounding will help prevent this disease. Parasitic dermatoses should be controlled and all wounds should receive prompt, consistent treatment. If healing does not progress properly, wounds should be evaluated as early as possible for *Pythium* infection, before the lesion becomes too large to be easily excised.

Histoplasmosis

Etiology

Equine histoplasmosis (**epizootic lymphangitis**) is caused by the organism *Histoplasma farciminosum*, a dimorphic fungus. The disease is seen primarily in Africa, Asia and Eastern Europe. It is spread by wound contamination and biting flies. The organism can survive in the soil for 2–3 mo. There are rare reports of this infection in humans and pigs.

Clinical signs and diagnosis

Unilaterally distributed, **firm nodules** on the face, neck, head, and sometimes the limbs are characteristic early in the course. The nodules become fluctuant, rupture and discharge a purulent exudate, which may contain blood. The ulcerated nodules tend to enlarge and the lymphatics become prominent. Spread to the contralateral side follows after several weeks. Rarely, spontaneous recovery occurs.

The differential diagnosis should include other causes of lymphangitis (glanders, sporotrichosis and ulcerative lymphangitis), other bacterial and fungal infections and sterile nodular panniculitis (*q.v.*). Since the organism is difficult to culture and grows very slowly, **cytologic examination** of exudate or biopsy for histopathologic evaluation is the best means of diagnosis. Yeast-phase organisms are seen primarily within macrophages in these preparations and are indistinguishable from those of *H. capsulatum*, the etiologic agent in histoplasmosis in small animals.

Treatment and prevention

The disease is reportable and managed by strict isolation and slaughter of affected animals. In herds, insect control, prompt wound care and good sanitation practices may help prevent spread of the disease to the non-affected animals. When implementing these measures, it should be remembered that the incubation period can be longer than 2 mo.

CONGENITAL/HEREDITARY SKIN CONDITIONS

Congenital skin conditions are rare in the horse. In many cases their etiology and mode of inheritance is obscure, as is their prognosis. Their treatment is of doubtful value.

HAIR FOLLICLE DEFECTS

Hair follicle dysplasia

Etiology

Dysplasias of black and white hair follicles are recorded more frequently in species other than the horse. The cause of the disorder is unknown.

Clinical signs

Characteristically there are areas of dystrophic, brittle, lusterless hairs where hair growth is persistently poor. In the Appaloosa breed, foals having apparently

normal follicles at birth show progressive loss of black hairs while non-black hair remains normal. There is no treatment.

Hypotrichosis

Etiology and clinical signs

Congenital hypotrichosis has been reported in a blue Percheron foal born with poorly circumscribed patches of alopecia affecting the trunk. Biopsies revealed severe follicular hypoplasia, but adnexal structures were normal. The alopecia was progressive.

Curly coat

Etiology and clinical signs

Curled hair follicles are abnormal in horses. Curliness of the haircoat has been recognized in several breeds, in particular the **Percheron**. The mode of inheritance of the defect is considered to be as an autosomal recessive trait. There is no treatment for this condition.

Mane and tail hair dystrophy

Etiology and clinical signs

This condition is characterized by dystrophic short, brittle, lusterless hairs that readily fracture leaving the affected area stubbly. The cause is unknown.

HYPERELASTOSIS CUTIS OR HEREDITARY EQUINE REGIONAL DERMAL ASTHENIA (HERDA), CUTANEOUS ASTHENIA (DERMATOSPARAXIS, EHLERS–DANLOS SYNDROME)

Etiology

Hyperelastosis cutis comprises a number of **heritable disorders** seen more commonly in the cat and dog than in the horse. In horses, the more profound collagen defects seen in some other species have not been recorded and defects have been confined to localized manifestation of skin hyperextensibility and fragility. Joint hyperextensibility is said to occur in some cases. Autosomal recessive transmission is suspected. The condition has been reported in Quarter Horses, a crossbred Arab and a Hafflinger.

Clinical signs

The signs are often mild with localized areas of hyperextensible, mobile skin. This may be readily torn and show evidence of healing with scar formation. The area most commonly affected is the back and thorax.

Diagnosis

Clinical signs of thin, hyperelastic skin in localized areas, thinning of the dermis and scarring. Histologic examination of biopsy material may show abnormal staining affinity to certain connective tissue stains. Electron microscopy may demonstrate abnormal collagen fibrillogenesis.

Treatment
Symptomatic; suture skin tears. Affected animals should not be bred.

EPITHELIOGENESIS IMPERFECTA (APLASIA CUTIS)

Etiology
An inherited, **congenital** condition reported in several breeds of horses. The mode of inheritance is ill defined but thought to be a simple autosomal recessive trait.

Clinical signs
There is an abrupt area of absence of epithelium, particularly of the limbs but sometimes involving the tongue. The condition may be lethal. The differential diagnosis includes skin trauma at foaling.

Treatment
Euthanasia is usually indicated.

JUNCTIONAL EPIDERMOLYSIS BULLOSA

Etiology
A defect in the expression of **laminin-5**, resulting in separation through the lamina densa of the dermoepidermal junction, has been documented in Belgian draft horses and two French draft horse breeds; an ultrastructurally similar defect has been described in American Saddlebreds. In American Saddlebreds the genetic defect has been mapped to chromosome 8, the locus for the *LAMA3* gene, and in the Belgian and French draft horses a defect in the *LAMC2* gene has been identified.

Clinical signs
Transient vesicles or bullae may be seen at or soon after birth. These rupture to form well-demarcated ulcers with exudation and crusting. Lesions typically affect the coronets, mucocutaneous junctions and skin over bony prominences. Hoof wall separation leads to sloughing; corneal lesions and dental dysplasia may be present. Affected foals are unable to feed; they become depressed, cachectic and die of septicemia.

Diagnosis
Biopsies reveal subepidermal clefts with the PAS-positive basement membrane zone attached to the dermal floor**.**

Treatment and prevention
Euthanasia is indicated. Parents of affected foals should not be used for breeding. The identification and localization of the genetic defects offers the option of a **molecular test** to identify carrier status and better management of breeding strategies.

DENTIGEROUS CYSTS

Etiology

Dentigerous cysts are a developmental anomaly associated with the first branchial pouch and the condition is seen in foals and young horses. The lesion may contain embryonic teeth.

Clinical signs

A bilateral or unilateral fistulous opening is associated with a firm swelling below the base of the ear. There is usually a persistent, milky, **purulent discharge** from the lesion.

Diagnosis

Radiography, exploratory surgery. The differential diagnosis includes foreign body, abscess and tumor.

Treatment

Surgical excision offers a good prognosis.

PIGMENTARY DISORDERS

CONGENITAL/HEREDITARY CONDITIONS

Albinism

True albinism probably does not occur in the horse, as **no albino gene** has yet been identified in this species. Horses with pink skin and white coat blue eyes, are usually the result of a **double dose** of the **cream dilution gene**, found at the albino locus, and are termed Cremellos. Phenotypically white horses can also result from other gene combinations that determine white coat patterns. The coloration is of little clinical significance except that affected animals may be at greater risk of suffering from photodermatitis, phototoxicity or photosensitization.

Lethal white foal disease

Lethal white foal disease results from the **homozygous expression** of the **autosomal dominant** gene which codes for the Frame pattern of coat coloration. Affected individuals have a defect in migration of neural crest cells resulting in absence of melanocytes and lack of myenteric plexuses in the intestinal trait. The defects of the intestinal tract, which include colonic atresia, are not consistent with survival. The condition is associated with a mutation in endothelin receptor B. DNA testing can be used to identify heterozygote carrier status, since phenotypic expression of the Fr gene may be minimal.

ACQUIRED DEPIGMENTATION

Mechanisms of pigment loss are not well understood. They may in some cases be post-inflammatory, autoimmune, neural or toxic.

Leukoderma

Etiology and clinical signs
Depigmentation follows traumatic injury to the skin or an inflammatory condition. Leukoderma is a common finding in horses, particularly in areas of tack damage. Localized depigmentation around the commissures of the lips and tail base may be due to the effect of chemicals contained in rubber tack such as bit guards and crupper straps.

Diagnosis
History of previous skin damage.

Treatment and prognosis
The loss of pigment may be temporary or permanent. There is no effective treatment. Avoidance of physical injury, particularly from ill-fitting tack, is indicated.

Vitiligo

Etiology and clinical signs
Vitiligo is a **disfiguring**, non-pruritic, non-painful, localized loss of pigmentation in focal areas of the skin, most commonly seen in **Arabian horses**. In the Appaloosa breed, the color pattern of the coat develops postnatally by progressive focal depigmentation, i.e. genetic loss of pigment. Some cases may have an autoimmune basis, but many are idiopathic. Breed predispositions indicate a probable genetic basis.

Diagnosis
Typical clinical findings and absence of preceding skin damage.

Treatment and prevention
There is no effective treatment, but occasional horses re-pigment.

Pinky syndrome, Arabian fading syndrome

Etiology
Idiopathic vitiligo of unknown cause.

Clinical signs
There is **progressive depigmentation** of the skin and hair, particularly around the commissures of the lips and muzzle and also the periorbital skin and eyelids; in some cases depigmentation extends to involve the perianal or perivulval area. Areas of loss of skin and hair pigment are non-pruritic, non-painful and non-crusting. Affected animals vary in age, but most are young (1–2 yr old).

Diagnosis
Based on typical history and clinical signs. Lesions should be differentiated from toxic or post-traumatic depigmentation.

Treatment
None proven as effective. Some investigators have supplemented the diet of affected animals with natural carotenoids (e.g. carrots) and considered these to have had a beneficial effect.

Leukotrichia

Loss of pigmentation of hair may follow inflammatory injury or may have an inherited basis.

Spotted leukotrichia

Etiology

A condition of unknown etiology mainly affecting Arab horses, but also seen in other breeds.

Clinical signs and diagnosis

Widespread, numerous, small clumps of white hairs over the rump and dorsum, arising spontaneously, which are non-painful and non-pruritic.

Treatment

Spontaneous resolution may occur. Cases require no treatment.

Reticulated leukotrichia

Etiology

This condition has been reported in Thoroughbreds, Quarter Horses and Standardbreds; it is of uncertain etiology, but is believed to be hereditary.

Clinical signs

A net-like pattern of crusts develops on the dorsum which, when the debris is shed, the hair grows through white.

Diagnosis

Based on history and clinical findings.

Treatment and prevention

Ineffective. Affected animals should not be bred because of the possible inherited nature of the condition.

Hyperesthetic leukotrichia

Etiology

Unknown; only reported in California.

Clinical signs

Multiple or single crusted lesions up to 4 mm diameter appear along the dorsal midline associated with extreme pain, similar to human *Herpes zoster* lesions. After a few weeks white hairs appear. Lesions spontaneously resolve after 1–3 mo. Once lesions have resolved the pain subsides but leukotrichia remains.

Differential diagnosis

Differential diagnoses include reticulated leukotrichia, dermatophilosis, *Culicoides* hypersensitivity and multiple dermoid cysts (*q.v.*) of the dorsal midline.

Treatment

No specific therapy is known.

ENVIRONMENTAL DERMATOSES

MECHANICAL DAMAGE

Pressure sores

Etiology and clinical signs

The type, severity and duration of the changes noted following mechanical trauma vary markedly and responses may be further modified by individual variations in skin reactivity. Mild pressure or low grade frictional forces applied repeatedly to an area of skin will stimulate **increased epidermal activity** leading to acanthosis and hyperkeratosis and either callus formation with loss of hair or, in thick coated animals, compression of the callus into the dermis and the production of "corns" or "sit-fasts".

If greater frictional forces are applied suddenly or in a sustained manner to an area of skin, tearing of dermal and epidermal tissue can result. This leads to the production of an **acute inflammatory reaction**, tissue disruption and the development of erosions or ulcers and exudation. This type of damage is frequently associated with badly fitting, worn or damaged harness and girths.

When a skin area is subjected to sustained and/or prolonged direct pressure, particularly when that skin area lies directly over bone, ischemia and other dermal changes result and the overlying epidermis becomes compromised. Epithelial death and sloughing may occur initially, followed by changes in dermal collagen resulting either in scarring, permanent loss of hair and the production of an atrophic and easily damaged epithelium, or, when damage is slightly less severe, the production of white non-pigmented hair. These types of change are frequently noted in association with **saddle sores**.

Treatment and prevention

The factors responsible for the production of mechanical damage must be identified and eliminated. Specific treatment of skin lesions may not be necessary. **Callosities** may require little treatment and resolve with time.

Corns and "sit-fasts" often respond to conservative treatment depending on their situation. If present on the back it is essential to ensure that the saddle is in good condition and has been properly fitted and that the area is protected with a thick numnah when the animal is ridden. The lesions may be excised or debrided when necessary, but this can result in more extensive, permanent damage and, as most protected lesions resolve in 6–8 mo, it should be considered a last resort.

Frictional sores and early pressure sores should be protected and treated as superficial wounds. Long-standing saddle sores present a difficult problem, as surgical removal is not usually possible and not advised. A conservative approach is recommended, ensuring that the lesions are well protected and further trauma is prevented.

BURNS

Etiology

Burns result from either direct exposure to high temperatures or overexposure to harmful short wave radiation (atomic, ultraviolet). Similar tissue damage may result from contact with electrical power or chemical agents.

Box 5.1 Classification of burns according to severity

- **First degree burns** present as erythema and superficial edema, accompanied by severe pain. This leads to superficial desquamation followed, in uncomplicated cases, by complete resolution of lesions and no permanent damage.
- **Second degree burns** present with hair loss, superficial blistering and epidermal necrosis accompanied by pain. Healing takes place within 7–10 days, provided secondary infection is prevented. Again, no permanent changes ensue.
- In **third degree burns** there is hair loss accompanied by a severe blistering reaction with loss of the epidermis and dermis but with absence of pain sensation, except at the periphery of lesions. Healing is slow, epithelialization only occurring from the periphery. Scarring often ensues, with loss of hair follicles, sweat and sebaceous glands and development of an atrophic epidermis.
- **Fourth degree burns** present with loss of both the epidermis and dermis, accompanied by necrosis and destruction of deeper tissues. Lesions heal slowly and scarring is a serious problem. Depending on the site and severity of the deep tissue damage, there may be serious impairment of function.

Clinical signs and diagnosis

The changes noted will vary according to the time, degree of exposure and the agent concerned. The presence or severity of the burns associated with electricity is related to the voltage, the area of electrical conductance and the duration of contact.

Thermal, electrical and chemical burns may be classified according to their severity (Box 5.1).

Alternatively, burn injuries may be more simply classified as superficial, involving only the epidermis and upper part of the dermis, or deep.

Treatment

Early assessment of the severity and extent of lesions is essential. Animals seriously burnt in, say, a prairie or stable fire, having widespread superficial burns that involve **over 50% of the body**, may need to be humanely destroyed. Euthanasia may also be indicated in animals with more localized deep burns that could impair future function. The salvage of any animal suffering damage to the foot or coronary band or smoke damage to the lungs and eyes should be seriously questioned.

Burn lesions should be **soaked thoroughly in cold water or ice packs** applied as soon as possible and for at least 30 min. The agents concerned in the production of chemical burns should be identified and may need to be specifically neutralized.

Plasma loss can present a serious problem in second, third and fourth degree burns, requiring fluid therapy with both colloids and crystalloids. It may be necessary to sedate and/or give analgesics in order to carry out wound treatment. Early assessment of burns can be difficult as lesions are frequently covered with charred hair and skin debris. Inserting a needle into the center of the lesion may aid diagnosis, as absence of pain is indicative of a

deep burn. All burns cases should be given a **broad-spectrum systemic antibiotic**. Short-acting steroids may be considered appropriate.

Individual lesions should be gently cleaned and then dressed either with antiseptic or antibiotic ointment. Silver sulfadiazine cream, gentamicin ointment, cetrimide cream and chlorhexidine have been recommended. Debridement of dead tissue enhances wound healing and reduces infection. Dressings reduce fluid loss and contamination, but the size and extent of burns often render this impractical. Leg lesions should be protected using a **non-adhesive dressing** under a protective bandage. Skin grafting (*q.v.*) may be indicated in the management of extensive, deep burns.

Finally, it is essential in severe burns cases that animals are placed on a high plane of nutrition (*q.v.*).

FROSTBITE

Etiology

Chilling in young, weak, undernourished or debilitated animals can result in generalized cooling (hypothermia) and/or focal skin damage (frostbite).

Heat loss, increased when the body is exposed to low environmental temperatures, is increased further when coat cover or other forms of insulation are absent or sparse, the skin and coat are wet and/or the body surface is subjected to cold air movements (wind chill factor). As a defense measure, muscular activity and shivering is used as a means of increasing body heat and piloerection of body hair is employed to trap an increased volume of insulating static air as a blanket within the coat. Vasoconstriction of cutaneous vessels helps to reduce cutaneous heat loss and to conserve central body temperature, but at the expense of reducing still further peripheral tissue temperatures and increasing the likelihood of frostbite.

When the previously described methods of heat production and conservation fail, central body temperature falls to **hypothermia**, typified by the subject becoming moribund, shivering ceasing, respiratory and heart rate falling and blood viscosity increasing. This further increases peripheral vascular resistance. If this process is not arrested and reversed, coma and death follow.

Local cutaneous changes associated with freezing are dependent on the rapidity of the freezing process. As the skin temperature drops, cellular activity also falls. Further slow reduction in temperature results ultimately in the formation of water crystals within dermal and epidermal cells and also the interstitial spaces. Rapid reduction in skin temperature results finally in gel rather than crystalline changes within cells.

In both hypothermia and frostbite, affected areas become **hard and inelastic**. Subsequent thawing causes further serious damage with marked disruption of tissue and cell membranes, particularly of the endothelial linings of capillaries and venules with extravasation of plasma and the production of edema and inflammation accompanied by serious disruption of the local circulation.

The susceptibility of cells to low temperatures and freezing is variable. Melanocyte function is easily destroyed, even by transitory cooling or freezing that fails to produce serious adverse effects in other cells of the dermis and epidermis.

Clinical signs and treatment

Frostbite is most frequently encountered in the very young, debilitated or **undernourished foal** in harsh climatic conditions. Most sufferers show evidence of hypothermia with **low rectal temperatures** (below 32°C), slow pulse and respiratory rates, general depression or coma. In such cases the foal should be **warmed slowly** by placing in warm water or blankets. **Warm glucose solutions** may also be given either IV or by stomach tube.

Frostbite usually affects the **ears and lower leg**. If areas are very cold, and the tissues are hard and inelastic then frostbite should be suspected and immediate attention should be given. Every effort should be made to thaw such areas by immersing in water kept at 42°C. The tissues must not be rubbed or traumatized.

In mild cases of frostbite, recovery may result initially in localized pain and slight local edema which resolves within a few days, leaving apparently normal skin which later may become covered with an area of depigmented hair. In severe cases, local edema becomes marked and, within 3–5 days, well-demarcated areas of hard, black, necrotic tissue become obvious surrounded by a rim of pink, edematous and weeping reactive tissue. The necrotic tissue will finally **slough** to leave an area of pink granulation, which will then slowly heal. Frostbite affecting the ear can result in small, stunted and distorted ear flaps due to damage to underlying cartilage.

In all cases of frostbite, affected areas should be protected and steps taken to control secondary infection.

IRRITANT CONTACT DERMATITIS

Etiology and clinical signs

Contact dermatitis may result when an agent capable of producing physical or chemical damage or of inducing an allergic response comes into direct or repeated contact with the skin surface (see allergic skin diseases *q.v.*).

Physical contact dermatitis is frequently associated with poorly fitting or poorly maintained harness or noted following exercise over coarse terrain or through heavy grit or mud. The severity of the skin changes is influenced by skin resilience, degree of hair protection and time of exposure and mode of application of agent. **Chemical contact dermatitis** results from direct exposure to irritant or corrosive substances.

The severity of the ensuing skin changes is related to the type of agent, its concentration, corrosive capacity and the exposure time. Powerful irritants and corrosives always produce severe cutaneous changes following initial application. Mild irritants or powerful corrosives in very low dilution may produce little change following initial exposure, but when applied continually or repeatedly may induce serious skin changes.

Chemical contact dermatitis in the horse is most frequently encountered following the inappropriate application of skin medicaments, cutaneous exposure to stable disinfectants or in association with cleaning agents used on harness or stable blankets, etc.

Clinical signs and diagnosis

Severe blistering, edema leading to exfoliation, hair loss and the production of weeping sores will be noted following the application of strong corrosives.

Milder agents may cause a low-grade inflammation accompanied by varying degrees of irritation, scaling and hair loss following either initial or repeated challenge. The response is always confined to the vicinity of the contact area and careful study of the sites involved usually gives an indication of the nature of the causative agent.

Treatment and prevention

Further contact with the agent must be avoided. It may be necessary to wash the agent off the skin or take other steps to neutralize its activity. Severe chemical contact reactions may require palliative treatment to allow healing to take place and to control secondary infection.

PHOTODERMATITIS

Cutaneous exposure to **sunlight** can result in dermatosis of varying severity.

Phototoxicity (sunburn)

Sunburn is a photochemical reaction involving the dermis and epidermis, which is produced by direct exposure to powerful ultraviolet (UV) rays contained within the 290–320 nm (UVB) wave bands, causing erythema, inflammation and tissue damage in unprotected, non-pigmented skin. The severity of the cutaneous changes is related to the time and degree of exposure, the skin area and the ambient temperature.

Photosensitization

Photosensitivity is a **severe cutaneous reaction** that follows penetration of the very much weaker UV rays in the range of 320–600 nm (UVA) into an unprotected, non-pigmented dermis and epidermis which contains **photoreactive molecules** derived from either the circulation or topical application. The response may be classified as primary, secondary (hepatogenous), photocontact or photoallergic.

Primary photosensitivity results from photosensitizing agents being deposited directly and usually unchanged into the skin after injection or ingestion. Ingestion and absorption of certain **pasture plants** can cause primary photosensitization as their tissues contain photodynamic compounds such as furocoumarins (bishop's weed, Dutchman's breeches and wild carrot), fagopyrin and photofagopyrin (buckwheat), perloline (perennial rye grass) and hypericin (St. John's wort).

Certain species of **aphid** are also capable of inducing primary photosensitivity when ingested by horses grazing infested pastures, in particular those containing trefoils. Primary photosensitivity has also been noted sporadically in horses grazing pastures containing Swedish clovers, lamb's tongue and certain species of plantain.

Skin changes only are noted in primary photosensitivity in the horse, with the possible exception of that associated with **rye grass** (*q.v.*), which can cause incoordination and a staggering gait with or without cutaneous changes.

Secondary or hepatogenous photosensitivity is the indirect result of **liver dysfunction** or damage and/or biliary stasis, which allows a number of substances that are normally broken down within the liver or eliminated from the body in the bile to become concentrated in the skin and other organs. The most important substance associated with hepatogenous photosensitivity in the horse is **phylloerythrin**, a powerful photosensitizer produced by the breakdown of chlorophyll by **bacterial action** within the bowel.

Liver damage leading to photosensitivity in the horse may be caused by plant and other poisons. The **pyrrolizidine alkaloids** are of particular importance and are present in a number of pasture plants that may be ingested by horses including certain species of heliotrope, ragwort**,** rattleweed, Salvation Jane (Patterson's curse), fiddleneck and tarweed. Liver damage has also been reported in other species in association with wild heliotrope, panic grass, alecrim, bog asphodel, ganskweed, bush pea and the coal oil bush, but ingestion of these plants is unlikely in the horse.

Liver damage may also occur, under adverse conditions, following the ingestion of alkaloids contained in water contaminated with **blue-green algae** or hepatotoxins associated with plant mold growing on rotting Bermuda grasses, lupins and stored grain. On very rare occasions, photosensitivity can be associated with carcinoma of the liver, lymphosarcoma, serum and antiserum reactions, liver infection and copper and phosphorus poisoning.

Photocontact reactions result when photodynamic agents come into direct contact with and are then absorbed by non-pigmented skin which is then exposed to sunlight; all animals so exposed show a similar reaction. Certain plants contain essential oils (furocoumarins), which are powerful sensitizers. These include some members of the carrot family, cow parsley, fennels, hogweed and possibly the buttercup family. Contact with certain coal tar products such as acridine, anthracine, phenathracine pyridine and creosote may also lead to photosensitivity, as may contact with acriflavine, anthraquinone, eosin and acridine dyes, but this is unlikely in the horse.

Photoallergic reactions are very rare and have not been confirmed in the horse. This type of response has been noted following repeated cutaneous exposure to phenothiazines, sulfonamides and halogenated salicylanilides in humans.

Clinical signs and diagnosis

Cutaneous changes associated with primary and secondary photosensitivity involve all areas of non-pigmented or partially pigmented skin and hair. Haircovered skin may be less severely affected or spared. Lesions present initially as severe inflammation and edema leading to skin splitting, exudation and finally skin necrosis. Dark-colored horses can present with edema and irritation involving the less protected skin of the lips and nose with milder changes involving the coronary bands.

All suspected cases should be subjected to a thorough clinical examination as hepatogenous photosensitivity is invariably accompanied by some evidence of liver dysfunction such as jaundice, weight loss, inappetance, malaise, generalized debility or, on some occasions, neurologic disorder. Examination of blood samples will reveal evidence of raised liver enzymes and phylloerythrin levels.

The diagnosis of photocontact dermatitis in the horse can present difficulties. Lesions involve only limited areas of the lips, nose and legs, and may present as patches or plaques of severe inflammation and edema leading to skin splitting and sloughing which are often confined to relatively small sections of non-pigmented skin areas.

After establishing the presence of photosensitivity, a detailed examination must be made of the history and also of the environment and diet to establish the cause.

Treatment

Affected animals should be placed in a **dark environment**. **Gentian violet dye** may be applied as a light barrier. Antibiotic therapy may be required and judicious use of short-acting systemic steroid therapy or non-steroidal anti-inflammatory agents may be of value in early cases.

Prognosis is good in cases of primary photosensitivity. Healing is usually rapid, but can result in scarring and permanent hair loss. The prognosis in hepatogenous photosensitivity is governed by the type and severity of the liver changes.

SELENIUM TOXICOSIS

Etiology

Selenium is an essential component of the enzyme glutathione peroxidase. While deficiency, with or without low levels of vitamin E, can precipitate symptoms of **muscular dystrophy** (*q.v.*) in rapidly growing foals and occasionally in older horses, excess intake of selenium from plants, cereals or contaminated water is also deleterious and produces symptoms of either acute or chronic toxicity. Naturally occurring selenium toxicity has been reported in localized areas of Australia, Canada, China, Colombia, Ireland, Israel, Mexico, Russia, South Africa and the USA.

Certain alkaline topsoils can contain very high selenium levels. The problem is amplified by low rainfall, which ensures that the element remains and is not leached out into the safety of the subsoil. The problem of toxicity is often worsened by the presence in pasture of so-called "indicator plants". These include certain species of *Acacia, Aster, Astragalus, Atriplex, Camandra, Grindelia, Gutierrezia, Haplopappus, Machaeranthera, Mentzelia, Morinda, Neptunia, Oonopsis, Oxytropis, Penstemon, Sideronthis* and *Stanleya,* all of which thrive on alkaline, selenium-rich soils. They are also referred to as "accumulators" as they possess the capacity to concentrate selenium within their tissue. Many are unpalatable, but if eaten can cause acute poisoning. When these plants die and decay, they contribute to raising the concentration of selenium in topsoil still further. All plants growing on selenium-rich soils absorb selenium in sufficient amount to cause toxicity. Concentrations above 4 ppm (either in herbage or cereals) should be considered dangerous if fed for any length of time.

Industrial pollution may also lead to increased levels of selenium contamination. An inappropriately high concentration of selenium added to compounded concentrate feeds may also lead to clinical toxicosis.

Clinical signs and diagnosis

If an animal ingests very high concentrations of selenium over a period of a few days, it will become **fatally ill**, showing symptoms of fever, respiratory distress and diarrhea, leading to collapse and death. Ingestion of lower concentrations of selenium over a longer period may result in chronic selenosis (alkali disease or bob-tailed disease).

During the early stages, mane and tail hair is shed and a generalized scaly and patchy alopecia develops accompanied by dullness, depression and emaciation. Lameness often occurs due to swelling of the coronary band which leads to interruption of normal hoof growth and the production of horizontal faults and cracks in the hoof wall, which finally splits and is shed. Neurologic symptoms, including blindness, staggering gait and head-pressing, may be encountered, leading finally to collapse and death.

Diagnosis is based on history of exposure and the presenting symptoms and may be confirmed by blood tests. **Whole blood selenium levels >4 ppm** are considered diagnostic. Selenium levels indicative of toxicosis may also be measured in hair and urine.

The **differential diagnosis** includes chronic arsenic toxicosis, chronic mercury poisoning and toxicosis due to ingestion of plants of the *Leucaena* genus (*q.v.*). Leucaenosis has been reported in Australia, New Zealand, New Guinea, the West Indies and Hawaii.

Treatment and prevention

The source of toxicity must be identified and steps taken to prevent further ingestion, either by removal of animals from contaminated pasture and/or changing the source of cereal feed. Despite taking these steps, further loss of hair may occur over the following week. The feet should be examined carefully for evidence of pathology and radiographed for evidence of laminitis (*q.v.*). Any hoof cracks should be sealed immediately using an epoxy resin and the feet trimmed. All animals should be placed on a high plane of nutrition. Supplementation with sulfur-containing amino acids may be of benefit.

There is **no effective antidote** to selenium poisoning but in the absence of life-threatening symptoms, exclusion of selenium from the diet will bring about a slow recovery.

MERCURY TOXICOSIS

Etiology

Mercury and mercurial compounds have been used widely in the textile, tanning, chemical and plastics industries, wood preservation, stains, paints, electroplating, electric dry cell batteries, gold and silver extraction and as antifungal seed dressings, diuretics, antiseptics and skin blistering agents.

Mercury poisoning usually results from **accidental ingestion**. It can follow inhalation and percutaneous absorption, but this is unlikely in the horse. The type and severity of symptoms associated with mercury poisoning are dependent on the chemical formulation, solubility, relative toxicity and the amount and rate of ingestion and absorption of the individual mercurial. Mercury is a **cumulative poison** that is only slowly eliminated from the body via the kidney and alimentary tract.

Ingestion of relatively large amounts of certain inorganic mercurials (mercuric chloride 8 g, mercurous chloride 12–16 g, bi-iodide of mercury 6 g) can cause an acute corrosive gastroenteritis resulting in straining, diarrhea, and severe colic followed rapidly by collapse and death. Ingestion of slightly smaller amounts of soluble inorganic mercurials, such as mercuric chloride, may produce milder enteric changes, but these compounds are readily absorbed from the bowel into body tissues, targeting the kidney and causing proximal tubular necrosis leading to irreversible renal failure (*q.v.*) within a few days.

Insoluble inorganic mercurials such as mercurous chloride can cause enteric upset, but are not readily absorbed. If retained within the bowel, these compounds can be broken down slowly into mercury and mercuric salts that can then be absorbed and give rise to symptoms of chronic poisoning which include cutaneous signs.

Chronic mercury toxicosis is frequently noted in association with ingestion of very low levels of organic or inorganic mercurial over many months.

Various ethyl, methyl and phenyl organic mercurials have been used as antifungal seed dressings and as diuretics and skin dressings. Organic mercurials may also be produced by the action of bacteria on inorganic mercurial industrial waste causing pollution of water and vegetation and leading to the incorporation of mercury into the food chain.

Ingestion of large amounts of organic mercurial will cause an **acute gastroenteritis** accompanied by colic and diarrhea. Enteric disturbance will not be observed when intake is lower, as may occur when treated grain or seed forms a small or intermittent part of the diet or when an animal has only limited access to contaminated water or vegetation, but such exposure may be sufficient to produce symptoms of chronic poisoning. Organic mercurials are readily absorbed from the bowel and, being lipid soluble, are then taken up preferentially by nervous tissue and fat.

As mercury levels rise in the nervous system, neurologic changes are noted, typified initially by stiffness and tremor, progressing to incoordination, ataxia, hyperesthesia, occasionally reduced vision and/or deafness and finally to coma and death.

Clinical signs and diagnosis

Chronic mercury toxicosis is typified by malaise, loss of weight and appetite and the following **cutaneous changes**: scaling of the skin which may become ulcerated, particularly over the anal and vulval areas and around the lips and gums, accompanied initially by loss of body hair and occasionally by loss of the mane, tail and leg feathers.

The symptoms of mercury poisoning are not pathognomonic, often making initial diagnosis difficult. It is essential that a careful and detailed investigation of the clinical history, environment, feed and all other in-contact animals is undertaken. Acute colic and/or gastroenteritis (*q.v.*) is more frequently associated with infection, other caustic poisons, plant poisons and mycotoxins. Neurologic changes in the horse may also be associated with plant poisons, certain molds and fungi, lead and arsenic (*q.v.*).

Chronic mercurial poisoning may be confused with all other debilitating conditions, many of which can on occasions induce cutaneous changes and

hair loss. Poor coat growth may also be noted in chronic arsenic poisoning. Loss of mane and tail hair can occur in association with chronic selenium poisoning, but hoof changes are not a feature of mercury poisoning. In certain parts of the world ingestion of *Leucaena leucocephala* will also result in the loss of mane and tail hair and cause ridging of the hoof.

When mercury poisoning is suspected, a **urine sample** should be taken and examined for evidence of mercury. High levels of urinary alkaline phosphatase and γ-glutamyl transpeptidase will often be present.

In acute poisoning post mortem examination may reveal evidence of an **acute corrosive gastroenteritis** and pale swollen kidneys and liver. Histologic examination of the kidney will reveal tubular necrosis in acute poisoning, while in chronic poisoning with kidney involvement there may be evidence of a membranous glomerulonephritis. Animals presenting with neurologic symptoms may display histologic evidence of cerebral and cerebellar atrophy with thinning of the granular layer, but no marked changes in the number or morphology of the Purkinje cells.

Post mortem and histologic examination of material obtained from cases of chronic poisoning not displaying evidence of neurologic or nephrotic changes is disappointing, but kidney assay will reveal mercury levels >5 ppm.

It is essential in all cases of suspected chronic mercury poisoning that a **thorough appraisal** is carried out into the feeds, the environment and potential sources of industrial contamination of vegetation and the water supply. All in-contact animals should also be assessed for evidence of poisoning.

Treatment

Treatment of animals presenting with acute gastroenteritis, nephritis and/or neurologic symptoms is unrewarding. In early cases of chronic poisoning identification and elimination of the source of mercurial compound is essential. Oral treatment with **potassium iodide** (4 g s.i.d.) for 10–14 days accompanied by **dimercaprol** (3–5 mg/kg IM) q.i.d. for 2 days then b.i.d. for a further 8–10 days may also be indicated.

ERGOTISM

Etiology

Symptoms of ergotism result from the ingestion of certain alkaloids and other pharmacologically active substances contained in the **plant fungi** *Claviceps purpurea* and *C. paspali*, which are capable of invading and multiplying in the seeds of many grasses and cereals. The organisms overwinter in the ground and germinate in the spring, developing stomata that produce and eject small ascospores.

The ascospores become wind-borne, finally penetrating rapidly developing seed heads where they undergo rapid hyphal proliferation, engulfing the germinal tissue and finally bursting out of the seed head to form hard, elongated, deep purple sclerotia. The sclerotia contain variable amounts of alkaloids and amines including ergotamine, ergometrine, acetylcholine, histamine and tyramine, which can cause changes in many organs such as the CNS, the uterus and the vascular system.

Active growth and spread of infection is noted during the **summer** and is markedly accelerated during or immediately after prolonged periods of wet weather or high humidity. Propagation can also occur in poorly stored hay and grain.

Clinical signs and diagnosis

The type and severity of symptoms associated with ergot poisoning are variable, being related to the concentration of ergot within the diet, the period of ingestion and the alkaloid content, together with the age and species of the animal involved.

Ergot poisoning is now rare and is most often encountered in cattle and sheep, less frequently in the pig and only extremely rarely in the horse. It is not uncommon to encounter ergot poisoning in cattle and sheep out at pasture while horses grazing the same pasture remain clinically unaffected.

Cases of suspected ergot poisoning may present in the horse as hyperesthesia, incoordination and convulsions, which can result in death. Such changes may be mimicked by mycotoxin poisoning (*q.v.*). Ergot poisoning may also result in smooth muscle spasm and endothelial damage to small peripheral arterioles and capillaries, leading to thrombosis and obliteration of small blood vessels. This results in gangrene of the extremities, particularly the lower leg and tips of tail and ears.

Affected animals present with symptoms of lameness with swelling and edema around and above the coronet on all four feet and accompanied by lack of sensation and warmth in the foot. Necrosis and sloughing of the skin and hoof may follow.

Diagnosis rests on the clinical symptoms and identification of ergot either in the forage or concentrate feed.

Treatment and control

There is no treatment for ergotism, but removal of the source of infection will bring about a slow remission of symptoms and changes in mild cases. Pasture contamination can be reduced by mowing affected areas using a high blade setting and removal of cuttings.

WOUNDS

ETIOLOGY AND CLINICAL SIGNS

Skin wounds may be produced by cutting, puncturing or tearing. The injury may involve damage to or loss of epidermal tissue, epidermis and upper dermis, or the whole of the epidermis and dermis and may involve deeper tissues as well as the skin.

The wound healing process is complex and involves the mobilization, reorganization and replacement of cells and tissues and the utilization of many biochemical mechanisms and pathways. The pattern of wound healing is influenced by the area and depth of tissue deficit, the extent of associated tissue damage, the presence or absence of bacterial infection, the physical status of the patient and area of the body involved.

Superficial wounds involving only loss of epidermis or the epidermis and superficial layer of the dermis heal rapidly, provided infection is adequately controlled and further trauma prevented. Healing is usually completed within 10 days and skin function and conformation are unimpaired. **Full thickness skin wounds** heal slowly unless the skin edges can be brought into close apposition. When closure is not possible, healing relies on the mobilization and utilization of three mechanisms: wound contraction, repair and regeneration (*q.v.*).

Wound contraction can reduce the size of a skin deficit on the flank of a horse by 30–50% within 10 days, but this mechanism is less efficient in wounds situated on the lower limbs. Although the causes of poor wound contracture in distal limbs have not been fully elucidated, previous research has suggested poor blood supply, relative hypothermia, decreased venous or lymphatic return, and imbalance of growth factors as possible contributors to delayed healing. In addition, minimal surrounding tissue is available for recruitment to allow primary wound closure and increased motion of the equine distal extremities causes dynamic tension and distraction of wound margins.

WOUND REPAIR

Wound repair is classically divided into distinct phases; these distinctions can enhance understanding and management of wounds, but are somewhat arbitrary. In reality, wound healing is a **dynamic process** during which multiple events occur simultaneously. Classically, the phases of wound healing are described as follows:

1. **Inflammatory phase.** Initially, local hemorrhage supplies red blood cells, white blood cells, platelets and fibrin to the site, forming a fibrocellular clot. Initial **clot formation** limits blood loss, and local vasoconstriction further attenuates hemorrhage. Within 10 min of clot formation, the local vasculature subsequently dilates, allowing more fibrin and clotting factors into the wound, accelerating the inflammatory process. The surface of the clot forms a scab, protecting the wound and providing early appositional strength. Just as importantly, the clot provides scaffolding for migrating white blood cells which begin the debridement phase under the influence of inflammatory mediators such as prostaglandins, serotonin, histamine and complement, as well as proteolytic and lysosomal enzymes.

2. **Debridement phase.** Stimulated by cytokines released from the first wave of white cells that arrived via initial hemorrhage, neutrophils and monocyte/macrophages arrive in increasing numbers by 6 h following injury. Neutrophils and macrophages both initiate and perpetuate debridement, and also act as antigen presenting cells, enhancing recognition of invading organisms. More specifically, neutrophils are recruited by **cytokines** (*q.v.*) such as complement, tumor necrosis factor (TNF-α) and interleukins (especially IL-1 and IL-8). They prevent local infection by phagocytosis of bacteria and foreign material, and themselves produce chemokines that attract other inflammatory cells, stimulating maturation of monocytes to macrophages within 24–48 h of arrival.

   Although neutrophils are important, **macrophages** are critical to healthy healing. Healing is markedly prolonged in the absence of macrophages. They

are recruited by cytokines including IL-1 and interferon-gamma (IFN-γ). They remove non-viable tissue, bacteria and foreign material in phagosomes by formation of proteolytic enzymes and generation of free radicals through inducible nitric oxide synthase (iNOS). Release of metalloproteinases from macrophages also contributes to tissue remodeling, and other macrophage-derived mediators such as tissue growth factor-β (TGFβ) and interferon-alpha (IFN-α) promote maturation by stimulating angiogenesis and connective tissue synthesis. Along with platelets, macrophages stimulate fibroblast infiltration and wound repair through the production of many factors including platelet-derived growth factor (PDGF), fibronectins and other cytokines.

3. **Repair phase.** Following elimination of local infection, debris, clotted blood and necrotic tissue, the process of **epithelialization** (*q.v.*) can begin. If manual debridement is performed and tissue is re-apposed with sutures, this process may begin within 12–24 h. Otherwise, the repair phase begins within 3–5 days following injury, after formation of healthy **granulation tissue**.

Granulation

Granulation tissue is an extraordinarily vascular complex of fibroblasts and macrophages within a matrix of collagen and fibrin. It is extremely important, as it provides early strength and blood flow to the wound, provides a surface for migration of epithelial cells and fibroblasts, and resists infection.

Fibroblasts are critical for development of healthy granulation tissue and are recruited by **cytokines** (*q.v.*) released from macrophages (especially PDGF, TGFβ, and fibroblast growth factor). In the absence of macrophages, fibroblast infiltration is delayed. Fibroblast infiltration is also stimulated by mild acidity and low oxygen tension in healing tissue. Fibroblasts are recruited from mesenchymal cells in the surrounding connective tissue.

After arrival in the wound, fibroblasts begin to produce collagen, fibronectin, proteoglycan, and elastin, called "ground substance". As more fibroblasts are recruited, they migrate into the wound across the wound surface via lamellipodia that adhere to the developing scaffold of fibronectin-coated fibrin and collagen established during the initial inflammatory phase. The amount of collagen peaks at 2–3 wk post injury, adding significant tensile strength after 5–15 days in a sutured wound. Early type III collagen fibers are replaced with mature type I fibers during this time.

Granulation tissue develops rapidly in horses, with a tendency towards overproduction, often called "**proud flesh**" (see below). Endothelial infiltration occurs following migration of fibroblasts, as existing blood vessels proliferate to form vascular loops. Lymphatic vessels develop more slowly, causing some lymphatic stasis and local edema in the first hours and days following injury.

Epithelialization

Epithelialization begins to occur immediately following formation of a healthy granulation bed (i.e. within 3–5 days), but will occur as early as 12 h after injury in a sutured wound. The **rete pegs** of the epidermis flatten, forcing cells at the wound edges to stretch across the defect.

Increased mitotic activity of basal cells begins early and enhances the rate of epithelialization, but this process occurs slowly, ranging from less than 0.2 mm/day in distal limbs to 0.8–2 mm/day on the flank. Epithelialization of large trunk wounds may take several weeks, while similar lesions on the lower legs may take several months.

During this process, cells begin to enlarge, separate from the basement membrane, and migrate across the wound gap. Epithelial cells secrete collagenases to allow **proliferation under scabs**; the scab will fall off once underlying epithelialization is complete.

Cell migration is guided by **collagen fibers**: basal cells flatten and stretch across the exposed collagen bundles via pseudopodia and microvilli. The cells should migrate across the defect until contact with other epithelial cells attenuates their progress (contact inhibition). Initially, the new epidermis is one cell layer thick, but it gradually thickens with time. Epithelial cells can also migrate down **suture tracts**, potentially leading to a foreign body reaction, or they may become keratinized, leading to sterile abscesses or scarring. The process of epithelialization is attenuated by the presence of fibrin or excessive amounts of other inflammatory products in the wound, by excessive granulation tissue, by overly frequent bandage changes, by topical corticosteroids, and also by antiseptics and ethyl alcohol (see below).

Wound contraction

Wound contraction occurs after suturing, or formation of a healthy granulation bed. Contraction may occur independent of epithelialization, but both processes appear to work in concert to achieve most rapid healing.

Contraction is mediated in particular by special cells called **myofibroblasts**. The cells, present in granulation beds, contain contractile proteins similar to the actin and myosin in smooth muscle. Myofibroblasts effectively anchor themselves to other cells and to collagen fibers in the granulation bed, and then contract, helping to draw the advancing wave of epithelial cells across the defect. This process stretches the existing cell layer, but continued collagen and epithelial cell proliferation restores the skin to normal thickness.

While the initial increase in wound strength is attributable to collagen synthesis in the early stages of healing, the greatest increase in strength occurs between 15 and 20 days post injury during the **maturation phase**. During this time, the number of fibroblasts begins to decrease, as does the concentration of capillaries.

Initially collagen fibers are arranged at random, but this matrix matures and reorganizes (more quickly in a sutured wound) because wound tension causes fibroblasts, collagen fibers and blood vessels to become oriented parallel to wound edges as functionally oriented fibers are strengthened. **Wound strength** may continue to improve with time, but the scar may only provide 80% of normal strength 1 year post trauma. Eventually an avascular, inelastic area of scar tissue is left within the dermis. After **severe trauma**, this tissue is often devoid of sweat and sebaceous glands and hair follicles, overlaid by a thick, friable epidermis that remains prone to traumatic disruption.

Rapid healing is contingent upon minimizing the total duration of each phase of the healing process. The initial inflammatory phase is essentially

unavoidable, but the duration of time that elapses between initial injury and first treatment is critical to successful primary intention healing (suturing). The "golden period" is generally defined as the first 6–8 h after injury. During this time, **bacterial numbers** will reach more than 10^5 organisms/g of tissue, or more if the wound was highly contaminated at the time of the injury. Non-viable tissue will begin to become necrotic, releasing large quantities of **pro-inflammatory cytokines** into the milieu, initiating the inflammatory phase of wound healing.

Thus, **physiologic wound care** involves attention to minimizing the duration of the inflammatory phase by removing debris, contamination, and non-viable tissue, while preserving homeostasis to promote rapid conversion to local repair phase of wound healing. Therefore, whenever possible, debris and other contaminants should be removed from the wound via **lavage** and **debridement** (*q.v.*), and obviously non-viable tissue should also be removed. These steps are critical components of wound care, as they can shorten the time required to return to normal tissue strength and architecture.

TREATMENT OF WOUNDS

Where possible, primary closure with sutures should be performed to re-appose tissue and minimize the need for granulation tissue formation, wound contraction and re-epithelialization.

Wounds that are **heavily contaminated**, chronic or swollen, or those involving synovial structures may best be handled by **delayed primary closure**, before the formation of granulation tissue, usually within 4–5 days of injury. Closure by **secondary intention** can be performed on chronic, severely contaminated or infected wounds after the formation of healthy granulation tissue; this allows optimal wound drainage and promotes gradual debridement of compromised tissue. Wounds with large skin defects on the upper limbs and body may be allowed to heal by second intention. **Skin grafting** (*q.v.*) may be necessary where the deficit exceeds the capability of wound contraction and epithelialization.

Initial assessment of wounds should include determination of more than depth and size of the wound. The possibility of involvement of **sensitive tissues** such as nerves and synovial structures should be definitively established. Wounds associated with blunt or superficial skin trauma may also involve fractures, although these typically produce more severe lameness. However, **bone trauma** is not always detectable during manipulation and palpation, especially when fracture fragments are non-displaced. Therefore, **radiographic evaluation** is indispensable for definitive evaluation of many wounds.

Wounds involving only the epidermis usually require minimal treatment. **Clipping hair** from the surrounding area and gently removing extraneous contaminants by washing the site with sterile physiologic saline solution (or a homemade solution, using one teaspoonful salt, approximately 5 g in 500 mL water) best maintains local homeostasis.

Antiseptic solutions and soaps, alcohol and hydrogen peroxide all **inhibit wound healing** by retarding physiologic inflammatory responses like wound contraction and re-epithelialization (see antiseptic lavage, below). Topical

antibiotic ointments and solutions enhance healing of minor wounds, and can be applied beneath a dressing before bandaging.

Wounds that are larger, deeper or more heavily contaminated, or those involving synovial structures can benefit from **aggressive wound care**, sometimes including antiseptics, joint and tendon sheath lavage and distal limb perfusion (see below).

Whenever possible, clients should be offered the option of general anesthesia as the optimal means for clinicians to assess, decontaminate and repair extensive wounds or those that involve compromise of synovial structures. However, many of these procedures can also be performed in the field under heavy sedation. After establishing that a patient is stable enough to tolerate sedation, administration of α_2-agonists (xylazine, detomidine) or a combination of α_2-agonists and opioids can enhance patient comfort and compliance. A sequential approach to wound management in the field includes many of the steps described below.

Systemic antibiotics

It has been shown that the use of **systemic antibiotics** given within 3 h of injury improves wound healing. The status of vaccination against **tetanus** (*q.v.*) must also be ascertained, and boosters given when indicated.

Broad-spectrum systemic antimicrobials should be administered early in the process, preferably immediately following preliminary evaluation of the wound. Although many lacerations may benefit from administration of routine antimicrobials (e.g. **trimethoprim–sulfa** at 30 mg/kg PO b.i.d., **procaine benzylpenicillin** at 22 000 IU/kg IM b.i.d.), heavily contaminated or chronic wounds may require more aggressive medications.

The combination of broad-spectrum antimicrobials with minimal rates of resistance (e.g. combined therapy with β-lactams and aminoglycoside such as **gentamicin** at 6.6 mg/kg IV or IM s.i.d.) is strongly indicated when wounds are contaminated or when compromise of synovial structures is suspected. For long-term medication, or when patients will not tolerate IM injection, several broad-spectrum **orally administered** antibiotics that penetrate deep soft tissue and synovial structures are available (e.g. **chloramphenicol** at 30–50 mg/kg t.i.d. or q.i.d., **doxycycline** at 5–10 mg/kg PO b.i.d.).

Antiseptic lavage

Initial management of most wounds is similar. Prior to shaving or clipping the surrounding hair, application of moist sterile sponges or sterile, water-soluble lubricant gel to the wound bed minimizes iatrogenic contamination of the wound.

Safety razors are convenient, produce very clean wound edges and may be more acceptable to reactive patients. However, razor burn due to skin sensitivity or inadequate soap/lubricant application can potentiate local infection. Even if not grossly evident, **microscopic irritation** of skin surfaces occurs when shaving with a safety razor, and this has been shown to affect rates of infection detrimentally. Clippers do not remove as much hair, and can be difficult to use on skin edges.

Some patients may not tolerate the sound or feeling of electric clippers, but cordless clippers are quiet, convenient and tend not to provoke patient responses. The surrounding skin should be cleansed with **dilute antiseptic**. Hydrogen peroxide and ethyl alcohol are ineffective at killing bacteria and are cytotoxic to epithelial and inflammatory cells. Although iodine and quaternary ammonium-based scrubs are more efficacious at killing bacteria, they are cytotoxic to epithelial and inflammatory cells, and their use is also contraindicated.

Extraordinarily contaminated or chronic wounds may benefit from a **single direct application** of dilute antiseptic solution such as povidone-iodine (0.1% or 10 mL of 10% proprietary Betadine solution in 1 L saline) or chlorhexidine (0.05%, or 5 mL of 10% proprietary Nolvasan solution in 1 L saline). These solutions offer excellent antibacterial activity and can therefore minimize the inflammatory and debridement phases of wound healing, but they have adverse effects on cellular function. Also available are **surfactant-based products** specifically designed to help remove bacteria and debris without adversely affecting the healing milieu (e.g. Constant Clens, Kendall Products), sometimes obviating the need for aggressive mechanical lavage.

In grossly contaminated wounds where some mechanical action is also required, a wound can be lavaged with **warmed sterile isotonic saline** solution delivered under pressure. A 50 mL syringe with an 18 G needle delivers a suitable pressure, although pressure bags, fluid pumps, and dedicated wound lavage systems are optimal. Lavage with water alone may cause cell swelling and rupture, but is convenient for wound irrigation and may be less injurious to tissues than antiseptics, especially if followed by lavage using 0.9% saline. Lavage through a metal cannula provides both a focused stream of fluid and a sterile instrument for probing to determine the extent of the wound.

Hemostasis

Although severe bleeding should be attenuated as soon as possible, **mechanical hemostasis** is less likely to potentiate local infection if performed after initial wound lavage. Small skin vessels may spasm following crushing with hemostats, but larger vessels typically require placement of ligatures.

The use of smaller suture material (0, 2-0) means less foreign material is ultimately left in the wound, but transfixation and double ligatures may be required to ensure that hemorrhage is completely controlled. Taper needles are less traumatic to vessels and surrounding connective tissue, and synthetic monofilament materials (e.g. PDS, Monocryl) combine moderate tissue time with decreased risk of iatrogenic infection. These materials are therefore indicated in contaminated wounds.

Local or regional anesthesia

Whenever possible, **regional anesthesia** (*q.v.*) is preferred. Anesthesia via caudal epidural and distal limb nerve blocks can be administered far from affected areas, minimizing complications. Regional anesthesia also tends to produce better pain control while using less total anesthetic solution. When local infiltration around a wound must be used, anesthetic should be

deposited in an aseptic fashion with attention to nerve supply, with most of the injection focused on the dorsal, rostral or proximal wound margins.

Although the toxic dose of **lidocaine** is 10 mg/kg (250 mL of 2% lidocaine in a 500 kg horse), much lower dosages (1.5 mg/kg) can produce signs of toxicity when rapidly absorbed. Subcutaneous injection of 60–90 mL of local anesthetic is generally safe in a 500 kg horse. Local anesthetic may be diluted to 10 mg/mL (1%) in young horses, ponies and miniature horses to minimize the risk of toxicity, although this may decrease duration of desensitization.

For injuries to the distal limb, **local anesthetic infiltration** at the abaxial sesamoids, low or high four point, or peroneal and tibial nerves will typically provide adequate anesthesia to distal regions. Depending on the site of injury, caudal (coccygeal) **epidural administration** of opioids (e.g. **preservative-free morphine** at 0.1–0.3 mg/kg) combined with local anesthetic (2–3 mL of 20% lidocaine in a 500 kg horse) provides excellent analgesia to the perineum and, when diluted into 20 mL (total volume) of sterile saline, migrates rostrally to provide partial anesthesia to pelvic limbs, pelvis, flanks and even to the caudal ventrum.

The **combination of opioid and local anesthetic** is preferred in part because of the difference in durations of action; epidural lidocaine desensitizes within 15 min but lasts only 4–6 h while epidural morphine takes 2–3 h to become effective and minimizes sensitivity for 12–18 h after administration. In cases needing longer-lasting hindlimb or perineal anesthesia, an indwelling epidural catheter may be placed to allow repeat administration.

Debridement/exploration

Aggressive debridement is a critical component of wound care as it minimizes the amount of debris, infection and non-viable tissue that must be removed from the wound by inflammatory cells. In particular, chronic wounds often require extensive debridement, both to remove necrotic tissue, debris and exuberant granulation tissue and to stimulate bleeding and inflammation prior to closure by second intention. Sterile gloves and instruments should be used to minimize contamination.

Complete exploration should also be performed at this stage. Flexible sterile probes can be used to determine the depth of subcutaneous tracts extending from the wound bed. Some deep tracts may require placement of **Penrose drains** prior to suturing to minimize **seroma** or **abscess formation** (*q.v.*) in the deeper layers.

Joint "needle" lavage

During exploration, it is critical to determine whether synovial structures are compromised. Synoviocentesis of joints and tendon sheaths should be performed early to identify the presence or absence of inflammation. Fluid analysis (gross appearance, total white cell count and morphology, and protein concentration as a minimum data base) should be performed on undiluted samples whenever possible. After a sample has been obtained, **injection of sterile saline** to distend joints, tendon sheaths and bursae can help to determine whether joint capsules communicate with wounds.

If saline introduced into the joint leaks via the wound, the joint is considered compromised. Due to the grave implications of long-standing **septic arthritis** or **tenosynovitis**, referral for general anesthesia and arthroscopic evaluation and lavage should be strongly encouraged. If this is not possible, standing needle lavage using **isotonic crystalloid solutions** is warranted to help minimize infection and inflammation in the joint. A single systemic dose of water-soluble, non-irritating antibiotic (e.g. sodium ampicillin, potassium or sodium benzylpenicillin) may be added to the lavage solution.

In addition to allowing drainage via the tract into the wound, additional needles should be placed to ensure **thorough lavage** of the entire synovial structure, including palmar/plantar pouches. While fluid pumps may not be available, infusion using a pressure bag or multiple large syringes may help expedite through-and-through lavage. Following synoviocentesis or joint lavage, intra-articular administration of 500–1000 mg of **amikacin** is strongly indicated.

Distal limb perfusion

Whether administered via IV or intraosseous routes, **distal limb perfusion** is a very effective technique for treating chronic infected wounds or septic joints and tendon sheaths. This procedure may be performed following sedation and regional anesthesia. In the field, it is most practical to place an 18 or 20 G 50 mm/2 inch catheter into the **palmar digital vein** for instillation of antimicrobials. Then, a **proximal tourniquet** should be placed using a pneumatic tourniquet, Vetwrap or, ideally, an Eschmark bandage. The flat rubber Eschmark bandage is applied very tightly, beginning at the hoof and forcing blood and extracellular fluid proximally to a point above the wound. The tourniquet is removed from distal to proximal, leaving the proximal-most band in place above the wound for a maximum of 45 min.

Typically, 1 g of **amikacin** is diluted in 20 mL of sterile crystalloid fluids and slowly infused via the pre-placed intravenous catheter. This procedure can be repeated on a daily basis, although repeated catheterization of palmar digital (or other) veins is challenging.

Antibiotic lavage

Following debridement and before primary closure, a final lavage of the wound bed can be performed using sterile saline with or without fortification with antibiotics. The decision whether to lavage with antibiotics should be based on degree of contamination, chronicity and proximity to sensitive structures. Antibiotics applied topically to wounds should be water soluble and non-irritant. Good choices include **sodium ampicillin**, **potassium benzylpenicillin** or **gentamicin**; typically one systemic dose of these antibiotics is placed in 1–3 L of crystalloids for lavage. As with antiseptic solutions, a pressure-bag attached via sterile IV tubing to a metal cannula allows both lavage and final exploration of deep tracts.

Sutures

Primary wound closure should begin with apposition of deeper tissue layers. Closure of fascial planes enhances cosmetic healing and minimizes scar tissue formation. Where deeper tracts or dead space remain, **drains** should be

placed with their origin in the deepest extent and with egress though the skin via a separate surgical incision.

Non-absorbable monofilament suture (e.g. nylon or other synthetic non-absorbable, size 0) can be placed percutaneously to fix the drain in place while still allowing removal after healing has progressed.

Apposition of dead space using "**walking**" **sutures** is important to minimize the risk of seroma formation. Walking sutures should be placed beginning at the deepest extent, using absorbable suture material. Braided absorbable suture material has relatively increased tissue drag, which can enhance ease of placement; however, braided suture can potentiate infection when contaminated. Subcuticular suture patterns are indicated to re-appose skin margins and minimize tension. **Small diameter absorbable monofilament suture material** is an excellent choice for subcuticular closure.

The skin should be sutured under minimal tension, employing tension-relieving techniques and **stents** where indicated. Placement of **far-near–near-far sutures** using no. 2 nylon or Prolene is an excellent choice when tension is greater, especially on distal extremities. Simple interrupted sutures or skin staples may be placed between the larger tension-relieving sutures to complete re-apposition of skin margins.

Bandages/dressings

When primary closure of wounds is not possible due to chronicity, gross contamination or infection, or wound edge contracture, **bandaging** can help prepare the wound bed for closure by second intention, or may produce excellent results without suturing. Even sutured wounds may benefit from the protection, immobilization and antimicrobial effects of dressings and bandages. Advanced wound care techniques seek to **augment physiologic healing responses** by minimizing infection and fostering normal cellular responses while avoiding the cytotoxic effects of overly frequent antiseptic application and bandage changes.

In general, mild exudate is desirable, as this fluid will contain beneficial inflammatory mediators, thus **enhancing re-epithelialization**. The end result should be more rapid healing with less scar tissue formation. Although traditional materials are less expensive than some of the advanced approaches outlined below, the relatively infrequent re-application (every 3–5 days) and more rapid healing mean that advanced wound care also tends to be cost effective.

Just like the dynamic process of wound healing, different bandages are appropriate for wounds depending on the degree of infection or stage of repair. Some of the more commonly utilized topical therapies and dressings and their intended applications are described below.

Many chronic non-healing wounds will respond to management using some of these materials. The finely tuned balance of growth factors and pro-inflammatory cytokines (*q.v.*) present in acute wounds is often lost in chronic wounds. Therefore, maintaining a moist wound surface rich in endogenous growth factors is one of the primary goals of the methods outlined below. It is also important to consider the fact that **too frequent bandage changes** can inadvertently debride epithelial cells, further prolonging the healing process. Bandages may be changed as infrequently as every 5 days, provided the exudate is not excessive, and infection is not present.

Some wounds become chronic due to excessive **motion of the affected area**. In these situations, splinting and casting is useful to minimize motion, allowing delicate epithelial cells to migrate across the wound surface. However, some very large wounds, especially those on the distal extremities, may require skin grafting (*q.v.*) for complete resolution.

When **excessive granulation tissue** is present, it is best managed by surgical excision and foam dressings with or without a cast, as mentioned above. In these situations, splinting and casting is useful to minimize motion, allowing delicate epithelial cells to migrate across the wound surface. Wounds that have healed with significant fibrosis or with compromise of function may benefit from **reconstructive surgery**. Some very large wounds, especially those on the distal extremities, may require **skin grafting** (*q.v.*) for complete resolution.

Triple antibiotic ointment

These ointments, typically containing neomycin, polymyxin B and bacitracin, are indicated for treating minor superficial infection. Long-term use may prevent fibrosis and scarring. However, severe infection, necrosis and exuberant granulation tissue are not amenable to treatment with these topical antibiotic ointments alone.

Steroid–antibiotic ointment

Classically used to minimize exuberant granulation tissue formation, steroid–antibiotic-based ointments work by inhibiting fibroblast activity. However, they also diminish activity of epithelial cells and can therefore prolong the healing process overall, sometimes resulting in static, non-healing wounds.

Silver sulfadiazine

Ointments containing silver sulfadiazine have excellent antimicrobial activity, especially on superficial infections caused by Pseudomonas. These salves also enhance epithelialization in open wounds but inhibit the activity of fibroblasts, therefore minimizing wound contraction, especially in the early phases of healing.

Hypertonic saline dressing

Dressings saturated in hypertonic saline solution (20% solution) are an **excellent first choice** for treating heavily infected or contaminated wounds, especially **chronic wounds**. Pre-made products are available (e.g. Curasalt, Kendall Products), but similar dressings can be made using sterile water and salt (sodium chloride). These dressings are bactericidal and also serve to draw extracellular fluid osmotically from the wound environment, minimizing local swelling and edema. These dressings are typically used as **wet-to-dry dressings**: they are applied moist to the surface of a wound and left in place for 24–48 h. They are dry when removed, thus helping to remove debris and dead cells from the surface of the wound. Repeat application of similar dressings may proceed until all necrotic material and debris is removed from the wound and a healthy granulation bed has begun to develop.

Hydrogel dressing

Hydrogel dressings (e.g. Curafil, Kendall Products) are useful in dry to lightly draining wounds. These gels help to promote autolysis of non-viable tissue when used with an occlusive dressing, and will not become dry, which can be useful in treating some burns (*q.v.*) and abrasions. Hydrogels stimulate macrophages to produce IL-1 and TNF-α, thereby stimulating fibroblasts and angiogenesis. They are therefore best indicated in the early repair phase of healing, when the production of granulation tissue is desired. However, following the development of a healthy granulation bed, it is most appropriate to stop using hydrogel-type dressings.

Calcium alginate dressing

Calcium alginate dressings (e.g. Curasorb, Kendall Products) are most useful in **heavily exudative wounds** where they promote formation of granulation tissue. Therefore, after development of a healthy granulation bed, alginate dressings should not be used, as they can stimulate the development of proud flesh. Although the contribution of the calcium component is poorly understood, calcium generally contributes to cell migration and remodeling during the repair phase. The alginate interacts with sodium present in wounds, creating a gel that provides an optimal moist healing environment. Calcium alginate dressings are very absorbent, holding approximately 20 times the dressing's weight in exudate. They do not adhere to the underlying wound bed, and their removal is therefore not uncomfortable for patients.

Fenestrated foam dressing

Foam wound dressings (e.g. Hydrasorb, Kendall Products) are indicated for use in heavily exudative wounds, including those with drains, because the foam material helps to wick excessive moisture away from the wound bed. Foam is contraindicated in infected wounds, but is excellent over **mature granulation beds** as it will inhibit excessive granulation tissue formation. Unlike topical ointments containing corticosteroids and antibiotics, foam does not inhibit inflammatory cells and epithelial cells, but preferentially minimizes the formation of proud flesh (*q.v.*).

Antimicrobial impregnated gauze dressing

Some antimicrobial-impregnated dressing materials are commercially available. One such product (Kerlix A.M.D., Kendall Products) is impregnated with polyhexamethylene biguanide (PHMB), an antimicrobial comparable to chlorhexidine. However, PHMB is minimally cytotoxic to inflammatory and epithelial cells, while still having excellent ability to minimize bacterial proliferation within the bandage or on the surface of a wound. These bandages can be applied in combination with any of those mentioned above, or they can be used alone. These are ideal materials for packing into large cavity wounds. PHMB-impregnated gauze is best applied wet, and can even be covered with a completely occlusive dressing, although this might not be necessary in heavily exudative wounds.

Skin grafts

Proper preparation of the graft site is an absolute prerequisite for successful skin grafting. Granulation beds must be free of infection and flush with the skin surface. Exuberant granulation beds are ideally **debrided and bandaged** 2–4 days prior to grafting procedures, as excessive bleeding beneath graft material can decrease acceptance of grafted skin. Grafts may be harvested from a variety of sites, using a variety of methods, most of which are best conducted under general anesthesia.

Ideal donor sites include the **cranial pectoral region** as well as the dorsal neck, especially under the mane. All subcutaneous connective tissue and fascia should be surgically removed from the donor skin prior to placement, and all bleeding from the recipient site must be attenuated. It is possible to achieve cosmetic results with smaller, full thickness wounds provided there is good acceptance of full thickness grafts and appropriately orientated hair growth.

Some full thickness grafts, such as pinch and punch grafts, may be collected from a standing sedated horse following local or regional anesthesia. These grafts are collected using a forceps and blade, or a biopsy punch instrument, and are inserted into pre-placed recipient holes in the granulation bed. Strips of full thickness tissue may also be harvested for placement into linear recipient sites, and sutured with 3-0 non-absorbable monofilament.

Because there is limited availability of full thickness donor skin for grafting, larger defects are typically managed using **partial thickness skin** from donor sites. It is difficult or impossible to harvest partial thickness grafts without the use of expensive **mechanized dermatomes**. These grafts must be obtained under general anesthesia, also allowing access to donor sites on the smooth, flat ventrum. Partial thickness grafts may be sectioned into strips to provide more complete coverage of large granulation beds.

Mesh graft expanders are also expensive, but are another means to accomplish coverage of large defects, and are especially good to minimize fluid accumulation beneath the graft in heavily exudative wounds such as burns (*q.v.*).

In **high-motion areas**, such as the dorsal tarsus, **tunnel grafts** maximize successful graft acceptance. This technique involves burying strips of partial thickness skin within tunnels created in a healthy granulation bed. The graft is placed using a 12 cm long cutting needle attached to adhesive tape on the haired side of donor tissue; the needle is passed through the granulation bed to implant the graft. The ends of the graft are sutured into place using 3-0 monofilament. After 7–10 days, the overlying granulation bed is excised, often necessitating a second general anesthetic. Although this technique is technically challenging, it requires less expensive equipment, and often achieves excellent results.

ALLERGIC SKIN DISEASES

URTICARIA AND ANGIOEDEMA

Etiology and clinical signs

Urticaria and angioedema are usually manifestations of **type 1 (immediate) hypersensitivity reactions** (*q.v.*). Antigens that have been implicated include

insect bites and stings, feedstuffs and additives, drugs, vaccines, infectious agents, parasites, topical applications, pollens, dusts, fungal and mold spores. The appearance of an urticarial reaction may be triggered by non-immunologic factors such as heat, cold, exercise, stress and physical pressure (dermatographism), but there is usually an underlying hypersensitivity state.

Urticaria or **hives** is characterized by the presence of **multiple edematous swellings** in the superficial dermis, often widely distributed over the body surface. The overlying epidermis is normal, although the accumulation of fluid in the dermis may result in overlying hairs appearing to stand up from the rest of the haircoat. Angioedematous plaques are larger in size, arise deeper in the dermis and are more often associated with serosanguineous oozing from dependent skin surfaces and subsequent crusting. There may be associated pruritus, although some animals seem unaware of the lesions. Urticaria may occur as a single episode only, or may be chronic with repeated episodes experienced over a period of time.

Diagnosis

The appearance of the clinical signs is typical. However, identification of the underlying cause of the hypersensitivity reaction can be extremely difficult. A thorough history of diet, management regimen and recent drug exposure is essential. A restriction or exclusion diet may be indicated. Alterations in management routine and intradermal skin testing may be employed in efforts to identify the causal allergen.

Treatment

In the acute phase clinical signs can be reversed, often rapidly, by parenteral administration of **glucocorticoids**. In chronic cases all attempts should be made to identify and subsequently avoid the causal allergen. If this is not possible then oral administration of prednisolone at a dose rate of 0.5–1 mg/kg/day should control the condition. Antihistamines may be helpful in preventing the appearance of lesions and also reduce the steroid dose requirements. Hydroxyzine hydrochloride at doses of 200–500 mg b.i.d. to t.i.d. has been reported to be effective.

ATOPIC DERMATITIS

Etiology and clinical signs

Hypersensitivity reactions (*q.v.*) may occur to aeroallergens such as tree, grass and weed pollens, dusts, animal and human danders, free-living mites, fungal and mold spores. The reactions may be **type I (immediate)** and/or **type IV (delayed)** (*q.v.*). Clinical manifestations of hypersensitivity to aeroallergens may affect the skin and respiratory systems, and allergy has also been implicated in some horses that head-shake. Cutaneous signs include marked pruritus with no primary lesions, and chronic urticaria. Secondary lesions due to self-trauma, such as excoriations, hair loss, thickening of the skin and lichenification, may develop. The condition may be seasonal in nature and age of onset is usually between 1 and 4 yr. As in other species, a genetic predisposition to develop allergy is likely.

Diagnosis

Food hypersensitivity and insect or parasitic hypersensitivity reactions should be ruled out. A tentative diagnosis can be made on history, clinical findings and ruling out other differentials. A circulating eosinophilia may be present. **Skin biopsy** often reveals a tissue eosinophilia, increased numbers of mast cells and a superficial perivascular inflammatory infiltrate. Intradermal skin testing may assist in identification of causal allergens. Drugs, stress and other factors may influence skin test results, and positive reactions can be seen in healthy (non-allergic) horses. Intradermal testing is best performed by experienced operatives, using proven allergen kits. Serologic tests are offered but there are few data demonstrating their reliability published.

Treatment and prevention

Avoidance of implicated allergens is the treatment of choice. This may necessitate major changes in management and feeding regimens, but in cases of indoor allergen reactions can be very successful in managing affected animals. **Hyposensitization** has been reported to be helpful.

Pharmacologic agents may be required to control symptoms and would include **antihistamines** and **glucocorticoids**. Hydroxyzine hydrochloride at doses of 200–500 mg b.i.d. to t.i.d. has been used, but other antihistamines may also be helpful. Prednisolone at doses of 0.5–1 mg/kg, initially daily, will control symptoms but should be administered on an alternate day basis long term. **Essential fatty acid supplementation** may be helpful in the management of the condition.

Owners should be warned about the possible inherited basis of atopy in the case of breeding animals.

FOOD ALLERGY

Etiology

Although frequently suspected in horses, food allergy is **extremely rare** in the horse, with only a few anecdotal reports in the literature. In other species adverse responses to ingested allergens may be manifested by changes involving the alimentary tract, respiratory system and/or the skin. Adverse food reactions may be non-immunologic (irritant, pharmacologic, toxic) or immunologic. The latter may involve **type I (anaphylactic)** and/or **type III (immune complexes)** and/or **type IV (cell-mediated)** hypersensitivity responses.

The mechanisms responsible for the initiation of an allergic response (*q.v.*) in an individual, to one particular food allergen, together with localization of the reaction to one body organ, are obscure. Sensitization to a food allergen, normally protein, is precise and specific and, once initiated, is life long.

Clinical signs

Skin responses that might be associated with ingestion of food allergens in the sensitized horse include a **generalized pruritus** with no evidence of macroscopic skin changes, a generalized papular urticaria, edematous plaques with pruritus with or without swellings of the head and vulva, or a generalized pruritus accompanied by inflammation leading to a generalized seborrhea.

Skin changes associated with food allergens are not pathognomonic and it is essential that they be differentiated from the more common skin changes associated with mite infestation and free-flying insects or atopic dermatitis, and also dermographism and drug reactions. It has been suggested that on rare occasions ingestion of food allergens may trigger off enteric changes involving either the small or large intestine and leading to diarrhea and thickening of the bowel wall.

Diagnosis

Diagnosis of food allergy in the horse is protracted as skin tests and serologic tests are unreliable for this purpose. Initially all suspect cases must be placed on an **elimination diet**. As food allergy has not been recorded in association with meadow or ley grass hay or grass, ideally animals should either be turned out to grass or fed only on hay and bedded on hay, shavings, rubber matting, dirt or sand.

If hay and grass alone are inadequate for the nutritional requirements of the horse, it is necessary to supplement the diet with a single cereal such as oats and observe for a period of not less than 4 wk for evidence of improvement. If this is not evident, the cereal should be changed and the animal monitored. Once improvement has been achieved then provocative challenge can be commenced, allowing at least 7–10 days between each new dietary constituent. Alfalfa may offer an adequate plane of nutrition as the sole foodstuff but has been implicated in adverse cutaneous food reactions and so would only be appropriate in a horse that had not previously received this food.

It is important to be aware that **inhalation** of allergens during feeding may result in allergic rhinitis, conjunctivitis, asthma and even cutaneous signs in sensitized animals. Food allergens may initiate such reactions, but they are more frequently encountered in horses sensitized to dust, fungal spores, yeasts or mite debris.

ALLERGIC CONTACT DERMATITIS

Etiology

Allergic contact dermatitis results from a **type IV (cell-mediated)** allergic response to an agent that has been repeatedly applied directly to the skin.

The capacity for agents to induce an allergic hypersensitivity response (*q.v.*) is extremely variable. Certain substances such as **dinitrochlorobenzene** are powerful contact sensitizers possessing the capacity to stimulate allergic responses in a very high percentage of animals within a few weeks. Other substances are immunologically inert and despite continuous or repeated contact rarely, if ever, induce an allergic response.

Most contact sensitizers are haptenic and require to become conjugated either covalently or otherwise to dermal or epidermal proteins before reaching full antigenicity and stimulating a T lymphocyte cell response. Contact allergens may be either very simple substances of low molecular weight (e.g. chrome, nickel, iodine) or be slightly heavier and complex (formaldehyde, oleoresins and certain synthetic dyes).

Unlike chemical contact reactions, a response is never noted following initial exposure, and continuous or repeated intermittent contact over many months

or several years is often required before an allergic response is induced. Between the time of exposure to the causal allergen and the sudden appearance of skin changes there is a lag phase that varies from 1 to 5 days.

The severity of the skin changes noted in allergic contact dermatitis is unrelated to the volume or concentration of the applied substances. Severe reactions often follow the application of only **molecular amounts** of allergen.

Clinical signs and diagnosis

The lesions of allergic contact dermatitis are **confined to the areas of exposure**. They may present as well-defined areas of hyperemia, scaling and irritation, cutaneous edema, exudation and irritation with varying degrees of hair loss, or pruritus only. If the condition continues undiagnosed and untreated, secondary changes including skin thickening, increased pigmentation, extensive hair loss and secondary infection may occur.

Close study of the skin changes and their distribution will usually give an indication as to the possible allergens responsible. Responses to fabrics are uncommon, but allergic responses to dyes in blankets, rugs and numnahs/saddle pads and reactions to chrome tanning agents in harness may be encountered. Less frequently, reactions to skin washes and dressings and certain plants may occur.

Treatment and prevention

Having identified the source of the allergy, steps should be taken to prevent further contact, as sensitivity, once established, will **persist throughout life**. Even after further contact has been prevented, irritation is likely to persist for some time and it is essential that affected areas be gently but thoroughly washed to remove as much allergen as possible. It may be necessary in some cases to use short-acting systemic steroid therapy.

Confirmation of the diagnosis may be obtained by **patch testing** an area of skin, either with the agent concerned or an extract, and observing the area every 8 h for at least 4 days for evidence of local irritation or other skin changes. Convenient test sites include the sides of the face and neck. Unless hair is very short, clipping is advised prior to application of suspect agents. **Skin biopsy** of test sites may be undertaken to demonstrate the typical histopathology of allergic contact dermatitis.

CULICOIDES HYPERSENSITIVITY

Etiology

Type I and type IV hypersensitivity reactions to the bites of *Culicoides* spp. (midges, "no-see-ums") are the cause of the syndrome also known as "sweet itch", "kasen", "Queensland itch", "muck itch", "dhobie itch" or "Sommerekzem" (*q.v.*). In most geographic locations these insects feed primarily at dusk and dawn, less so during the night, and not during the day. Windless conditions with temperatures above 10°C are ideal for their activity. *Culicoides* spp. breed in areas of moist, muddy ground around ponds, marshes, ditches and tidal flats.

Clinical signs and diagnosis

The onset of this problem occurs between 1 and 4 yr of age or between 1 and 4 yr after first exposure to the insects. It is seasonal, occurring in the summer and early autumn. In tropical and subtropical locations the season may last for 9–10 mo of the year. During the **first year**, the condition tends to be mild, worsening each year thereafter as long as exposure to the insects continues.

Pruritus is the major manifestation of this condition and causes the self-inflicted lesions. The classically described disease affects the head, ears, mane, withers, rump and tail. However, some species of the *Culicoides* insect prefer to feed in other areas on the animal, resulting in lesions with a different distribution. Ventrally distributed lesion may also occur involving the intermandibular space, chest, upper forelegs, the ventral abdomen and the inguinal region. The pruritus experienced by hypersensitive horses causes rubbing and self-trauma which results in alopecia, lichenification, crusting, erosions, ulcerations, fissures, wrinkling or corrugation of the skin, and secondary infections.

Diagnosis is based on history and clinical signs. Intradermal skin testing can be useful for confirming the clinical diagnosis, although appropriate antigens may not be available commercially. Biopsy findings of perivascular cuffs of mononuclear cells and eosinophils suggest allergic dermatitis but are not diagnostic for an etiologic agent. The parasitic manges, other insect hypersensitivities and cutaneous onchocerciasis should be ruled out (*q.v.*).

Treatment and prevention

Treatment requires **prevention of further exposure** to the insects and relief of inflammation. Exposure to the insects is eliminated by housing in **insect-proof stables** from late afternoon until well after dawn. Where stabling is not possible, use of insect-proof blankets may offer protection. Daily to twice daily application of insect repellents containing **permethrins** may be useful, but is likely to be ineffective without stabling. Fine-mesh screening or netting, ceiling fans or strategically placed box fans, and automated insecticide misters may aid in situations where the stables cannot be fully enclosed. **Drainage** of ponds, marshes and boggy areas where the *Culicoides* insects breed may be helpful when environmental regulations allow such alterations. Transfer of affected animals to higher, drier pastures or to drier geographic locations often results in complete or near-complete resolution of signs.

Inflammation is treated systemically with **glucocorticoids**. Initial doses of prednisolone or prednisone required to control the severe itch may be as high as 2 mg/kg daily. If insect exposure is not controlled, it is impossible to reduce this induction dose to lower and safer levels. Some relief of pruritus can be achieved by bathing in tar and sulfur-based shampoos. Secondary bacterial infections should be treated appropriately.

Nightly stabling of affected animals should begin from before the onset of the insect season and continue until the insects subside in the fall. A single night's exposure during the insect season can cause itching that may last as long as a month.

This condition has been seen in related animals, suggesting a **genetic predisposition**. Affected animals should be removed from breeding programs.

OTHER IMMUNE-MEDIATED CONDITIONS

PEMPHIGUS FOLIACEUS

Etiology

Pemphigus foliaceus is the most common autoimmune skin disease (*q.v.*) of horses. Autoantibodies directed against epidermal cell surface antigens result in loss of intercellular cohesion, acantholysis and the formation of vesicles in the epidermis.

Clinical signs

Skin lesions often begin on the **face or limbs**, but in younger horses commonly become generalized; in older horses the lesions may be restricted to the coronary bands, ergots and chestnuts. The primary lesion is a **pustule or vesicle**, but these are transient and the usual presentation is of a crusting, scaling dermatosis with oozing, annular erosions and alopecia. Lesions are variably **painful or pruritic**. A **Nikolsky sign** may be present (separation of upper epidermis by pressure, indicating poor cellular cohesion). Many horses show concurrent systemic signs.

Diagnosis

Cytologic examination of vesicle or pustule contents reveals acantholytic keratinocytes and non-degenerate neutrophils and/or eosinophils, with an absence of bacteria. Histologic examination of intact primary lesions is diagnostic. The characteristic pathology consists of intragranular to subcorneal intraepidermal vesico-pustules containing acantholytic cells.

Direct immunofluorescence testing reveals diffuse intercellular deposition of immunoglobulin (IgM, IgG) and, usually, complement in the epidermis. However, false negative results may be obtained after administration of glucocorticoids, and false positive results may be seen in other skin diseases.

Treatment

Therapy of pemphigus foliaceus depends upon the use of **immunosuppressive drugs** and permanent therapy is often required. The initial drug of choice is **prednisolone**, at doses of 1 mg/kg s.i.d. by mouth. Improvement should be evident within 7–10 days, and alternate day therapy can be initiated once lesions are controlled, reducing to the lowest possible maintenance dose. An alternative glucocorticoid is dexamethasone, at doses of 0.2 mg/kg PO s.i.d.

If the condition is resistant to corticosteroids or unacceptable doses are required to control lesions, **gold salts** (chrysotherapy), e.g. **sodium aurothiomalate** (Myocrisin, Myochrysine), have been used successfully in the management of equine pemphigus foliaceus, as an adjunct to steroid therapy. Aurothiomalate is given IM, initially in two test doses of 20 and 40 mg 1 wk apart, followed by weekly injections of 1 mg/kg. There is usually a 6–12 wk lag phase before a response is seen. Once the condition is controlled, injections may be given monthly. It may be possible to withdraw concurrent steroid therapy. Adverse reactions are reported in other species, including blood

dyscrasias, proteinuria and skin eruptions, and periodic hematologic examinations and urinalysis are advised. Azathioprine has been used in a few animals but there is little published information available regarding its use.

BULLOUS PEMPHIGOID

Etiology

Bullous pemphigoid is a rare autoimmune skin disorder (*q.v.*) of the horse resulting from autoantibodies directed against basement membrane of skin and/or mucosa. This results in subepidermal cleft formation due to dermoepidermal separation and vesicobullous formation.

Clinical signs

The primary lesions are vesicles or bullae, but these rapidly ulcerate. Lesions may affect oral mucosa, mucocutaneous junctions and skin, particularly in the axillae and inguinal areas. Ulcers, crusts and epidermal collarettes are the usual lesions, with variable pain or pruritus. Systemic signs of anorexia, fever and depression may be present.

Diagnosis

Bullous pemphigoid must be differentiated from viral diseases such as horsepox, herpes coital exanthema and vesicular stomatitis, systemic lupus erythematosus and drug eruptions (*q.v.*). **Skin biopsy** is strongly suggestive or diagnostic, as long as intact vesicles are obtained. Histopathologic findings are subepidermal vacuolation, clefting and vesicle formation with mild to moderate perivascular inflammatory infiltrates. Direct immunofluorescence testing demonstrates linear deposits of immunoglobulin and, usually, complement at the dermoepidermal junction. Correct choice of biopsy site and absence of steroid therapy is important for immunofluorescence testing.

Treatment

High doses of **glucocorticoids** are indicated in the management of bullous pemphigoid. Therapy, if successful, is prolonged, if not permanent. Prednisolone 1 mg/kg PO b.i.d. or dexamethasone 0.2 mg/kg PO s.i.d. is the initial treatment of choice, reducing to the lowest possible maintenance dose on alternate mornings. Chrysotherapy, azathioprine and chlorambucil have been used in the management of bullous pemphigoid in dogs and humans, but reports of successful management of equine cases are lacking.

SYSTEMIC LUPUS ERYTHEMATOSUS

Etiology

Systemic lupus erythematosus (SLE) is a rare multisystemic autoimmune disorder (*q.v.*) of horses. Several factors, including genetic predisposition, viral infections, hormones, ultraviolet light and immune disorders, are involved in the etiology of SLE.

Clinical signs

Cutaneous signs described in the rare reports of equine SLE include symmetrical alopecia, seborrhea, scaling, panniculitis and edema of the extremities. Systemic involvement may include hemolytic anemia, thrombocytopenia, arteritis, proteinuria, fever, depression and weight loss.

Diagnosis

Definitive diagnosis of SLE can be **challenging** and depends on demonstration of multisystemic involvement and the identification of various autoantibodies. A positive antinuclear antibody test and lupus erythematosus cell test supports the diagnosis, but results must be interpreted with care as both false positives and negatives may occur. The dermatohistopathology in SLE can be variable, but an interface dermatitis with hydropic degeneration, single cell necrosis of the basal cell zone, focal thickening of the basement membrane, hyperkeratosis and lymphocytic dermal inflammation are typical features. Direct immunofluorescence testing may reveal linear deposition of immunoglobulins at the basement membrane zone of epidermis and hair follicles.

Treatment

Cases of equine SLE have been treated with **prednisolone** at initial doses of 1 mg/kg PO b.i.d., reducing to the lowest possible maintenance dose on an alternate day basis. However, the response to therapy is unpredictable and the prognosis guarded.

CUTANEOUS (DISCOID) LUPUS ERYTHEMATOSUS

Etiology

Cutaneous, formerly discoid, lupus erythematosus (DLE) is thought to be a benign variant of SLE (*q.v.*) with cutaneous manifestations and no systemic involvement. **Ultraviolet light** seems to be an aggravating factor, with exacerbation of lesions in sunny weather. It is a rare dermatosis of the horse.

Clinical signs

Skin lesions are seen on face, ears and neck, and typically consist of areas of patchy alopecia, erythema, scaling and crusting, sometimes with leukoderma and leukotrichia. Affected horses are well in other respects.

Diagnosis

Histologic examination of skin biopsies reveals hydropic and lichenoid interface dermatitis. Direct immunofluorescence testing reveals deposits of immunoglobulin and/or complement at the dermoepidermal junction. Antinuclear antibody tests and lupus erythematosus cell tests are negative.

Treatment

The management of DLE includes avoidance of sunlight by stabling during daylight hours, use of topical sunscreens and the use of topical corticosteroids

(1% hydrocortisone, 0.1% betamethasone valerate). Refractory cases may require systemic glucocorticoids, prednisolone at initial doses of 1 mg/kg PO once or twice daily (or dexamethasone 0.2 mg/kg PO s.i.d.), reducing to the lowest possible alternate day maintenance dose.

This more benign autoimmune skin disease carries a better prognosis than those described above, but long-term management regimens may be required to keep the condition in remission.

DRUG ERUPTIONS

Etiology

Many classes of drugs can potentially cause a reaction, which may include cutaneous eruptions. Drugs that have been implicated in horses include antibacterial agents, particularly **penicillin** and **sulfonamides**; **phenothiazine tranquilizers**; non-steroidal anti-inflammatory agents, particularly **aspirin** and **phenylbutazone**; **local anesthetics**; **anticonvulsants**; certain **biological products**; and various **topical preparations**. Cutaneous eruptions may follow systemic administration by any route or topical application. Hypersensitivity reactions are thought to be involved in the etiopathology of drug eruptions, but non-immunologic mechanisms such as toxicity, photosensitivity (*q.v.*) and idiosyncratic reactions may also be involved. Drugs may be immunogenic in their own right or may act as haptens that bind to host proteins. Type I, II, III and IV hypersensitivity reactions (*q.v.*) may be involved.

Clinical signs

Drug eruptions can mimic many dermatoses, and no specific type of reaction is seen. Possible manifestations include urticaria, papular dermatitis, generalized dermatitis, vesicular dermatitis and ulcers secondary to vasculitis. Histopathologic findings are similarly varied with perivascular dermatitis, interface dermatitis, intraepidermal and subepidermal vesicular dermatitis all being possible reaction patterns in biopsies. A drug eruption may occur after only short exposure to an offending drug or after years of administration, and may even appear a few days after drug therapy has stopped.

Definitive diagnosis can be difficult. All other possible causes of the skin lesions must be excluded. A high index of suspicion and a detailed history of drug administration are required. Withdrawal of the offending drug should result in resolution of lesions within 10–14 days. It may be difficult to pinpoint the causal agent in animals on several drugs, and intentional re-exposure to the suspected drug to confirm the diagnosis is contraindicated since it may result in fatal anaphylaxis.

Treatment and prevention

All suspected medications should be discontinued, and appropriate supportive measures indicated. Drug eruptions are often poorly responsive to corticosteroids. If concurrent disease requires continued therapy, then unrelated drugs should be substituted. Chemically related compounds should be avoided in the future.

CUTANEOUS VASCULITIS

Etiology

Cutaneous vasculitis (*q.v.*) is an uncommon disorder in horses, thought to involve type I and III (immune complex) hypersensitivity reactions (*q.v.*). In most cases the etiologic agent is unclear. However, cutaneous vasculitides may accompany certain infections, notably **streptococcal infection** (strangles), *Corynebacterium pseudotuberculosis* infection, salmonellosis, equine viral arteritis and equine influenza (*q.v.*). In some cases lesions restricted to white-skinned and white-haired areas implicate photoactive mechanisms.

Clinical signs

The lesions of idiopathic cutaneous vasculitis commonly occur on the distal limbs, lips, pinnae and periocular regions and consist of purpura, edema, erythema, necrosis, ulcers and crusts. Oral involvement may be seen. Lesions may be painful and affected horses may show systemic signs including pyrexia, anorexia, depression and weight loss.

Purpura hemorrhagica (*q.v.*) is the manifestation of the cutaneous vasculitis that may complicate infectious conditions of the horse. Cutaneous lesions consist of edematous, hemorrhagic subcutaneous swellings of the distal limbs, ventrum and head. Exudation, necrosis and sloughing may follow. Petechial and ecchymotic hemorrhages are seen on mucous membranes.

Diagnosis

Cutaneous vasculitides must be differentiated from autoimmune disease, equine viral arteritis, drug eruptions and toxicosis (*q.v.*). The definitive diagnosis is based upon history, physical examination and biopsy. Histopathologic findings consist of neutrophilic (leukocytoclastic), eosinophilic, lymphocytic or mixed vasculitis, often with fibrinoid degeneration. Diagnostic changes are most likely to be found in lesions 8–24 h old. Horses with purpura hemorrhagica may show mild anemia, neutrophilia with left shift, elevated plasma fibrinogen and globulin concentrations. Platelet counts are normal. Direct immunofluorescence testing may demonstrate immunoglobulin and/or complement in vessel walls, but is not essential for diagnosis.

Treatment

Once a diagnosis of vasculitis has been made, attempts must be made to identify and eliminate underlying causal factors. The progress of the disease depends on the extent of damage in each individual case. There may be only a single, short-lived episode or the disease may be chronic or recurrent.

In idiopathic cases many horses will respond to **glucocorticoid** therapy (prednisolone 2 mg/kg/day PO in single or divided doses; dexamethasone 0.2 mg/kg/day). Maintenance alternate day therapy may be needed. In cases of purpura hemorrhagica the prognosis is better if therapy is initiated early and consists of aggressive **appropriate antibiotic therapy** (e.g. penicillin 22 000 IU/kg b.i.d.), control of edema with **diuretics** (e.g. furosemide) and limitation of the hypersensitivity response (glucocorticoids). Hydrotherapy, gentle exercise, massage and bandaging may be beneficial.

Prevention

Avoidance of sunlight is indicated in cases where photoactive factors are implicated. Any other agents that are identified as possible causal factors should similarly be avoided.

ERYTHEMA MULTIFORME

Etiology

The pathogenesis of this cutaneous reaction pattern is not fully understood, although many triggering factors have been recognized. Hypersensitivity reactions are believed to be involved. In the horse, erythema multiforme has been associated with **potentiated sulfonamide therapy** and idiopathic cases are described.

Clinical signs

Erythema multiforme is a rare, acute, self-limiting dermatosis. The skin lesions are urticarial plaques, maculopapular or vesicobullous lesions, which clear centrally and expand peripherally to give annular (doughnut), arciform and polycyclic shapes. These lesions persist for days to weeks. Scaling, crusting and alopecia are not features. The cutaneous lesions are generally asymptomatic.

Diagnosis

Definitive diagnosis is based on typical clinical findings and skin biopsy. The characteristic histopathologic features are a hydropic interface dermatitis, single cell necrosis in the basal epidermis, with or without superficial dermal edema. Massive subepidermal edema and confluent areas of full thickness coagulation necrosis may result in the development of vesicular lesions.

Erythema multiforme is a cutaneous reaction pattern and evaluation for the presence of underlying causes such as a drug reaction, infection and neoplasia is indicated.

Treatment

Any underlying cause identified should receive appropriate management. The cutaneous lesions are usually self-limiting and require no specific therapy, resolving within 3 wk to 3 mo. Avoidance of implicated causal factors is necessary to prevent the condition.

CUTANEOUS AMYLOIDOSIS

Etiology

Secondary or reactive amyloidosis associated with chronic infections rarely produces skin lesions. **Primary amyloidosis** is usually restricted to the skin and/or upper respiratory tract. Cases with simultaneous cutaneous and systemic amyloidosis have been reported rarely. The amyloid fibrils in cutaneous amyloidosis are derived from immunoglobulin light chains. There is usually no known triggering factor.

Clinical signs

Cutaneous amyloidosis is a rare skin disease of horses, characterized by papules, nodules and plaques and most commonly affecting the head, neck

and pectoral region. Lesions are firm, well circumscribed, non-painful and non-pruritic and covered by normal skin. Although in some cases early lesions may appear urticarial and regress initially, they recur and the condition becomes chronic and progressive.

Diagnosis

Histopathologic examination of skin biopsies reveals amorphous, homogeneous hyaline, eosinophilic deposits of amyloid intra- and extracellularly with an accompanying granulomatous dermatitis with numerous multinucleated, histiocytic giant cells. Congo red stain demonstrates amyloid in tissue, with an apple-green appearance when viewed by polarizing microscopy. Other special stains that may be used include crystal violet and thioflavin. Transmission electron microscopy reveals characteristic amyloid fibrils, 6–10 nm thick, twisted but straight and unbranched.

Treatment and prognosis

There is no effective treatment for amyloidosis. Glucocorticoid therapy has been ineffective. However, if there are no respiratory or systemic lesions then horses may survive for prolonged periods. It may be wise to advise against breeding affected animals since there is evidence of inheritance of certain forms of cutaneous amyloidosis in humans.

EQUINE EOSINOPHILIC EXFOLIATIVE DERMATITIS AND STOMATITIS

Etiology

Eosinophilic exfoliative dermatitis and stomatitis (EEDS) is a rare disorder characterized by eosinophilic infiltration of epithelial tissues, predominantly affecting skin and intestinal tract and associated organs. The condition has been reported in Canada, Australia, the USA, Sweden, the UK and France. The etiology is unknown, but hypersensitivity mechanisms and epitheliotropic cell-associated virus and genetic predisposition in Standardbreds have been postulated.

Clinical signs and diagnosis

Skin lesions often appear in the winter in stabled horses of any age, sex or breed. Scaling, crusting, oozing, alopecia and fissures are seen affecting the face and/or coronary bands. Early in the course of the condition oral ulceration is common. There is progression to a generalized exfoliative dermatitis with extensive alopecia, scaling, exudation, crusting and ulceration. Variable pruritus may be encountered. Systemic signs of progressive, severe weight loss become apparent, despite a normal or even increased appetite.

Laboratory findings that may be present include hypoalbuminemia, leukocytosis and mild anemia. Circulating eosinophilia is rare. Dermatohistopathology reveals superficial and deep perivascular dermatitis. The infiltrate is eosinophilic and lymphoplasmacytic. Irregular ortho- and parakeratotic hyperkeratosis with irregular epidermal hyperplasia is seen, together with necrosis of single keratinocytes. Eosinophilic microabscesses and granulomas may also

be features. Eosinophilic inflammation of other epithelial organs is common. Direct immunofluorescence testing has given negative results.

Treatment

There is no known effective treatment. Immunosuppressive doses of glucocorticoids have failed to reverse the condition, which progresses over a period of months, ultimately requiring euthanasia.

EQUINE SARCOIDOSIS/GENERALIZED GRANULOMATOUS DISEASE (GGD)

Etiology

This is an uncommon condition of unknown etiology characterized by granulomatous inflammation of many organ systems with cutaneous involvement. The disease resembles human sarcoidosis.

Clinical signs and diagnosis

Skin lesions are the major presenting sign, with generalized scaling and crusting with varying degrees of alopecia most commonly described. Cutaneous nodules may be present in addition to the exfoliative dermatitis or as the only skin lesions. Peripheral lymphadenopathy may be present. Systemic signs include weight loss, decreased appetite and persistent pyrexia.

Laboratory findings may include leukocytosis, increased fibrinogen, elevated globulins and, in severe cases, mild anemia. Hepatic and renal function tests may be abnormal.

Definitive diagnosis is based on histopathologic examination of skin biopsies. The major feature is the presence of non-caseating granulomas consisting of aggregates of epithelial cells and multinucleated giant cells located in the superficial to mid dermis. Sarcoidal granulomas are also found in many other tissues including lymph nodes, lungs, gastrointestinal tract, liver and spleen. Direct immunofluorescence testing of affected skin has been negative, as have attempts to demonstrate involvement of pathogenic organisms.

Treatment

Although a few horses have undergone spontaneous remission, most cases suffer progressive dermatitis and wasting requiring euthanasia. The administration of high doses of **glucocorticoids** early in the course of the disease may be helpful. Prednisolone should be given at doses of 2 mg/kg PO initially, reducing the daily dose once a response is seen, ultimately to alternate day therapy. However, equine sarcoidosis would appear to be a more severe disease than human sarcoidosis, justifying a guarded to poor prognosis.

NEOPLASTIC SKIN CONDITIONS

Skin tumors account for two thirds of all reported equine neoplasms. As in any species, neoplastic change can occur in any component of the skin but in horses

certain tumor types predominate. In approximate descending order these are sarcoid, squamous cell carcinoma, melanoma, papilloma and others (*q.v.*).

To enable appropriate management, including prognosis and treatment, a **specific diagnosis** should be obtained in all cases. While clinical features may be suggestive in many cases, only histopathologic examination can give a definitive diagnosis. Treatment modalities (*q.v.*) including surgery, cryotherapy, electrocautery, irradiation, chemotherapy and immunotherapy may be used individually or in combination; the tumor type and site will dictate which is most applicable.

SARCOID

Etiology

Equine sarcoids are **locally aggressive**, **non-metastatic fibroblastic tumors**. The term is often used to encompass fibroma, fibroma-like tumor, neurofibroma and low-grade fibrosarcoma as well. While these other tumors can be distinguished histopathologically, the clinical appearances, behavior and treatment are similar. Equine sarcoid is a **common clinical entity** that may cause loss of use of the horse and also an **esthetic problem**. A viral etiology has been suggested, with bovine papillomavirus DNA detected in many samples. Possible transmission routes may include flies, rubbing posts and shared equipment. A **genetic predisposition** is also suggested.

Clinical signs

Based on gross appearance, sarcoids can be divided into four groups: occult (flat), verrucous (warty), fibroblastic (proud flesh-like) and mixed verrucous–fibroblastic. Some classifications also include nodular (overlying skin normal) and malevolent (invasive and infiltrative) types.

The most common is the **fibroblastic type**, which presents as a firm, mobile nodule up to several centimeters in diameter within the dermis; this form must be differentiated from other tumors including melanoma, fibroma and neurofibroma/sarcoma (*q.v.*) as well as inflammatory conditions including cutaneous habronemiasis and other nodular skin diseases (*q.v.*). This type of sarcoid may become ulcerated and more exuberant in appearance with a hemorrhagic and purulent discharge; in this state it may be mistaken for granulation tissue (*q.v.*) and must also be differentiated from squamous cell carcinoma (*q.v.*).

The second form is the so-called "**verrucose sarcoid**" with a dry, keratinized, warty appearance; this type should be differentiated from squamous papilloma and dermatophytosis (*q.v.*). The third, **mixed form**, is a combination of the fibroblastic and the verrucose types. The **occult form** presents as a thickened plaque-like area of roughened skin with scant hair. The occult and verrucose forms may develop into the fibroblastic sarcoid, especially when subjected to **repeated trauma**. Although in many cases the physical appearance may be typical of an equine sarcoid, a definitive diagnosis requires histopathologic examination and this should be performed before treatment is started.

Sarcoids can affect any breed and either sex, and there is no association with coat color. There may be an increased incidence in young adult horses. The tumor may be solitary but in a third of cases there will be multiple lesions.

Predilection sites include the ventral abdomen, groin and inner aspect of the thigh, the axillae and head, in particular the lip commissures, periorbital tissue and the base of the ears. When sarcoids occur in the groin and axilla it is not uncommon for **"kissing" lesions** to be present on touching skin folds, suggesting transplantation of neoplastic tissue.

Prognosis

The success of treatment depends on a number of factors and this should be explained to the owner at the outset. The location, size and number of lesions are important considerations; sarcoids of the extremities, axilla and groin may be more difficult to treat, while those affecting periocular regions have been found more responsive to treatment. **Recurrence** of sarcoids is a common problem and repeated treatment may be required for complete resolution in some individuals.

Treatment

Simple **surgical excision** has a high failure rate (50%). Recurrence, usually within 6 mo, may be due to incomplete excision or to iatrogenic transplantation at the time of surgery. Electrocautery may help control blood loss but does not significantly increase the success rate.

Cryotherapy (with or without diathermic resection) (*q.v.*) gives the most consistent results with a high success rate (up to 95%), although **repeated treatments** may be required. The procedure may be possible using local anesthesia and sedation but more commonly general anesthesia is required. The size and position of the lesion, the temperament of the horse and the facilities available are factors influencing this decision.

Stimulation of the host immune system can be achieved by the administration of foreign material. For the treatment of equine sarcoids, various preparations of the vaccine strain of *Mycobacterium bovis* **bacillus Calmette–Guérin** (BCG) have been used. In the UK only the live, freeze-dried form is available as human percutaneous BCG vaccine, but cell wall preparations have also been used with greater efficacy and fewer side effects. Reported side effects after administration of live BCG include anaphylaxis and death (rare), fever, diarrhea, laminitis and active granulomas. The tumor becomes edematous and painful following treatment; this progresses to ulceration with a purulent discharge. Regression of the lesion proceeds from the second or third week but may take several months before it is complete.

Unlike cryotherapy, BCG immunotherapy (*q.v.*) is relatively free from significant scarring and therefore is particularly useful for **sarcoids of the eyelids**. The response to therapy can be good with reported success rates ranging from 50% to 75%. However, the potential for significant adverse reactions should always be considered before embarking on BCG immunotherapy.

Immunotherapy with non-viable ***Propionibacterium acnes*** is available in the USA and good results are claimed.

Many **topical products** have been used in the treatment of sarcoids, including the antimetabolite **5-fluorouracil** and **podophyllin**, an irritant used in management of warts. Bloodroot extracts and other caustic chemicals may induce sloughing of lesions. Good success can be obtained with a topical ointment

available from the University of Liverpool[1], **AW4-LUDES**, which contains a variety of heavy metals and antimitotic compounds. Imiquimod cream, which stimulates the production of a variety of cytokines including interferons, is also anecdotally of benefit.

Intralesional injections of an emulsion of cisplatin (*q.v.*) in oil and water after surgical debulking (1 mg/cm^3 of tissue on four occasions at 2 wk intervals) have given good relapse-free survival rates without side effects.

Radioactive implants (iridium-192 and gold-198) (*q.v.*) have been used with a high success rate (up to 100%) with minimal complications. However, this form of therapy can only be performed on designated premises by a suitably qualified person; the cost of implants may be prohibitive for certain cases.

SQUAMOUS CELL CARCINOMA

Etiology

Although squamous cell carcinoma (SCC) may arise at any site on the skin, it more commonly occurs at **mucocutaneous junctions**. In particular, the conjunctiva, the eyelids, the prepuce, the penis and the vulva appear to be predilection sites (a fuller discussion of these affected sites is given elsewhere). Chronic exposure of poorly pigmented, relatively hairless areas to **UV light** has been implicated in the development of SCC involving the eye and periocular sites, and **smegma** has been associated with SCC of the penis and prepuce.

Clinical signs

Unlike humans and cats, SCC in the horse tends to be a **proliferative** rather than an erosive lesion. The clinical appearance ranges from a sessile nodular mass that has to be differentiated from a sarcoid through to an exuberant cauliflower-like growth with secondary ulceration, hemorrhage and infection. SCC must be differentiated from granulation tissue, sarcoid, cutaneous habronemiasis and other cutaneous tumors (*q.v.*); definitive diagnosis should be by histopathology.

Prognosis and treatment

SCC is a locally invasive tumor. It does not commonly metastasize and then only as far as the draining lymph node; the lungs are rarely involved. SCC of the **prepuce and penis** tends to be more aggressive and metastasis is more common than from other sites. Treatment of SCC may be by radical excision, cryosurgery or radiotherapy (external beam or implant (*q.v.*)). Intralesional **cisplatin** and topical 5-fluorouracil have also been beneficial (*q.v.*).

MELANOMA

Etiology

Melanoma is a common skin neoplasm in horses, especially in **aged grays**. The tumor is rare in animals <6 yr old. Approximately **80% of gray horses >15 years old** have melanotic masses; however, not all are truly neoplastic. In some cases, a disturbance of melanin metabolism occurs and **focal hyperplasia** of melanocytes occurs; this can predispose to malignant transformation.

[1] Contact Professor Derek Knottenbelt (e-mail address: knotty@liv.ac.uk)

Clinical signs

Melanoma can develop at **any site** but areas of predilection include the perineum, vulva, the underside of the dock, the male genitalia, and also the limbs, neck and ear. The tumors can be solitary or multiple, hard or soft nodules in the subcutaneous tissue. The cut surface is typically dark brown or black but the less common amelanotic melanoma is unpigmented. Definitive diagnosis requires histopathology, although needle aspirate cytology can be useful. However, in gray horses the physical appearance alone may be sufficient to make the diagnosis.

Prognosis

Clinically, three growth patterns exist. The most common is a **slow growth** over a period of years without metastasis; the second is a similar initial pattern but with **sudden malignant transformation and metastasis**; and, finally, melanoma can behave in a **malignant** manner from the outset. Metastatic spread is often widespread to all organs of the body. Melanomas in non-gray horses tend to be more aggressive than in grays.

Treatment

Treatment of melanomas, especially advanced cases, can be unrewarding. Local resection of early solitary lesions or masses that are frequently traumatized can be of benefit. Immunotherapy and irradiation are of little value, although a polyvalent allogeneic antigen-supplemented vaccine has been used in horses with multicentric melanomas (*q.v.*). **Cimetidine** (*q.v.*) has been reported to produce partial to complete remission using an initial dose of 2.5 mg/kg t.i.d., reducing to a lower maintenance dose if there is a favorable response. Others believe cimetidine is of little therapeutic benefit.

MAST CELL TUMOR

Etiology and clinical signs

Mast cell tumors are rare in horses and, in fact, may be hyperplastic aggregations rather than true neoplasms. The lesions of up to 20 cm diameter are usually solitary, occurring most commonly on the head and limbs. The mass may vary from well to poorly circumscribed and may be dermal or subcutaneous. Ulceration, alopecia and hyperpigmentation may occur. The masses are usually self-limiting and regress spontaneously; metastasis has not been reported.

Treatment

Surgical excision has a high success rate, and intratumoral (*q.v.*) corticosteroid therapy is useful to control solitary lesions.

CUTANEOUS LYMPHOMA

Etiology and clinical signs

Lymphoma (*q.v.*) in the horse can occur as a cutaneous neoplasm with solitary or multiple dermal or subcutaneous nodules. Concurrent systemic involvement

is usually present with lymphadenopathy, depression and weight loss, although the disease may be restricted to the skin alone, at least initially. The physical appearance of the skin lesions varies from firm nodules with relatively normal overlying skin to ulcerating plaques; lesions can occur at any site on the body. Lymphoma in the horse tends to be progressive and is ultimately fatal. Biopsy is necessary to confirm the diagnosis.

Treatment

No successful treatment has been found. Corticosteroid therapy may give some palliation.

ADNEXAL TUMOR

Benign (adenoma) and malignant (adenocarcinoma) tumors of the sebaceous and sweat glands and the hair follicles are rare in horses.

BASAL CELL TUMOR

Basal cell tumor is a rare condition in the horse. This neoplasm is not known to metastasize or to undergo transformation to its malignant counterpart, squamous cell carcinoma. Wide excision is curative.

KERATOMA

Etiology and clinical signs

Keratoma (*q.v.*), a benign tumor of the keratin-producing cells of the hoof wall, is not a common condition of horses. It may not be a neoplasm but rather may represent a **chronic localized hyperplastic reaction** following injury to the hoof wall or coronet. The mass develops between the hoof and the third phalanx and may cause lameness if it impinges on the underlying sensitive laminae and/or bone; in some individuals it is an incidental finding.

Keratomas appear more frequently to affect the toe region. The mass may cause deformation of the hoof or deviation of the white line. Commonly, however, there are no external signs and the problem can only be localized by selective nerve blocks or radiography. Necrosis of the pedal bone due to the pressure of the mass shows as focal loss of bone.

Treatment

Treatment is by surgical excision. As long as complete removal is achieved, the prognosis is good.

OTHER TUMORS

Other tumors of the skin have been reported but may be considered rare. Treatment should be by wide surgical excision and/or cryotherapy. In the main, prognoses have to be based upon extrapolation from other species and should, at least, be guarded.

CUTANEOUS ENDOCRINOPATHIES

HYPERADRENOCORTICALISM (CUSHING'S SYNDROME)

Etiology

The plasma glucocorticoid concentration is elevated, most commonly due to excessive secretion of adrenocorticotropic hormone (ACTH) arising from **adenoma of the pars intermedia** of the pituitary gland (*q.v.*). Loss of sensitivity to dopaminergic feedback control from the hypothalamus is postulated. In addition to increased ACTH production from pituitary adenomas, other peptides such as β-endorphins, melanocyte-stimulating hormone and corticotropin-like intermediate lobe peptide may be secreted. There is failure of negative feedback mechanisms and, under the continual drive of ACTH, hyperplasia of the adrenal cortices ensues, with hypersecretion of cortisol and adrenocortical androgens. Occasionally, the disease may arise as a result of **adrenal neoplasia**.

Clinical signs

The disease is common, recorded in 10% of rescued horses in one study. The most striking feature of equine hyperadrenocorticalism is **hirsutism** (*q.v.*), the exact mechanism of which is unclear. Animals show an excessively long, dense and often curly haircoat, with failure of normal shedding. The mane and tail are usually spared. **Hyperhidrosis** is common, possibly due to abnormal hypothalamic thermoregulation as well as the effects of the thick haircoat. The underlying skin may appear relatively normal, although seborrhea may be present. Other cutaneous findings that may be present include infections and xanthomatous nodules. Bulging of the supraorbital fat pads may be present.

Systemic signs of hyperadrenocorticalism (*q.v.*) include **muscle wasting** and **pot-bellied appearance**, laminitis, chronic infections and often marked polydipsia (up to 80 L/day) and polyuria. Concurrent diabetes mellitus is quite common. Neurologic signs are present occasionally.

This is a condition of older horses and ponies: the average age at diagnosis is 19 years, and hyperadrenocorticalism is rare in horses <10 years old.

Diagnosis

Hematologic findings may include neutrophilia, lymphopenia and eosinopenia, although total white cell count may be normal unless secondary infection is present. Liver enzymes are usually elevated and hyperglycemia is common. Urinalysis reveals a low specific gravity, often glucosuria and sometimes evidence of urinary tract infection.

Definitive diagnosis depends upon the results of **hormonal assays**. Resting cortisol values may be elevated, but dynamic tests are required to confirm the diagnosis. ACTH stimulation tests and/or dexamethasone suppression tests (*q.v.*) may be employed.

Measurement of plasma ACTH concentration may be used to confirm the diagnosis. Although the test is sensitive, data on specificity are limited, but values >50 pg/mL indicate a probable diagnosis of the condition. Blood samples require special handling since ACTH is very labile.

An increase in plasma cortisol in response to thyrotropin-releasing hormone (TRH) injection (samples taken before and 30 min after injection) is also indicative of hyperadrenocorticalism, but the test has low sensitivity and specificity, particularly in horses with high basal cortisols or those that are unwell for other reasons.

A **combined dexamethasone suppression–TRH stimulation test** has been described which has increased sensitivity and specificity and allows easier interpretation than either test alone. The protocol is as follows:

1. A baseline blood sample is taken, followed by IM injection of 40 μg/kg of dexamethasone.
2. Three hours later a second blood sample is taken and 1 mg of TRH is given IV.
3. Half an hour later a third blood sample is taken.
4. The final sample is taken 22–24 h after the dexamethasone injection.
5. Samples are submitted for cortisol measurement.

In normal horses the baseline cortisol concentration is suppressed by dexamethasone, is unaffected by TRH administration, and remains suppressed the following day. Affected horses may show some initial suppression of basal cortisol 3 h after dexamethasone, but the concentration returns to basal or above after TRH and remains unsuppressed.

Treatment and prognosis

The prognosis for equine hyperadrenocorticalism is poor, **progression** of disease being likely. However, clinical signs can be ameliorated in many horses with treatment. The dopamine agonist **pergolide**, which interferes with peptide secretion by the pituitary tumor, is more effective than cyproheptadine, a serotonin antagonist, which probably interferes with ACTH secretion. A daily dose of pergolide of 1 mg daily for a 500 kg horse (0.002 mg/kg) is cost effective. If the response to treatment is suboptimal the dose can be increased incrementally to a maximum of 0.01 mg/kg PO daily. Anorexia and depression may occur at higher dose rates.

Trilostane, an inhibitor of steroid synthesis now licensed for the treatment of canine hyperadrenocorticalism, has been shown to be effective in improving clinical and laboratory abnormalities in horses with hyperadrenocorticalism, with no side effects observed. A dose of 1 mg/kg once daily in the afternoon or evening has been recommended.

A high plane of nutrition and good standard of care is required by these debilitated animals. The expense of treatment and the nature of the condition often result in owners requesting euthanasia.

HYPOTHYROIDISM

Etiology and clinical signs

Naturally occurring hypothyroidism (*q.v.*) is a rare condition of horses with few confirmed cases described in the literature. Deficiency of, or interference with uptake of, dietary iodine is the usual cause.

Clinical signs of hypothyroidism may be varied and diverse (*q.v.*). Cutaneous signs may include dry, scaling skin, dull haircoat, delayed shedding, alopecia and myxedema, particularly of the face and lower limbs. Histologic examination of skin biopsies reveals orthokeratotic hyperkeratosis, follicular keratosis, sebaceous gland atrophy, telogen hair follicles and dermal mucinosis.

Diagnosis

Basal thyroid hormone measurement is unreliable since many illnesses and concurrent drug therapy may result in low T_4 and T_3 concentrations. Dynamic testing is required to demonstrate hypothyroidism. A dose of 2.5 IU of thyroid-stimulating hormone (TSH) administered IV results in at least a doubling of baseline T_4 concentration 4 h later in normal horses. Since TSH is difficult to obtain and is expensive, the **thyrotropin-releasing hormone (TRH) response test** is likely to be the test employed. Blood samples are taken prior to and 4 h after IV injection of 1 mg TRH (0.5 mg in fit horses). The response in euthyroid horses should be 1.5–2 times the basal concentration, and within the normal range.

Treatment

For dietary-induced hypothyroidism **iodinated casein** at a dose of 5 g/day PO may be administered. Alternatively, supplementation with sodium levothyroxine (T_4) at a dose of 10 mg daily has been reported to be effective.

MISCELLANEOUS SKIN CONDITIONS

EOSINOPHILIC GRANULOMA (NODULAR NECROBIOSIS, COLLAGENOLYTIC GRANULOMA)

Etiology

The etiology is unknown, but is thought to be an **allergic response**. This is the most common nodular skin disease of the horse. There is no sex predilection and it occurs mainly in adult horses. It is rare in heavy horses and Thoroughbreds and more common in riding horses. The condition is seen more commonly in summer than winter months and for this reason **insect hypersensitivity** has been thought to play a role in the cause.

Clinical signs

Multiple, firm, nodular lesions are present located within the dermis, unattached to underlying tissue. No systemic signs have been described. The lesions are usually non-pruritic and, in most cases, non-ulcerating, spherical masses 1–2 cm in diameter. There is no associated hair loss, although the overlying hair may appear raised or tufted. Where lesions are close together coalescence may occur giving plaque-like masses of 10 cm diameter or more. Older lesions may become mineralized and some may show a small central ulceration in which white calcareous material may be seen. Lesions are mainly confined to the trunk, neck and upper limbs and are particularly common in the saddle area.

Diagnosis

Definitive diagnosis is based on history, clinical findings and skin biopsy. Histologic examination shows areas of granulomatous inflammation with fragmentation of collagen fibers, the predominant cell type present being the eosinophil. It has been demonstrated that true collagenolysis is not present, and the disrupted collagen fibers surrounded by eosinophilic material are now termed **collagen flame figures**. No parasites or other microorganisms are found in lesions. Eosinophilic folliculitis or furunculosis may be seen. Long-standing lesions show mineralization. **Differential diagnosis** includes bacterial furunculosis, abscess, mycetoma, urticaria, fibroma, lymphosarcoma, amyloidosis and viral papular dermatitis.

Treatment

Where lesions are numerous and there is no mineralization, oral prednisolone or prednisone at 1 mg/kg s.i.d. for 2–3 wk may be employed. Isolated lesions may be treated with intralesional corticosteroid, methyl prednisolone acetate 5–10 mg/lesion or triamcinolone acetonide 3–5 mg/lesion. Mineralized lesions will not respond to this treatment. Care should be taken to ensure that not more than 20 mg total of triamcinolone acetonide is administered at any one occasion as a precaution against precipitating laminitis.

Prognosis

The prognosis is guarded. Some cases will resolve spontaneously within weeks, but others may persist for many months, permanently mineralized. It is rare for the condition to make the horse unrideable provided adequate padding is used under the saddle.

UNILATERAL PAPULAR DERMATOSIS

Etiology and clinical signs

Unilateral papular dermatosis is a rare nodular skin condition that mainly affects finer skinned breeds with a predisposition for **Quarter Horses**. No age or sex predilection has been established. The condition presents with the sudden appearance of large numbers of papules and nodules on one side of the trunk with no accompanying systemic response, and no pain, pruritus, or hair loss. Lesions appear to be circumscribed, benign and resolve spontaneously within a few months. Occasional recurrences on the same or opposite side of the body are known. The etiology is unknown.

Diagnosis

Clinical signs of unilateral nodular/papular lesions. Skin biopsy reveals eosinophilic folliculitis and furunculosis with no etiologic agents. Cultures are negative. Differential diagnosis includes furunculosis, collagenolytic granulomas and sterile panniculitis.

Prognosis

Guarded to favorable. If spontaneous remission does not occur then oral prednisolone or prednisone at 1 mg/kg PO s.i.d. may be given.

KERATINIZATION DISORDERS

Generalized seborrhea

Etiology

Seborrhea, by definition, implies an excess production of lipid secretion from the sebaceous glands. Although some skin disorders are accompanied by increased greasiness of the skin and coat, the disorders referred to are really of **increased production of skin scale**. Thus the clinical condition of seborrhea characterized by increased epidermal turnover, which may be accompanied by more or less lipid secretion, is a scaling defect. Seborrhea is a clinical sign rather than a specific disease.

Primary seborrhea is rare in horses while **secondary seborrhea** may be a clinical sign accompanying a wide variety of clinical disorders, e.g. ectoparasitism (lice, mites); fungal infection (dermatophyte invasion of surface keratin); bacterial infection; abnormal lipid metabolism (hepatic disease); deficiency diseases (zinc deficiency); autoimmune disease (pemphigus foliaceus); or endoparasitism (chronic strongylosis).

Mane and tail seborrhea

Etiology

Obscure; no predilection by age, breed or sex.

Clinical signs

Excessive accumulations of skin scale within the hair of the mane and tail.

Diagnosis

Elimination of other causes of excess scale formation, see above.

Treatment

Regular bathing in antiseborrheic shampoos containing coal tar, sulfur and salicylic acid. For greasy seborrhea, benzoyl peroxide shampoos are helpful. If the scale is dry, emollients and humectants may be used as rinses or sprays.

Linear keratosis

Etiology

Unknown, but is thought to be a developmental anomaly similar to epidermal nevus of man. The disorder has been reported mainly in the USA where there appears to be a predilection for young (1–5 yr) **Quarter Horses**, **Morgans**, **Standardbreds** and **Percherons**, but it has also been recognized in the UK.

Clinical signs

Unilateral linear lesions, mostly orientated vertically on the neck, thorax, shoulder and extending down the forelimb to the pastern. The length of the lesion may be up to 50 cm with width 0.25–0.75 cm. The surface of the skin is covered in a thick seborrheic mass arising from non-painful, non-pruritic papular

eruptions, the surface of which becomes covered in hyperkeratotic orthokeratotic debris. Once established, the condition appears to be permanent.

Diagnosis
The clinical signs are highly suggestive. Biopsy reveals epidermal hyperplasia and orthokeratotic hyperkeratosis. Differential diagnosis includes dermatophilosis, dermatophytosis, trauma and possible larval migration.

Treatment
There is no specific therapy. Antiseborrheic preparations may be helpful. Topical creams containing vitamin A have been found of some value in controlling the scaling. The value of more potent retinoids in the condition does not appear to have been investigated.

Cannon keratosis ("stud crud")

Etiology
Cannon keratosis is an uncommon chronic dermatosis of the horse affecting the anterior surface of the cannon area of both hindlimbs, with no breed, age or sex predilection. The etiology is obscure. It is likely that the cause is multifactorial, such factors as hygiene, urine splashing, infection and individual susceptibility to repeated wetting all playing a part.

Clinical signs
Non-pruritic, non-painful scaling with matting of hair in crusted plaques on the dorsal surface of the cannon area of both hindlimbs.

Diagnosis
Typical clinical signs, on fine skinned horses. Bacterial and fungal infection must be ruled out. Skin biopsy is not definitively diagnostic, showing chronic inflammatory changes including epidermal hyperplasia with ortho- and parakeratosis and mild, chronic, dermal inflammatory changes. Photoactivated vasculitis, which may have some clinical similarities, needs to be ruled out.

Treatment
Topical antiseborrheic preparations and glucocorticoid creams b.i.d. Cleansing, removal of crusts, dressing with an astringent (potash alum solution) followed by the application of an emollient cream may also be of value. Particular attention should be paid to management.

NODULAR PANNICULITIS

Etiology
Sterile panniculitis, although a well-recognized condition in the dog, is a condition of great rarity and unknown etiology in the horse. Lipid freed into the tissues following damage to adipose tissue acts as a potent inflammatory

agent once it is hydrolyzed to glycerol and free fatty acid and gives rise to further inflammatory reactions.

Clinical signs

Multiple subcutaneous nodules, sometimes extending to form plaques, from a few millimeters to several centimeters in diameter, mainly affecting the trunk. These rupture and drain producing an oily discharge. Varying degrees of pain are associated with the condition and there may be systemic signs of illness.

Diagnosis

Definitive diagnosis is based on the appearance of the lesions, sterile cultures and excisional biopsy. Histologic findings are of lobular to diffuse pyogranulomatous and granulomatous panniculitis. Differential diagnosis includes all causes of nodular skin lesions of the horse, collagenolytic granulomas, bacterial and fungal infections, foreign bodies and traumatic lesions and immunologic and hypersensitivity reactions.

Treatment

1.0–2.0 mg/kg prednisolone or prednisone once daily for 7–14 days. The prognosis is guarded.

ANHIDROSIS (DRY COAT, EQUINE ANHIDROTIC SYNDROME)

Etiology

The physiologic mechanisms of sweating in horses are complex and still not completely understood. Although not fully determined, the **non-sweating syndrome** of horses appears to be associated with a number of factors that precipitate exhaustion of the sweating mechanism, for example temperature and humidity. Horses reared in temperate climates and transported to regions of high humidity and temperature may **fail to acclimatize**. Certain individuals have a poor response to sweat stimulation by adrenalin (epinephrin). Animals involved in **strenuous exercise**, e.g. racing and other competitive events, may become stressed in a hot humid climate.

Clinical signs

In acute cases sweating is much reduced or absent; this is accompanied by respiratory distress, labored breathing, fever, collapse and occasionally death. **Chronic anhidrosis** is characterized by dry lusterless coat, seborrhea and partial alopecia, particularly affecting the face and neck. Horses also show poor exercise tolerance and loss of condition.

Diagnosis

Diagnosis is based on a clinical history of non-sweating. Anhidrotic horses show a very slow sweat response to an **intradermal skin test with various dilutions of adrenaline (epinephrin)**. After injection of 0.5 mL of 1:1000 adrenalin (epinephrin) intradermally the response producing sweating is delayed 5 h or longer.

Treatment

Symptomatic and empirical. Application of cold water to reduce body temperature is recommended. Affected horses have been housed in air-conditioned barns but should be removed to a cooler, less humid environment.

HYPERHIDROSIS

Etiology

Factors resulting in hyperhidrosis include high ambient temperature, infection, administration of drugs, excessive muscular exertion, pain, hyperadrenocorticalism and temperament.

Clinical signs

Excessive sweating may be generalized or localized over the neck, base of ears, around the nostrils and thighs. The coat appears dark and wet with sweat. Specific therapy depends upon the cause.

Chapter 6

The ear, nose and throat

T. Greet (Consultant Editor), S. Howarth

Chapter contents

INTRODUCTION

Diseases of the ear, nose and throat occur relatively commonly in the horse. In many cases an accurate diagnosis followed by a specific medical or surgical treatment can result in a successful outcome. Advances in imaging technology such as endoscopy during treadmill exercise, combined with the increasing availability of novel techniques such as gamma scintigraphy and magnetic resonance imaging, have resulted in an improved understanding of the disease processes affecting the region. Dental disease has been included in this chapter because of the relationship of maxillary dental disease to lesions of the nasal passages and paranasal sinuses.

THE NASAL PASSAGES

EXTERNAL NARES

The external nares are the openings to the nasal passages. The comma-shaped **alar cartilages** support the external nares dorsally, medially and ventrally. Lateral dilatation of the nares is achieved by muscular activity that regulates airflow to the nasal passages, larynx and lower airways. The external nares are the major site of upper respiratory resistance to airflow, therefore in the normal horse the distensible nature of the external nares is vital for athletic function. Narrowing or loss of muscular support to the external nares results in collapse of the nares during the inspiratory part of the respiratory cycle. Upper airway obstruction produced by the external nares can be considered to be either **functional** or **static/luminal**.

Trauma

Lacerations of the external nares are not uncommon. They usually heal well because of the abundant blood supply and musculature in this region. If left to heal by secondary intention the resultant scar formation may produce **stenosis**, limiting dilatation of the nares. Accurate anatomic repair with at least two-layer closure is therefore obligatory. Stenotic nares may be corrected using a cosmetic double apposing Z-plasty technique.

Neurogenic disorders

Facial nerve (cranial nerve [CN] 7) **paralysis**, a result of either peripheral (dorsal buccal branch) injury or a more centrally located lesion, will produce failure of nostril dilatation at deep inspiration. If present bilaterally a **functional obstruction** will result which may necessitate a tracheotomy to relieve the dyspnea, or as a long-term salvage procedure, resection of the lateral wall of the nares.

NASAL DIVERTICULUM (FALSE NOSTRIL)

The false nostril is positioned dorsolaterally to the external nares. Its floor and medial wall are formed by the **alar fold**, a rostral soft tissue extension of the

ventral turbinate. Vibration of the alar fold on expiration during exercise is a normal physiologic occurrence that produces the noise recognized as "**high blowing**".

Abnormal alar folds

Partial airway obstruction may occur if either the alar folds are excessively thick or the external nares are relatively small. An inspiratory vibratory noise is produced and airflow to the nasal passages is restricted by dynamic collapse of the vestibule.

The subjective assessment of the alar folds and their contribution to an upper respiratory noise is difficult, particularly in the absence of visible or palpable abnormality. However, some assistance may be obtained in confirmation by placing a temporary mattress suture through each alar fold to the skin of the external nares, thus obliterating the space within the false nostril. If the previous respiratory noise is eliminated or significantly reduced in volume during a subsequent exercise test, then **bilateral resection** of the alar fold can be recommended to alleviate the horse's condition.

Atheroma/epidermal inclusion cyst

Atheromas present as spherical, non-painful, unilateral swellings of the caudo-dorsal aspect of the nasal diverticulum. Generally, they are a **cosmetic problem** seldom obstructing the nasal passages.

Recognized usually in younger horses, the cyst contains a thick, gray sterile fluid of keratinized and non-keratinized cells produced by aberrant location of epithelial tissue. Local drainage, curettage of the cyst lining and daily irrigation with povidone-iodine may be performed under sedation and regional anesthesia. This technique may be advised on cosmetic considerations, however recurrence can be expected if there is inadequate removal of the cyst lining. Complete dissection of the unpunctured cyst and primary skin closure under general anesthesia gives more reliable results.

NASAL CHAMBERS

The nasal passages have a number of physiologic functions apart from acting as the initial conduit for air to the lower respiratory tract. They warm and moisturize the ambient inspired air, they are involved in thermoregulation, act as a crude filtering system of airway contaminants and debris, and provide a location for olfactory receptors. The mucosa of the nasal chambers is closely adherent to the supporting structures of the dorsal and ventral turbinates and midline nasal septum.

The well-developed blood supply that courses through the submucosa of the nasal passages during exercise undergoes vasoconstriction. This causes the mucosal epithelium to adhere more closely to the underlying cartilage, maximizing the airway diameter and resisting potential collapse. The mucosa becomes engorged during general anesthesia and in association with **Horner's syndrome** (*q.v.*), producing significant upper respiratory obstruction. This is due in the latter case to impairment of sympathetic control to the nasal vasculature.

Trauma

Depression fractures of the rostral nasal and incisive bones, such as might arise from head-on collisions or kicks, will lead to loss of support to the external nares. If left to heal naturally, this may result in **luminal stenosis**. Surgical correction aims to provide support to the airway, preventing stenotic complications.

Foreign bodies

Nasal foreign bodies are uncommon, however inhalation of grass seeds or twigs will produce persistent clinical signs of head shaking, epistaxis and snorting (*q.v.*).

Fungal infection

Mycotic infection (*q.v.*) is sporadic in occurrence and usually opportunistic, dependent either on impaired local resistance or the presence of devitalized tissue. Clinically, a **fetid serosanguineous/mucopurulent and generally unilateral, nasal discharge** is observed; however, in some horses this discharge may be minimal. A diagnosis can be made endoscopically by recognizing **mycotic plaques** and occasionally granulomas on the turbinates and nasal septum. A definitive diagnosis is obtained by **biopsy and culture** of the lesion.

A wide variety of isolates have been reported including *Aspergillus fumigatus, Coccidioides immitis, Cryptococcus neoformans* and *Rhinosporidium seeberi*.

Treatment involves **topical application** of antifungal agents, e.g. **ketoconazole** or **natamycin**, via an external irrigation system that utilizes the paranasal sinuses as a reservoir. This may be supplemented by using systemic antifungal agents and surgical removal of the plaques and granulomas, which is usually best achieved by use of endoscopic or endometrial biopsy forceps, under direct endoscopic visualization. In some cases the lesions may be self-limiting without treatment.

Ethmoidal hematoma

Ethmoidal hematoma is a progressive, expansile, encapsulated lesion of unknown etiology; there is no histologic evidence of neoplasia even though the lesion may act like a tumor. The lesion usually develops from the ethmoidal region, however paranasal sinus origin is also not uncommon.

The lesion is typically encountered in middle-aged to older horses, presenting with an **intermittent, unilateral, serosanguinous nasal discharge** unrelated to exercise. Depending on the lesion size and position there may be altered nasal airflow and a respiratory noise at exercise may also be detected.

Endoscopic examination reveals a typically yellow-green-brown space-occupying lesion extending rostrally along the nasal meatus. Radiography can be used to delineate the extent of the soft tissue mass and determine the presence of possible secondary lesions. It should be noted that if a lesion is restricted to the paranasal sinus, the only finding may be a trickle of hemorrhage from the sinus ostium in the middle meatus.

Surgical treatment involves resection using a frontomaxillary sinus bone flap approach to the nasal chamber. Access to the ethmoidal region is then through the floor of the frontal sinus and is inevitably a bloody procedure. The lesion may recur following excision depending on the completeness of lesion removal.

The use of a **transendoscopic laser** (Nd:YAG or diode) to ablate the hematoma has provided a much less invasive procedure, but may be less effective in the confined areas of the ethmoidal region. Injecting lesions with a **10% formalin solution** on repeated occasions has also proved effective, although if large volumes are used there is a risk of fatal encephalitis. Such an injecting system can be purchased or made up by attaching a needle to a piece of stiff tubing and carefully inserting it down the biopsy channel of the endoscope. Both the formalin injection and laser techniques can be used for intrasinus lesions, via direct sinus endoscopy.

Neoplasia

Neoplasia of the nasal passages is rare although squamous cell carcinoma, adenocarcinoma, lymphosarcoma, fibrosarcoma and ossifying fibroma (*q.v.*) have all been reported. Presenting signs reflect the presence of an expansile, space-occupying lesion within the nasal passages, i.e. nasal discharge, epistaxis, altered nasal airflow, respiratory noise at exercise and facial swelling/distortion. The degree of local expansion, accessibility and the size of the area involved before recognition determine therapy and prognosis.

Treatment is by lesional excision through a facial flap, but other than for well-encapsulated benign lesions like an ossifying fibroma, the prognosis is very poor.

Nasal amyloidosis

The etiology of this very rare condition is unknown. Following sustained immunologic stimulation (possibly the result of chronic infection), macrophages deposit glycoprotein fibrils in the form of nasal and cutaneous plaques and nodules. These are non-painful and often ulcerate, producing the clinical signs of nasal discharge, epistaxis and reduced exercise tolerance. The plaques can be recognized endoscopically and are distributed throughout the nasal passages. Diagnosis is confirmed by histopathology of biopsy samples. Palliative treatment involves cauterization and surgical resection. Successful therapy is rare and must address the primary cause.

NASAL SEPTUM

The nasal septum extends from the external nares caudally, dividing the nasal passages as far as the ethmoidal region.

Deviation

Congenital deviation of the nasal septum ("wry nose" or rhinocampylus lateralis) occurs in utero, in association with deviation of the premaxillae.

Difficulties in **suckling and prehension** may result from severe deviation. This can be corrected by a radical surgical technique, first sectioning and then realigning the premaxillae using internal and/or external fixation. Finally, the deviated rostral nasal septum is resected. Such surgery is seldom carried out.

Acquired deviation may develop following external trauma or as a consequence of continuous pressure from space-occupying lesions of the nasal passages, e.g. neoplasia or turbinate distension from sinus cyst formation.

Thickening

A rare congenital **cystic degeneration** of the nasal septum may result in nasal septal thickening. Airway obstruction is marked and the thickened septum can be palpated digitally. Treatment involves resection of the affected portion of the septum using embryotomy wire inserted via trephine holes into the sinus and exiting the nasal passages.

Choanal atresia

Choanal atresia is a very rare congenital malformation associated with failure of perforation of the bucconasal membrane at the choanae or posterior nares. The condition may be uni- or bilateral. Failure to perform an emergency tracheostomy at birth will result in asphyxiation of a foal with bilateral obstruction.

Nasal polyps

Nasal polyps consist of inflammatory connective tissue attached to either the turbinates, nasal septum or an alveolar socket. They may act as a space-occupying lesion producing the clinical signs of respiratory stertor, exercise intolerance and mucopurulent nasal discharge. Treatment involves resection and cauterization of their origin.

THE PARANASAL SINUSES

The paranasal sinus system consists of the bilaterally paired rostral and caudal maxillary, frontal, ethmoidal and sphenopalatine sinuses. Functionally, the sinus system reduces the weight of the bony covering that supports the skull contents and protects them from external trauma.

The external landmarks of the maxillary and frontal sinuses are readily palpated. A line from the medial canthus of the eye to the nasomaxillary notch marks the dorsal margin of the maxillary sinus and the lateral margin of the frontal sinus. The ventral margin of the maxillary sinus lies parallel and just ventral to the facial crest. The rostral maxillary sinus extends to a line drawn perpendicular to its dorsal margin that intersects the rostral end of the facial crest. The caudal limit of the caudal maxillary sinus is defined by a line bisecting the orbit. The left and right frontal sinuses are divided on the midline by a complete bony septum. The caudal limit of the frontal sinus is represented by a line perpendicular to the midline bisecting the temporomandibular joint.

The most rostral extension of the frontal sinus lies within the dorsal turbinate (the concho-frontal sinus) and is delineated by a transverse line halfway between the medial canthus of the eye and the infraorbital foramen.

The paranasal sinus system is lined by mainly pseudostratified, columnar, ciliated epithelium and goblet cells. **Drainage of the mucus** that is produced by this respiratory lining is assisted by the coordinated beating of cilia toward the caudal maxillary sinus. The frontal, ethmoidal and sphenopalatine sinuses drain and communicate directly with the caudal maxillary sinus. Normally, a complete bony septum overlying cheek teeth four and five divides the rostral and caudal maxillary sinuses. Continuation of this septum divides the naso-maxillary opening through which the whole sinus system drains to the middle nasal meatus.

SINUSITIS

Sinusitis may be divided into **primary (infectious)** or **secondary sinusitis**. The predominant clinical sign of sinusitis is a **unilateral nasal discharge**. Complete obstruction of drainage from the sinuses results in fluid and soft tissue accumulation within the sinuses and turbinates creating internal pressure which may be recognized clinically as facial swelling, reduced airflow at the nostril, respiratory noise at exercise and a dulled resonance and pain on percussion of the sinuses. If the internal sinus pressure causes obstruction of the nasolacrimal duct as it courses through the maxillary sinus, **epiphora** may also be observed. **Neurologic signs** produced by caudal extension of a disease process through the cribriform plate are rare complications of sinusitis.

Diagnosis is confirmed **endoscopically** by recognizing turbinate distension and a discharge emanating from the caudal middle meatus. Radiography is used to determine the extent of sinus involvement and the presence of fluid within the paranasal sinus system, and to evaluate possible **dental involvement**.

Primary sinusitis

Primary sinusitis is a consequence of an **upper respiratory infection** extending to involve the paranasal sinus system, altering the normal mucociliary clearance mechanism and reducing normal drainage. The presence of fluid within the sinus system is demonstrated by a horizontal fluid–gas interface on a standing lateral radiographic image of the paranasal sinuses. Confirmation of the diagnosis and isolation of the etiologic agent can be achieved following **sinucentesis** of the affected sinus. This is most easily achieved via insertion of a Steinmann pin through the facial bone plate into the sinus, and then aspiration via a needle, catheter or swab.

Treatment must be aggressive to prevent secondary complications of inspissation of accumulated pus and bone necrosis. The primary aim of treatment is to re-establish normal drainage to the nasal passages. Systemic broad-spectrum or, ideally, sensitive specific **antibiotic therapy** should be instituted in association with daily **irrigation and lavage** of the sinus. Large volumes of **physiologic sterile saline** should be administered through an ingress balloon catheter (12–16 G French) positioned in the affected sinus through a small

trephine hole. Therapy should be continued for 7–14 days, during which time exercise is encouraged to assist drainage. (Drainage from the nasomaxillary aperture is temporarily improved during exercise as the nasal mucosa undergoes physiologic vasoconstriction.)

Chronic cases often fail to respond to this conservative management and adequate drainage can then only be established surgically, using a facial flap approach.

Secondary sinusitis

Dental

The last four cheek teeth of the maxillary arcade lie within the maxillary sinus. The development of a **periapical abscess** affecting any of these teeth is likely to produce a **secondary sinusitis**. This occurs most commonly in middle-aged horses and most frequently it is the **4th cheek tooth** that is affected. The resulting unilateral nasal discharge that is produced is characteristically **fetid**.

Accurate recognition of dental involvement requires a thorough examination of the oral cavity and **oblique radiographs** highlighting the roots of the suspected dental arcade. Both procedures can be performed in the standing horse, as can gamma scintigraphy, which is exquisitely sensitive in identifying periapical inflammation. The use of computed axial tomography (CAT) scanning or magnetic resonance imaging (MRI) can also provide high quality detail of dental structures and surrounding alveolar bone. However, both of these techniques normally require the horse to be anesthetized.

Treatment involves removing the affected tooth. Nowadays this is best achieved by oral extraction in the **standing horse**. However, the affected tooth may be **repelled** into the oral cavity and sinus contamination with food prevented by **packing the alveolar socket** with dental wax or methyl methacrylate bone cement, providing **postoperative irrigation** and ensuring adequate drainage of the affected sinus.

Two surgical approaches are commonly employed. They differ in the degree of surgical exposure provided and the amount of postoperative management of the alveolar socket that may be performed. **Trephining** directly over the affected tooth root requires accurate localization, using radiographic images and facial structures (facial crest, medial canthus of eye, nasolacrimal duct and other indicators of sinus topography). Postoperatively the alveolar socket may be irrigated daily and the development of granulation tissue monitored. An approach using a **sinus bone flap technique** provides excellent surgical exposure of the affected tooth roots and more confidence in complete removal of all affected dental tissue. Using either technique, postoperative radiographs are mandatory to ensure complete removal of all dental tissue. Thereafter, management consists of **twice-daily lavage** of the sinus using a balloon catheter system placed in the frontal sinus ensuring normal drainage to the nares.

Maintaining the **alveolar plug** in position while the alveolar socket granulates can be difficult and is imperative for successful surgical management. Dietary management has little effect in preventing leakage around the plug and further sinus contamination.

Traumatic sinusitis

Secondary sinusitis may develop following external trauma to the sinus region. Open lacerations and/or depression fractures will produce **epistaxis** and **facial swelling**. Radiography should be used to confirm the presence of fracture fragments, fluid or hematomas within the sinus. Specific attention should be paid to the dental arcade to determine any damage to the tooth roots, the consequence of which may affect the prognosis. However, it is amazing how often such lesions resolve with minimal complication.

Fracture fragments may be removed or, if accurate anatomic reduction and stable fixation can be achieved, they may be retained. The sinus should be lavaged to remove organizing hemorrhage and contaminating organisms. Postoperative irrigation is advised. Open wounds should be treated aggressively to prevent **sinus fistulae** developing. Chronic fistulae can be treated using periosteal flaps, allowing osteogenesis to occur over the defect.

PARANASAL SINUS CYSTS

Paranasal sinus cysts primarily affect the **maxillary sinus** but they may also occur in the **frontal sinus**. They have a true cystic lining that contains a characteristic sterile, amber/yellow fluid formed from blood breakdown products. They may be found at any age but there is a predilection for the younger horse ($\leqslant$1 yr) and older horses ($\geqslant$9 yr).

The clinical signs are a **mucopurulent/serous nasal discharge**, which is usually scanty, facial swelling and reduced airflow at the affected nares. Endoscopy reveals turbinate distension. Radiography demonstrates a contained soft tissue density, which may show areas of mineralization, and tooth root distortion but no evidence of periapical abscessation. Rarely there may be additional bizarre dental structures, or anomalous dental eruption. **Sinucentesis** can be used to confirm the presence of the characteristic amber fluid.

Complete surgical excision is performed by blunt (digital) dissection through an appropriate sinus bone flap, ensuring adequate drainage to the nares and placement of a postoperative irrigation system. The prognosis following surgery is good and recurrence rates are low.

Rarely, more extensive lesions involve multiple sites and can prove extremely difficult or impossible to remove.

NEOPLASIA

Squamous cell carcinoma, adenocarcinoma, osteosarcoma, fibrosarcoma, lymphosarcoma and ameloblastoma (*q.v.*) have all been recognized in the paranasal sinuses of the horse. Although more common in older horses, neoplasia has also been reported in young horses and rarely congenitally. The size and distribution and invasive nature of the majority of lesions at presentation usually preclude successful therapy.

SUTURE PERIOSTITIS

Suture (diastasis) periostitis is a **non-painful bony swelling** over the margins of the paranasal sinuses that is commonly attributed to a traumatic etiology;

however, often there is no history of trauma. These swellings are a **cosmetic problem** only. They are caused by instability at suture lines, usually between the nasal, frontal and maxillary bone plates. Radiography can be used to monitor the periostitis that develops and also rule out the presence of depression fractures, sequestra or neoplasia. The periostitis is self-limiting. It leaves a permanent, residual swelling although this gradually reduces with time.

Similar swellings can be associated with pressure from expansile sinus masses. Such cases always have evidence of soft tissue density within the sinus and treatment should be directed at the primary cause. Sometimes such suture instability may follow facial flap surgery.

DENTITION[1]

The horse is particularly well adapted to a herbivorous diet. The efficiency of mastication (*q.v.*) of ingesta is maximized by molarization of the premolar dentition, which has evolved so that they are almost indistinguishable from the true molars.

Narrowing of the interdental space between neighboring teeth also assists in creating a continuous grinding, occlusal surface. Furthermore, naturally occurring ridges and troughs orientated transversely across the occlusal surface of the maxillary and mandibular arcades interdigitate with each other and create a particularly abrasive surface on which ingesta may be ground down.

In order to ensure a continuous grinding surface and to account for continual wear of the dental tissue the horse has developed teeth that have abundant reserve crown and that erupt continuously.

To assist the grinding action, the mandible has a great range of lateral and rostro-caudal movement provided by the incongruous articulation of the temporomandibular joint. Finally, the main muscle of mastication, the masseter muscle, is well developed with a broad area of attachment rostral to the temporomandibular joint; this maximizes the crushing force that is produced at the occlusal surface.

NORMAL DENTAL DEVELOPMENT

The incisors have a simple anatomy with a deep enamel invagination on their wearing surface. This infundibulum is filled with cement. The cheek teeth of the mandible and maxilla are more intricate in their appearance due to marked infoldings of the enamel layer. During embryologic development the tooth germs of the maxillary arcade develop more quickly and consequently at eruption have a more complicated construction than mandibular teeth. The maxillary tooth also has a true infundibulum that produces enamel lakes on the occlusal surface that at eruption are incompletely cement filled. Mandibular teeth have a more rectangular cross-sectional area than the maxillary teeth.

The normal eruption times of the deciduous and permanent teeth are well documented and are set out in Table 6.1.

[1] For a review of equine dental disorders see Dixon, P.M. and Dacre, I. (2005) A review of equine dental disorders. *The Veterinary Journal* 169, 165–187.

Table 6.1 Normal eruption times of deciduous and permanent teeth in the horse

Deciduous dentition		Dental formula		
		i	c	p
		3	0	3
		3	0	3
	Tooth	**Eruption time**		
Incisors	Di 1	Birth–1 wk		
	Di 2	4 wk		
	Di 3	6–9 mo		
Premolars	Dp 2			
	Dp 3	Birth–2 wk		
	Dp 4			
Permanent dentition		**Dental formula**		
		i	c	p	m
		3	1	3/4	3
		3	1	3	3
	Tooth	**Eruption time**		
Incisors	I 1	2.5 yr		
	I 2	3.5 yr		
	I 3	4.5 yr		
Canines	C	4–5 yr		
Premolars	P 1	5–6 mo		
	P 2	2.5 yr		
	P 3	3 yr		
	P 4	4 yr		
Molars	M 1	9–12 mo		
	M 2	2 yr		
	M 3	3.5–4 yr		

I, i, incisor; C, c, canine; P, p, premolar; M, m, molar; D, deciduous.

The Triadan system

Recently a new system of dental nomenclature has been adopted from the human dental field. Thus each tooth is defined by a 3-digit number. The first digit defines the quadrant, i.e. 1 for upper right, 2 for upper left, 3 for lower left and 4 for lower right.

The teeth are then numbered from central incisor 1 through to 3rd molar as 11; this allows for a wolf tooth on both upper and lower jaws (tooth 5). Thus the upper right canine will be 104 and the lower left 4th premolar will be 308.

Normal eruption

The timing of normal eruption and wear of the incisors is consistent enough to allow accurate estimation of a horse's age. Eruption is a consequence of vascular activity of the tooth roots forcing the tooth along its normal eruption pathway. Non-painful, bony swellings are often recognized overlying the roots of erupting teeth in juvenile horses. Radiography of the dental roots shows evidence of **periapical hyperemia** and **alveolar bone resorption**. These dental germs, particularly in the mandible, are prone to external trauma and injury.

Abnormal eruption

Rotation, displacement or impaction is most commonly seen affecting the third cheek tooth because this is the final permanent tooth to erupt and it has to do so between the second and fourth permanent teeth. Abnormal eruption may also occur as a consequence of external trauma to developing tooth germs.

Displacement or maleruption of the **wolf tooth** (the rudimentary remnant of the permanent first premolar) may occur and be a genuine cause of bitting problems, warranting extraction. (Normal eruption of the wolf tooth is unlikely to be clinically significant.)

Pseudopolyodontia (deciduous tooth retention)

Retained deciduous incisors are usually loosely attached and readily removed with dental forceps. If they are more firmly attached and displace the erupting permanent teeth lingually, **sharp dissection** may be required.

Deciduous cheek teeth "dental caps" may remain attached to the surrounding gingiva during eruption of the underlying permanent tooth, disrupting mastication. Their **sharp edges** may lacerate the surrounding soft tissues producing signs of oral **pain and quidding**.

Regular dental rasping will encourage the shedding of dental caps, some of which may require more aggressive treatment. Removal can be undertaken using sedation or, if firmly attached, under a general anesthetic. The technique involves manipulation with dental forceps and elevator to lever the dental remnant from its attachment.

NORMAL WEAR

Anisognathism

At any point, the distance separating the mandibular arcades is 30% narrower than the corresponding maxillary distance. The mandibular arcades are also straighter in their orientation. The maxillary arcade curves outwards to the buccal cavity.

These normal features, in conjunction with the continual lateral and rostrocaudal grinding movements of the mandible, produce characteristic wear of the occlusal surfaces. The wearing surface slopes down towards the buccal cavity creating sharp enamel points on the lingual surface of the mandibular arcade and on the buccal surface of the maxillary arcade. **Large dental "hooks"** may also develop on the rostral and caudal ends of the arcades. Regular (biannual) rasping is usually sufficient to prevent occlusal dental problems.

ABNORMAL WEAR

Shear mouth

Excessive angulation of the occlusal surface results in prominent enamel points preventing lateral movement of the arcades. This condition can be

attributed to either inadequate width of the mandibular arcades or restricted lateral grinding movements of the mandible following temporomandibular trauma or arthropathy.

Wave mouth

Abnormal mastication and/or differential rates of wear between individual teeth results in exaggerated development of the normal troughs and ridges of the occlusal surface. This provides a sigmoid pattern to the dental arcade when viewed laterally. The impaired mastication and quidding that develop in severe cases necessitate leveling of the dental arcade using rasps and chisels under general anesthesia. Motorized rasps may also be used.

Step mouth

Severe differential wear between adjacent teeth or following tooth removal produces marked variation in the height of adjacent teeth. Mastication is markedly impaired, which may result in malnutrition. Treatment aims to level off the step-like profile of the arcade.

Smooth mouth

Smooth mouth is a **geriatric condition** of the horse that develops as teeth are lost or worn down to the gingival surface. Mastication is severely affected as the grinding efficiency of the occlusal surface is severely limited. Poor condition, colic and malnutrition may develop. Smooth mouth may also be seen in young animals if excessive, frequent and improper rasping is performed.

Enamel hypoplasia

Abnormal enamel development will produce excessive dental wear in young or middle-aged horses. The effect of this is to produce a smooth mouth conformation in a non-geriatric horse.

ABNORMAL DEVELOPMENT

Brachygnathism/prognathism

Congenital shortening of the mandible or maxilla results in malocclusion of the incisor arcade and if severe will also involve the cheek teeth. These are inherited conditions, the most common being **mandibular brachygnathism (parrot mouth)**. This terminology describes the relative shorter length of the mandible compared to the maxilla.

An assessment of the presence of mandibular brachygnathism is usually determined at 2 yr of age when the degree of contact of the central incisors is evaluated. The condition is defined by a complete failure of occlusal contact.

Maxillary prognathism (sow mouth) is a less common developmental abnormality with relative shortening of the maxilla compared with the mandible.

Cosmetic surgery to disguise the signs of either condition is of questionable ethical value. However, attempts at restricting mandibular or maxillary elongation by using braces or wires are frequently carried out, particularly in North America. Treatment is usually unnecessary but rasping and/or cutting of overlong teeth may be needed.

Nutritional secondary hyperparathyroidism (big head/miller's disease)

A generalized skeletal disease is found in horses fed a dietary intake of excess phosphorus in relation to calcium. The presenting signs are facial swelling, nasal obstruction, nasal discharge, mandibular distortion and abnormal development of tooth germs. This condition is of historical importance but is rarely seen with modern balanced diets.

Mandibular cysts

Mandibular cysts produce a **unilateral swelling of the mandible** in the young horse. There is no history of trauma and the horizontal ramus is usually affected. The lesion tends to occur rostrally near the mandibular synostosis. Radiographic examination reveals an expansile lesion containing large radiolucent areas. The etiology of this lesion is unknown, but it does not appear to be inherited. Treatment involves vigorous curettage of the cyst lining. Dental development postoperatively is usually unaffected by this treatment.

Polyodontia

Supernumerary teeth usually occur in the incisor arcade and are generally a cosmetic problem only. If there is abnormal wear and trauma to the surrounding soft tissue, the additional teeth may be surgically removed. Supernumerary cheek teeth may also occur medially or at the ends of the cheek teeth arcades. Their presence usually leads to malocclusion, food impaction and periapical abscessation. If this does occur, surgical removal is indicated.

A particular syndrome occurs occasionally, involving the **eruption of a seventh upper cheek tooth**, caudal to the third molar. These two teeth are frequently separated by a wider gap (diastema) than is usual. Food material may penetrate the caudal maxillary sinus causing a severe sinusitis. The extraneous tooth can usually be removed per os and the sinus treated in the usual way via a facial flap approach. It is seldom necessary to place a protective dressing in the alveolus to avoid food penetrating the sinus, other than for the first two or three days.

Oligodontia

The development of a less than normal number of teeth is known as oligodontia. **Pseudo-oligodontia** develops following either external trauma or surgical removal. True congenital oligodontia may result from nutritional secondary

hyperparathyroidism of the foal (see above). Normal tooth germs fail to develop correctly and those teeth that erupt may do so abnormally.

Heterotopic polyodontia (dentigerous cysts)

Abnormally positioned tooth germs of the branchial arch typically produce **cystic swellings of the temporal region** in yearlings. The dental tissue is well developed and contained within a cyst lining of stratified squamous epithelium. A **fistula** is often present on the leading edge of the nearest pinna, producing a characteristic oily discharge. Treatment requires complete removal of the cyst lining as well as the contained dental tissue. Care must be taken in removing the tooth as it may be fused to the underlying cranium.

PERIODONTAL DISEASE

Periodontal disease may affect any tooth and is usually associated with abnormal wear or abnormal dental eruption that allows food material to accumulate between individual teeth.

The clinical signs are **quidding** and **painful mastication**. Inflammation of the gingival sulcus is followed by erosion and enlargement of the gingival recess, the sequel of which is food impaction. The continued inflammation, infection and erosion of the supporting alveolar bone produce gross gingival pocketing, further food retention and weakening of the periodontium. The abnormal wear creates shearing forces that accelerate loosening of the tooth's normally firm attachment to the supporting alveolus. Ultimately the periodontal attachments of the tooth in the socket are compromised, providing a direct route to the periapical region and subsequent development of a suppurative process.

If untreated, periodontal disease will result in **periapical abscessation** with resultant facial swelling, discharging sinuses to the skin, secondary sinusitis, halitosis and loss of the affected tooth. **Regular prophylactic dental care** to maintain normal mastication is advised to prevent onset of periodontal disease.

PERIAPICAL ABSCESSATION

Sepsis of dental radicles may develop from an extension of periodontal disease via hematogenous spread following dental or alveolar bone fracture, or in the maxillary arcade following impaction of food into the infundibulum. The infundibulum of the maxillary tooth is normally only partially filled with cement. At the depth of the infundibulum the cement is hypoplastic and a potential space persists which may become impacted with food.

Fermentation of entrapped ingesta, and resulting **acidic dissolution** of the surrounding enamel and dentine, erodes the surrounding tooth, weakening it and leaving it liable to potential fracture. Secondary dentine is normally produced as a protective response to this "caries" lesion, however continued dissolution may ultimately bridge the dentine and allow infective agents direct access to the root pulp, the consequence of which is **pulpitis**, followed by periapical abscessation.

Periapical abscessation produces halitosis and painful swelling centered over the affected tooth root. If the tooth is present within the maxillary sinus, secondary dental sinusitis and nasal discharge will result.

Radiographic examination of suspected **periapical abscessation** must include oblique radiographs of the affected dental radicles. Markers and probes are useful to accurately determine the affected root. Radiologically, periapical abscessation is characterized by distortion of the dental roots, a radiolucent halo around the affected root, osteitis of the surrounding bone and loss of the normal distinct lamina dura and periodontal membrane.

Treatment involves repulsion of the affected tooth using a **trephine hole** and punch or sinus bone flap technique for those teeth within the maxillary sinus. Periapical infections of the rostral maxillary and mandibular teeth may also be approached using a lateral buccotomy approach. The exposure using a buccotomy approach is good following resection of the lateral alveolar bone and therefore enhancing complete removal of all dental tissue. Postoperative packing is assisted by using an oral plug and ribbon gauze that can be led out to the skin either dorsally or ventrally. This packing can be gradually removed as the socket granulates. Care must be taken when performing the buccotomy approach to avoid the facial artery, vein, nerve and parotid duct.

DENTAL NEOPLASIA

Odontogenic tumors may be of epithelial, mesenchymal or mixed origin. They are usually encountered in younger horses and may be congenital. **Ameloblastomas** are the most common and benign, however the local invasion is extensive and produces facial swelling, dysphagia, halitosis and weight loss.

Treatment is limited by the lesion size on presentation. If resection is inadequate, recurrence is common.

THE NASOPHARYNX

The pharynx is a muscular tube divided in two by a horizontal muscular sheet, the soft palate. The ventral half is continuous with the oral cavity and is called the **oropharynx**. The dorsal half, the **nasopharynx**, is continuous with the nasal passages.

The soft palate, which is subject to complex muscular actions, forms a continuous sheet from the hard palate rostrally to the dorsal pharyngeal roof caudally. There is a hole in this sheet through which the rostral laryngeal cartilages fit during respiration, much like a button in a buttonhole. This junction is an airtight seal that prevents food leakage from the oropharynx into the airway.

On the lateral walls of the nasopharynx the cartilaginous flaps of the guttural pouches are situated. During deglutition, the nasopharynx is closed by elevation of the soft palate, opening of the guttural pouch flaps and rostroventral movement of the nasopharyngeal roof. The larynx moves rostrally and closes and food is propelled from the oropharynx into the esophagus by action of the base of the tongue and progressive caudal constriction of the pharyngeal muscular tube. Immediately after this the pharynx and larynx resume their respiratory positions. The whole process lasts <1 s.

There is widespread lymphoid tissue throughout the nasopharynx with a particular concentration in the pharyngeal recess situated dorsally between the cartilage flaps of the guttural pouches. In young horses these lymphoid follicles may become quite large.

PHARYNGEAL DISEASE

Abscesses

A **pharyngeal abscess** may develop after a respiratory tract infection. Typically it forms in the retropharyngeal lymph nodes following infection by *Streptococcus equi equi* but commonly other *Streptococcus* spp. or other bacteria may be involved. In some cases the abscess may rupture into the guttural pouches producing empyema (*q.v.*). An abscess may form lateral to the nasopharynx as well as in a dorsal position and may occur secondary to infection of a localized injury such as penetration of the pharyngeal mucosa by a foreign body.

Affected horses usually have obvious **pharyngeal swelling** and show signs of **upper airway obstruction**. There may be a respiratory noise and, if the obstruction is severe, **dyspnea** may be marked with the horse adopting an "air hunger" position with its head and neck extended. In the acute phase there may be pyrexia and dullness and elevated hematologic and blood biochemical parameters (leukocyte count, serum proteins and fibrinogen) usually indicate a severe inflammatory lesion.

Endoscopic examination of the upper airway will usually reveal marked nasopharyngeal stenosis, or if there is empyema of the guttural pouches a purulent discharge may be noted from one or both ostia. Lateral radiographic views of the pharynx will usually demonstrate an increased area of radiodensity in the retropharyngeal tissues with concomitant narrowing of the nasopharyngeal airway or reduction in size of the guttural pouch air shadow. In some cases radiologic evidence of **guttural pouch empyema** (*q.v.*) may be noted. Rarely there may be evidence of dysphagia, which can be demonstrated by a barium swallow study.

Treatment with broad-spectrum antibiotics and anti-inflammatory drugs may be the only practical course of action unless a superficial abscess can be drained surgically. In severely dyspneic cases surgical drainage may be carried out as an emergency procedure or as an alternative to insertion of a temporary tracheostomy tube. Although *Streptococcus equi equi* is sensitive to penicillin, some clinicians consider that the course of the disease may be prolonged and the resultant immunity poorer if such treatment is followed instead of a more conservative approach of topical compresses and/or abscess drainage. However there is little scientific basis for this view. Treatment of secondary guttural pouch empyema is employed where indicated (*q.v.*)

Foreign bodies

Although horses are considered to be selective grazers, they will occasionally ingest pieces of twig such as blackthorn or hawthorn. This happens usually while grazing at the edge of hedgerow or as a result of ingesting hay that

contains such a twig. Affected horses will show severe discomfort and often **cough paroxysmally**. Usually there is **marked inappetance**. Occasionally there may be **slight epistaxis**.

Upper airway endoscopy may reveal the foreign body typically situated in the piriform recess or it may just be visible appearing under the edge of the soft palate. Rarely, a long twig may be seen extending from the oropharynx across the laryngeal aditus into the cranial esophagus. Twigs trapped in the oropharynx may remain invisible to endoscopy of the nasopharynx. Radiographic views of the pharynx frequently reveal little evidence of such a foreign body.

Removal of pharyngeal foreign bodies can usually be achieved manually via the mouth with the horse under a general anesthetic although it may also be possible in some cases under heavy sedation.

Neoplasia

Tumors of the nasopharynx are rare but **squamous cell carcinoma** (*q.v.*) formation in older horses can produce signs of dyspnea or dysphagia and there is usually severe halitosis. Endoscopic examination of the nasopharynx will usually reveal a soft tissue mass although in some horses the lesion may be confined to the oropharynx and only visible by examination under general anesthesia. A biopsy will confirm the diagnosis. There is no treatment for the condition. **Lymphosarcoma, melanoma** or **adenocarcinoma** (*q.v.*) may produce similar clinical signs, and sometimes epistaxis may be noted.

Nasopharyngeal lymphoid hyperplasia

The tonsillar/adenoidal lymphatic tissue of the horse is very widely distributed throughout the nasopharynx and mucosa of the guttural pouch. Lymphoid follicles may be found in large numbers in young horses in all sites but particularly on the nasopharyngeal roof. The dorsal nasopharyngeal recess has a particularly dense concentration of lymphoid tissue, which has been described colloquially as the **pharyngeal tonsil**. Endoscopy is the diagnostic method of choice.

The lymphoid follicles in young horses are often quite prominent; the mucosa may appear reddened and mucus production may be profuse. This lymphatic reaction is usually a response to antigenic challenge (e.g. respiratory viruses or environmental allergens). Clinical signs are usually minimal or those of respiratory viral infection (i.e. mucopurulent nasal discharge, cough and pyrexia). Prominent nasopharyngeal lymphoid follicles may be responsible for mild upper airway obstruction and an abnormal respiratory noise at exercise.

Topical treatment with anti-inflammatory sprays has been advocated although this is not usually necessary or constructive.

Pharyngeal cysts

Pharyngeal cysts in the nasopharyngeal roof, soft palate and particularly subepiglottic tissue (*q.v.*) are occasionally found in young foals, and rarely in

mature horses. Typically, affected foals make an **abnormal respiratory snoring noise** and dysphagia may be noted. The cyst can usually be seen on endoscopic examination of the upper respiratory tract.

Treatment in any site other than subepiglottic may be extremely difficult although there are reports of successful resection of cysts from the edge of the soft palate. Some subepiglottic cysts are associated with epiglottal entrapment (*q.v.*) and in young foals there may be a secondary aspiration pneumonia (*q.v.*), which should be managed appropriately.

Soft palate defects

Midline clefts of the soft palate may be short or involve the whole length of the soft palate. Affected foals usually regurgitate milk down the nose and **secondary aspiration pneumonia** (*q.v.*) may occur. While oral inspection may reveal a cleft of soft or hard palate, a definitive diagnosis can be made by **nasopharyngeal endoscopy**. Asymmetric defects of the soft palate may present a much greater diagnostic challenge as nasal regurgitation of milk often does not occur. In fact, gross dysphagia is sometimes not noted and the major clinical sign may be an abnormal respiratory noise at exercise or exercise intolerance in an older horse.

There is **no satisfactory treatment** for palatal defects and affected horses are not suitable for athletic purposes.

Laryngopalatal dislocation

The normal horse is an obligatory nasal breather and has a unique anatomic relationship by which its larynx fits intimately through a hole in its soft palate. This is temporarily disrupted during swallowing.

If laryngopalatal dislocation occurs at fast exercise, a loud "gurgling" noise is produced and severe respiratory embarrassment results. This respiratory obstruction is usually transient and is corrected by deglutition when the soft palate returns to its respiratory subepiglottic position. Such respiratory obstruction is known colloquially as "**choking up**" or the horse is described as having "**swallowed its tongue**". Affected horses usually stop dramatically and then swallow and continue, showing few signs when examined after exercise. Typically the problem affects racehorses towards the end of a race. Commonly such horses may be galloping freely without difficulty, only "choking" when the jockey attempts to make the horse accelerate. The condition is less commonly encountered in event horses on the cross-country course or even hunters exercising on heavy land.

The cause of this severe transient respiratory obstruction is often obscure but **stress** may play a role, particularly in the racehorse. The mechanism is unknown but some believe that caudal retraction of the larynx by the sternohyoid and sternothyroid muscle groups is involved. Recent work from North America has proposed that neuritis of the pharyngeal nerves may initiate palatal displacement.

In a proportion of cases, a primary respiratory problem may be recognized (e.g. **laryngeal hemiplegia** or **small airway disease**). In these circumstances treatment should be directed toward management of this primary respiratory

problem. However, in a large number of cases no primary specific respiratory disease is identified.

While some horses may respond to conservative treatment such as ensuring the horse is completely fit, using a dropped noseband to close the horse's mouth, a tongue strap to limit tongue retraction, or a milder bit, in many cases such methods are ineffective. **Surgical resection** of the sternohyoid and sternothyroid muscle groups and/or the edge of soft palate, or cautery of the palate using a firing iron via the mouth or a Nd:YAG laser per nasum may be effective, but in a significant proportion of cases no treatment is useful. The insertion of a **tracheostomy tube** may help some horses but a number of horses must be retired from racing to less arduous pursuits with which the condition does not interfere.

Fourth branchial arch anomaly

Fourth branchial arch anomalies are occasionally encountered. Affected horses may suffer rostral displacement of the palatopharyngeal arch as a consequence of cricopharyngeal muscle aplasia or hypoplasia. This pair of muscles constitutes the proximal esophageal sphincter, and their absence results in **aerophagia** and thus **eructation** and **tympanitic colic**. Affected animals often have maldevelopment of the laryngeal cartilages, which results in the production of an abnormal respiratory noise at exercise.

Endoscopic examination often reveals the palatopharyngeal arch to be displaced rostral to the corniculate processes of the arytenoid cartilages, and in some horses it is possible to look down the esophagus from the nasopharynx because of hypoplasia of its proximal sphincter. The condition may be unilateral, in which case it is usually right-sided. There may be an asymmetry of the rima glottidis that can be confused with a recurrent laryngeal neuropathy.

An **air-filled cranial esophagus** is usually noted on lateral radiographic views of the area. There is no treatment for the respiratory obstruction produced by the anomaly.

Hyoid bone fracture

Fracture of the hyoid bone is a rare condition that is usually associated with a pharyngeal injury or can occasionally occur secondary to an inflammatory or neoplastic disease. The usual clinical signs are dysphagia or pharyngeal discomfort and the diagnosis is made by radiographic or endoscopic means. There is no need to treat the fracture except by short-term use of **anti-inflammatory drugs**. It will usually heal by fibrous union. In the absence of neurologic signs the prognosis is good.

GUTTURAL POUCHES

The guttural pouches are paired **air-filled diverticula of the auditory (Eustachian) tubes** peculiar to Equidae and the hyrax (a tree shrew). They are situated ventral to the cranium and dorsal to the nasopharynx and larynx. Each guttural pouch has an opening into the nasopharynx by means of a

cartilaginous flap that opens during deglutition. The function of the pouches is obscure but they are lined by mucous membrane containing follicular lymphoid tissue similar to the nasopharynx (*q.v.*) that may be hyperplastic in younger animals.

Each pouch is divided by the stylohyoid bone in the caudal part, producing a smaller lateral and larger medial compartment. The pouches share a common medial septum. The wall of the lateral compartment is closely associated to the maxillary artery (branch of external carotid), the facial nerve (CN 7) and the parotid salivary gland. Cranial nerves 9, 10, 11 and 12, along with the sympathetic nerves and cranial cervical ganglia, are closely associated in a fold of mucous membrane with the internal carotid artery in the caudal wall and roof of the medial compartment. The retropharyngeal lymph nodes lie ventral and caudal to the pouches. Each pouch is directly connected to the middle ear (*q.v.*).

DISEASES OF THE GUTTURAL POUCHES

Empyema

Following some bacterial respiratory infections a retropharyngeal lymphadenopathy and abscess formation may occur. Classically, such a **pharyngeal abscess** is associated with infection by *Streptococcus equi equi* but any bacterium may be involved. The abscess may rupture into one or both guttural pouches producing **empyema**.

Affected horses may be dull and/or pyrexic, and often there is swelling caudal to the vertical ramus of the mandible. A purulent nasal discharge is common and may be bilateral or predominantly unilateral. The discharge may be fetid. Rarely there may be no nasal discharge, typically because there has been **inspissation** of purulent material within the pouch. In such cases **pharyngeal swelling** may be marked and there may be dyspnea and even dysphagia, although this latter sign is uncommon. Dyspnea is the result of nasopharyngeal obstruction, and dysphagia may follow pharyngeal obstruction or pharyngeal neuritis (*q.v.*).

Endoscopic examination of the nasopharynx will usually reveal **a purulent discharge** from the ostium of one or both guttural pouches and there may be evidence of marked **nasopharyngeal obstruction**, particularly when both pouches are involved. **Endoscopic inspection** of both guttural pouches should be carried out to assess the extent of the infection. However, if the pouch is full of purulent material it may be difficult to insert the endoscope and it may also be difficult to visualize the normal anatomy. In chronic cases the purulent material may have become inspissated forming so-called "**chondroids**", which are balls of dried pus. In some chronic cases the normally thin translucent mucosa of the guttural pouch becomes very thickened and inflamed.

Standing lateral radiographic views of the pharynx will show loss of the normal radiolucent guttural pouch air shadow. Fluid levels may be noted; these may be multiple if both pouches are involved. Irregular increased radiodensity in the guttural pouch area may be present if the purulent material has become inspissated or formed chondroids.

The **treatment** of guttural pouch empyema depends on the clinical severity of the case. If there is dyspnea it may be necessary to insert a temporary

tracheostomy tube or to carry out **emergency drainage** of purulent material with the horse standing. In mild cases it may only be necessary to treat the horse with an appropriate antibiotic as determined by bacterial culture of nasal or nasopharyngeal swabs. In most cases the use of **antibiotics** should be augmented by **lavage of the pouch** using an indwelling balloon catheter. Such lavage using saline, tap water or even a 0.5% solution of **povidone-iodine** or **hydrogen peroxide** should be carried out twice daily until the nasal discharge has resolved. Concentrated solutions of such irritant chemicals may induce neuritis of the adjacent cranial nerves.

If chondroid formation has occurred, it may be necessary to **drain the pouch surgically** via Viborg's triangle (defined by the caudal border of the mandible, the linguofacial vein and the tendon of the sternomandibularis muscle) or a modified laryngoplasty approach (*q.v.*). Such surgery is usually carried out under general anesthesia and care must be taken to avoid the pharyngeal nerves. Usually the wound is left to heal by second intention. It is preferable to avoid surgical drainage if at all possible.

The prognosis for guttural pouch empyema is good provided irreversible pharyngeal nerve damage has not occurred, and that appropriate lavage or surgical drainage and removal of chondroids has been instituted.

Tympany

Air-filled distension of one or both guttural pouches is an uncommon condition usually seen in foals although, rarely, older animals may be affected. It is said to be more common in Arabians and Thoroughbreds in the UK. Affected foals typically have a "**bullfrog**" appearance with marked pharyngeal distension. Although the condition is most commonly unilateral the swelling may appear bilateral because the common medial septum and the soft tissues of the pharynx are flexible. The distension may be intermittent. Affected foals usually make a **snoring respiratory noise, particularly when suckling**, but in bilateral cases dyspnea may be severe.

The etiology of the condition is uncertain, although a ball-valve effect of the mucous membrane fold associated with the cartilaginous flap of the guttural pouch has been suggested. Endoscopic examination of the nasopharynx may be helpful in determining whether the condition is unilateral or bilateral. The nasopharyngeal roof sags asymmetrically in unilateral cases and there may be severe symmetrical collapse of the nasopharyngeal roof in bilateral cases.

The most useful diagnostic aid is a standing lateral radiographic view of the pharynx, which will demonstrate a massively enlarged guttural pouch air shadow. It should also be possible, by assessing the contours of this shadow, to decide whether the condition is unilateral or bilateral.

In unilateral cases the condition may be treated by **fenestration of the common medial septum**. This can be achieved in the standing horse under endoscopic control using a laser or diathermy but is more commonly carried out under general anesthesia via a Viborg's triangle or modified laryngoplasty approach. This technique is obviously ineffective in bilateral cases.

A second surgical method, useful for bilateral cases, involves **ventral enlargement of the nasopharyngeal ostium** of the guttural pouch using a

hooded blade, again via a Viborg's triangle approach, or using a Nd:YAG laser, under endoscopic control.

The third, least invasive and the preferred method is the enlargement of the guttural pouch ostium by **chronic catheterization** using an indwelling balloon catheter. This results in damage and necrosis to the cartilaginous flap, producing a permanently open ostium. Although the catheter must be left in place for 4–6 wk this method can be used in bilateral cases and obviates the need for a general anesthetic.

The most common complication of chronic catheterization is the premature removal of the catheter by the patient, in which case the catheter must be reinserted. Complications of the first two techniques usually arise from iatrogenic damage to the pharyngeal nerves resulting in **dysphagia** (*q.v.*) and **gangrenous aspiration pneumonia**. Occasionally guttural pouch tympany can be complicated by secondary infection and empyema, which can usually be treated effectively by lavage and antibiotic therapy.

The prognosis for resolution of guttural pouch tympany using the above techniques is good provided iatrogenic pharyngeal nerve damage can be avoided and that bilateral cases are recognized and treated appropriately.

Mycosis

Mycotic plaques associated with the guttural pouch mucosa are not rare and typically affect the roof of the medial compartment adjacent to the internal carotid artery and the cranial and sympathetic nerves. Rarely the lesion may be found on the lateral wall of the lateral compartment, associated with the maxillary artery. The fungal lesions appear to develop at these sites in association with **arterial aneurysms** (*q.v.*) although the cause of aneurysm formation is unknown. A variety of fungal and bacterial species have been identified in association with the lesion including *Aspergillus* spp., *Nocardia* spp. and *Pseudomonas* spp.

The most common clinical sign is **epistaxis**, which is usually **bilateral**, is not associated with exercise and may be massive. Such nasal hemorrhage is fatal in a significant proportion of cases if the lesion remains untreated. There is often a foul smelling nasal discharge. Other clinical signs are related to cranial or sympathetic nerve damage, the most common of which is **pharyngeal hemiplegia** resulting in **dysphagia**. Other clinical signs include facial, laryngeal and lingual hemiplegia and signs of sympathetic nerve damage such as patchy sweating, colic or **Horner's syndrome** (*q.v.*). A useful additional clinical sign in these cases is parotid pain, although its severity is variable.

Endoscopic examination of the upper respiratory tract is the diagnostic technique of choice, although visualization may be difficult in horses that have had recent severe hemorrhage. In such cases there may be considerable bleeding in the nasopharynx; however, a characteristic sanguineous discharge from a guttural pouch ostium is usually discernible.

The endoscope should be passed into the pouch with care to avoid disturbing a clot over the artery and consequent hemorrhage. The endoscope is best inserted by passing a biopsy forceps through the biopsy channel of the instrument to open the flap. Sometimes the pouch is full of blood or a **hematoma** making visibility impossible. However, if a clear view can be obtained, a

mycotic plaque is usually easy to see over the roof of the medial compartment; in some horses the lesion may be quite extensive and spread over much of the medial compartment, even extending through the common medial septum to the other pouch. Primary bilateral lesions are extremely rare and lesions affecting the maxillary artery in the lateral compartment are also uncommon. Other endoscopic features may include **pharyngeal or laryngeal hemiplegia** (*q.v.*) and food is often seen in the nasopharynx, larynx and trachea in horses with dysphagia.

Plain radiography is not usually of much value in cases of guttural pouch mycosis. However, lateral radiographic views of the pharynx or a similar view using image intensification after oral administration of a **barium sulfate** suspension may be of great value in determining the presence of pharyngeal paralysis.

Another radiographic technique that is useful in cases of mycosis is obtaining lateral views of the chest in horses with **gangrenous aspiration pneumonia**. Carotid angiography under general anesthesia may also be valuable to determine the presence of **arterial aneurysms** and anomalies. Angiography may be particularly helpful for the inexperienced surgeon in elucidating the arterial anatomy of the carotid tree, which may be variable. However, it is time consuming and unnecessarily prolongs anesthetic time in a potentially poor risk patient and is therefore performed infrequently.

In horses with **epistaxis** (*q.v.*) there is a major risk of **fatal hemorrhage**; the aim of treatment is to prevent this. Although such horses occasionally will recover spontaneously, presumably following thrombosis of the internal carotid artery, **surgical ligation** of the artery via a hyovertebrotomy approach is the treatment of choice. Although simple proximal ligation has been shown to be effective there is a risk of retrograde hemorrhage via the circle of Willis, and most surgeons usually opt to occlude the artery distally. As the artery distal to the typical site of leakage is inaccessible the most satisfactory method of occluding it is by the insertion of an intra-arterial balloon catheter from a proximal site to beyond the leak. This is combined with proximal ligation.

In any horse with pharyngeal paralysis there is a risk of **aspiration pneumonia** (*q.v.*).

Some horses appear to recover from pharyngeal hemiplegia, presumably because the neuritis may be reversible or because the horse adapts to an altered method of deglutition.

Antifungal medication of the plaque via an indwelling catheter may be helpful in resolving the lesion but is of secondary importance to depriving the plaque of its blood supply. A weak solution of approximately 250 mL **natamycin** is injected via a catheter syringe and an indwelling balloon catheter into the pouch. Alternatively a smaller volume may be nebulized into the pouch via the catheter. These treatments are seldom carried out these days other than at the time of surgery, unless neurologic signs are present. However, in horses showing no signs of hemorrhage, medical treatment alone is indicated.

Neoplasia

In gray horses, melanin deposition submucosally in the guttural pouches is quite common and the development of **melanomas** (*q.v.*) is not uncommon.

Such lesions seldom develop to produce clinical signs although pharyngeal obstruction may eventually result if the lesion enlarges. Rarely the guttural pouch may become a site for development of other tumors such as a squamous cell carcinoma (*q.v.*). However, these tumors usually arise primarily in the nasopharynx adjacent to the pouch (*q.v.*).

Allergic parotiditis

Allergic parotiditis is confused frequently with diseases producing guttural pouch distension. The problem occurs only **at grass** and affected horses show a bilateral enlargement of the parotid salivary glands, which may occur to a marked degree. In the most severe cases, **facial edema** develops because of impaired facial venous drainage as a result of parotid gland enlargement. The condition rarely produces respiratory obstruction.

The most striking feature of the condition is the **rapid recovery** when affected horses are brought indoors. Several horses may be affected in one field, and some fields appear more likely to induce the condition than others. Samples of blood collected at the time may show an eosinophilia. It has been assumed that the problem is caused by an **allergy** to some factor in the outdoor environment, possibly some ingested plant material. Treatment is not usually indicated and affected horses may be returned to the same pasture eventually without developing the condition.

THE LARYNX

The equine larynx consists of five cartilages (the epiglottis, paired arytenoid, thyroid and cricoid cartilages). The **rima glottidis** (arytenoid cartilages and vocal cords) of the larynx acts like a biological valve. When fully abducted it permits an adequate flow of air to the lungs at fast exercise and when fully adducted it helps prevent aspiration of food during deglutition.

During quiet respiration the rima glottidis adopts an intermediate position. Movements of the rima glottidis are controlled by muscular action from the vagus (CN 10). The only abductor muscle is the cricoarytenoid dorsalis, innervated by the **recurrent laryngeal nerves**; the other muscles all produce adduction. The only muscle innervated by the cranial laryngeal nerve is the cricothyroid muscle.

On each side of the larynx is a pair of folds (vestibular and vocal) composed of muscle and the covering mucous membrane. The lateral ventricle is a small mucous membrane outpouching situated between these folds on each side. These structures have a role in vocalization. The subepiglottic mucosa is loosely attached to the oral surface of the epiglottis. This permits dorsocaudal movement of the cartilage during deglutition.

The rostral laryngeal cartilages fit snugly through a hole in the soft palate. During deglutition this relationship is disrupted when the soft palate is elevated and the larynx moves rostrally. At this movement the epiglottis is tipped dorsocaudally and the glottis is closed, preventing food entering the lower airway.

DISEASES OF THE LARYNX

Recurrent laryngeal neuropathy

The most important laryngeal disease is paralysis, which usually presents as **left-sided laryngeal hemiplegia** or hemiparesis. The cause of this disease is unknown but a "dying-back phenomenon" is noted histologically in the left recurrent laryngeal nerve. The routes of the left and right nerves are different in the horse, the left being much longer and traveling around the aortic arch before supplying the larynx. It is generally considered that it is the length and route of the nerve that is responsible for the disease. The idiopathic disease probably has a heritable component, which is complex in nature.

The disease is characteristically found in larger male horses but may occur in females and smaller horses or ponies. The disease occurs on the right side in a small proportion of cases. However, many cases that appear right-sided have a branchial arch anomaly (*q.v.*). Bilateral paralysis is extremely rare.

Laryngeal hemiplegia can follow a **specific cause** (e.g. accidental perivascular injection of irritant chemicals around the jugular vein, mediastinal mass, guttural pouch mycosis or lead poisoning) but occurs most commonly in its **idiopathic form**.

The clinical signs of the disease are an **inspiratory musical** "**whistle**" or harsher "roar" in more severe cases. Respiratory tract obstruction may occur, depending on the severity of the disease and the occupation of the horse. The disease is more likely to produce dyspnea when affected animals are required to gallop for an extended distance. It should be noted that a small reduction in laryngeal airway diameter produces a relatively large increase in airway resistance. After exercise, **gentle palpation** of the larynx may reveal **fremitus**. There is often obvious atrophy of the left dorsal cricoarytenoid muscle and on careful palpation of the area it is possible to feel the muscular process of the left arytenoid more easily than the right because it is denuded of its associated muscle. After exercise, pressure on the right arytenoid cartilage (the arytenoid depression test) may further narrow the rima glottidis in an affected horse and exacerbate the abnormal respiratory noise.

There is **no cure** for laryngeal hemiplegia and in many mild cases there is no need for treatment. Simply making the horse become fitter will often reduce the noise. In many instances the degree of respiratory obstruction is not severe enough to impair performance. However, the disease can be **progressive** and the paralysis may worsen with time.

Traditional treatment for the disease involves left **ventriculectomy** with or without **cordectomy** via a **cricothyroid laryngotomy**, or using a Nd:YAG or diode laser under endoscopic control.

However, in severely affected horses that are required to perform athletically this procedure is often ineffective. In such horses a **ventriculectomy** is usually combined with a **laryngoplasty** (tieback procedure) in which the collapsed left side of the larynx is **fixed in abduction** by the insertion of retrolaryngeal sutures. The **surgical approach** is ventral to the linguofacial vein. The suture(s) is inserted from the caudal border of the cricoid cartilage to the muscular process of the left arytenoid cartilage under the pharyngeal musculature. When tightened and tied, the sutures mimic contraction of the defunct left dorsal cricoarytenoid muscle.

The most serious complication of this operation is the induction of **severe dysphagia** in a small percentage of cases. Aspiration of food material results from failure of laryngeal protection during deglutition. While a postoperative cough and subtle dysphagia may occur more frequently, such cases can often be managed by dietary adjustment or the horse may be able to adapt to it. Most owners are prepared to accept this because of the improvement in exercise tolerance. If the problem cannot be managed, removal of the implants is indicated.

Laryngoplasty may not improve the laryngeal airflow adequately in some cases, particularly when horses are required to perform at the highest level in flat racing.

Epiglottal entrapment

Dorsal displacement of the subepiglottic mucous membrane over the epiglottis produces **epiglottal entrapment**. The condition may be persistent or transient. A significant proportion of cases are asymptomatic but the mucous membrane pouch produced can be responsible for abnormal respiratory noises at fast exercise or even slower paces. The noise is usually harsh and inspiratory but a fluttering or gurgling expiratory noise may be produced in some horses.

The condition may induce **laryngopalatal dislocation** during galloping. It is common to see **ulceration** of the entrapping mucous membrane in those horses producing abnormal respiratory noises. This may be related to laryngopalatal dislocation or to pressure from the underlying epiglottic tip. The condition in its persistent form can be diagnosed easily by endoscopy. In transient cases it can be much more difficult to identify. Stimulating swallowing during endoscopy can induce the condition although in some cases entrapment may last only a second or so. It has been suggested that endoscopy during treadmill exercise may be helpful in such cases.

The etiology of the condition remains obscure although it can occur in horses with **epiglottal hypoplasia** (*q.v.*) or with a **subepiglottal cyst** (*q.v.*) or mass.

Treatment of horses making a respiratory noise is either by **ablation** of the entrapping mucous membranes via a **cricothyroid laryngotomy**, or by splitting the tissue with a hook knife per nasum, or using a Nd:YAG or diode laser, under endoscopic visualization in the standing horse. Transient cases may be most easily treated by the first technique. In some horses speculative resection of the subepiglottic mucosa may be the only option.

Epiglottal hypoplasia

The epiglottis appears extremely varied in size and shape in the normal horse. Normally, epiglottic size is assessed endoscopically but more accurate measurement can be made from a lateral radiographic view of the area. Gross hypoplasia is extremely rare but has been reported, particularly in the Standardbred. Secondary epiglottal entrapment or laryngopalatal dislocation is the usual consequence.

Traditionally there has been no effective treatment for the condition, although some clinicians have been successful in mild cases using

subepiglottal augmentation, increasing epiglottal bulk by submucosal injection of Teflon or a similar polymer.

Arytenoid chondritis

Arytenoid chondritis has been recognized with increased frequency in recent years. The cause is usually unknown although some cases follow surgical or accidental insult to the laryngeal cartilages. Typically there is swelling and distortion of the **arytenoid cartilage**. If the condition is unilateral there is usually an abnormal respiratory noise at exercise and exercise intolerance in some horses.

The condition may be bilateral with consequent severe laryngeal obstruction. There may be a discharging sinus from the affected arytenoid and "kissing" ulceration of the contralateral arytenoid cartilage is common. Characteristically, even in subtle cases there is swelling of the medial face of the arytenoid cartilage and usually there is gross interference with movement (abduction or adduction) of the affected side of the larynx. Although an endoscopic diagnosis is usually straightforward, care must be taken to differentiate the more subtle cases from laryngeal hemiplegia (*q.v.*). Both left and right sides appear to be involved with similar frequency.

Treatment is by partial or subtotal **arytenoidectomy** via a cricothyroid laryngotomy under general anesthesia. The latter method has been associated with postoperative dysphagia. In the mildest cases there may be little obstruction to the glottis. Laser ablation may be effective when the arytenoid enlargement mainly consists of granulation tissue. In severe cases a **tracheostomy** may be the most practical method of case management.

Laryngeal granuloma

A granuloma associated with the larynx is almost always the **sequel to previous surgery** or to an accident but may be associated with chondritis (*q.v.*). Removal of the granuloma in uncomplicated cases is usually effective, particularly when the granuloma is a sequel to ventriculectomy and is attached to the vocal cord. The condition has been reported in the UK associated with an exotic disease, **rhinosporidiosis**.

Subepiglottic cysts

Congenital pharyngeal cysts in a variety of sites occur rarely in young foals (*q.v.*), producing respiratory obstruction and sometimes dysphagia. The predilection site is the loosely attached subepiglottic mucosa. Small cysts may be asymptomatic but in the majority of cases there is an associated snoring or gurgling noise that may be most obvious during suckling or feeding. With large cysts there may be marked respiratory obstruction.

It is not uncommon for such cysts to be associated with **epiglottal entrapment** (*q.v.*). An endoscopic diagnosis is usually readily made although lateral radiographic views of the pharynx, especially after the oral administration of barium sulfate, may be helpful in confirming the condition.

Treatment is by radical excision of the cyst via a cricothyroid laryngotomy incision. The subepiglottic mucosa should also be resected if there is

concomitant epiglottal entrapment. In most cases excision is effective, but the lesion may be very rostral in a small number of cases requiring removal per os using a snare under endoscopic control.

Neoplasia

Laryngeal tumors are extremely rare in the horse although cases of **lymphosarcoma** and **squamous cell carcinoma** (*q.v.*) have been reported. Surgical resection appears to carry a poor prognosis.

THE EAR

The equine pinna is erect and able to rotate about its long axis under muscular control. The horizontal and vertical canals are relatively inflexible which makes examination of the tympanic membrane extremely difficult in the conscious horse. Typically a thick, dark waxy material is present in the normal ear, representing a secretion from the ceruminous glands. The middle ear and the auditory tube are connected with the guttural pouches. The middle and inner ears are contained within the petrous temporal bone.

DISEASES OF THE EAR

Deafness

Deafness is thought to be uncommon in the horse but is extremely difficult to assess. It may be congenital or result from inflammatory changes in the inner or middle ears or guttural pouches.

Epidermal hyperplasia

Raised white plaques are found quite commonly on the inside of the equine pinna. Histologic examination reveals epidermal hyperplasia. The plaques are asymptomatic but may appear unsightly and are of more concern to the owner than the horse. There is no effective treatment for the condition.

Ear mites

Psoroptic mites (*q.v.*) have been reported as an incidental finding in the horse. However they can be associated with otitis externa and severe aural irritation or even head shaking (*q.v.*). Treatment, if necessary, is with eardrops containing gamma benzene hexachloride.

Otitis externa

Although a dark, waxy material is present in the external ear canal of the normal horse, otitis externa is rare. Clinical signs of aural discharge, head shaking, ear-rubbing or even an aural hematoma have been seen. Otitis has been associated with **ear mite** infestation (*q.v.*), **neoplasia** of the ear canal, a **foreign**

body in the external ear canal or **iatrogenic** causes such as attempted treatment of epidermal hyperplasia with ointments or local abrasion.

Treatment of the primary cause of the problem is usually effective and proprietary ointments or eardrops containing mixtures of antibiotics, gamma benzene hexachloride and corticosteroids plus parenteral non-steroidal anti-inflammatory drugs are usually helpful. General anesthesia may be necessary to carry out this treatment effectively and aural lavage may also be of value.

Aural hematoma

Aural hematoma is rare but usually results from direct **trauma** or **self-mutilation** by the horse because of **otitis externa**. The lesion is best treated as in the dog or cat, by surgical drainage under general anesthesia combined with treatment of any underlying otitis externa.

Aural neoplasia

Tumors of the ear canal are rare in the horse although **papilloma**, **melanoma** and **squamous cell carcinoma** (*q.v.*) have been reported. Usually there is an aural discharge and obvious ear shyness or irritation. Diagnosis is usually by biopsy following auroscopy. The treatment involves local excision of the neoplastic tissue. A lateral ear canal wall resection, as used in the dog, has been employed to give better surgical exposure in cases of squamous cell carcinoma. The prognosis for any lesion other than a papilloma is very guarded.

Sarcoids (*q.v.*) affecting the pinna have been reported and are usually managed by resection and/or cryotherapy or laser treatment of the lesions or by the intralesional injection of BCG (Bacille Calmette–Guérin).

The parotid gland adjacent to the ear is an extremely common site for **melanoma** (*q.v.*) development although the lesion seldom involves the ear itself.

Dentigerous cysts

The development of aberrant embryonic epidermal tissue around the base of the ear is usually associated with a swelling and a sinus discharging sebaceous material near the rostral edge of the pinna. Contrast radiography may be of value in defining a **dentigerous cyst** (*q.v.*), which is often associated with single or multiple aberrant teeth attached to the petrous or squamous temporal bones. Oblique radiographic views should be obtained in each case to identify such structures.

Surgical excision of the cyst and associated teeth should be carried out under general anesthesia. Care must be taken in removing the teeth as these are usually solidly embedded in the bone and excessive force may result in skull fracture or intracranial hemorrhage.

Peripheral vestibular disease

Inflammatory changes involving the vestibular system occur infrequently in adult horses. The etiology in many cases is obscure but may follow an ascending

infection from the **guttural pouch** or a descending infection from the **external ear**. Affected horses are usually ataxic with a head tilt or nystagmus and sometimes show signs of other deficits (CN 5 or 7). Diagnosis is based on a neurologic examination and recognition or elimination of possible causes of similar signs such as guttural pouch disease or a fractured skull.

Some cases are associated with an **arthropathy** of the **hyoid apparatus**. Radiographic examination of such cases will usually reveal new bone formation affecting the proximal hyoid bones.

Treatment is by the prolonged administration of **parenteral corticosteroids** (prednisolone is probably best, the recommended daily dose being 1 mg/kg PO and reduced by 50% 1 wk before complete cessation of treatment). Nonsteroidal anti-inflammatory drugs may also be helpful. This regimen must be allied to treatment of the primary condition in those cases where this can be identified. The prognosis appears to be variable but many cases will respond to prolonged medication. However, in some horses resection of a portion of the stylohyoid bone is required to resolve the condition.

Head shaking

Head shaking (*q.v.*) may be a clinical sign of a variety of diseases (e.g. **guttural pouch** or **paranasal sinus** lesions). However, there is a well-recognized syndrome that typically involves involuntary rapid dorsoventral head movements at ridden exercise. This dramatic behavioral problem (*q.v.*) is most commonly seen in the warmer months of the year in horses used for general riding purposes but more especially if they are being schooled for more sophisticated disciplines such as dressage. Occasionally, affected horses will try to rub the nose on a foreleg or the ground at the canter. In many cases the horse is either unrideable or extremely dangerous to ride. Usually no clinical, endoscopic or radiologic lesion can be identified to explain the dramatic behavior. The condition is often intermittent and may be weather related.

No specific diagnosis can usually be made and although some horses recover spontaneously, in many cases the problem is persistent. Bilateral infraorbital neurectomy has been found to be effective in a proportion of cases although the reason for its efficacy is unclear. Similarly destruction of the ethmoidal nerve by injection of 10% phenol in almond oil using a long spinal needle has also shown to be effective in a small number of cases, although the improvement may be temporary or incomplete.

In some cases the symptoms may be relieved by the use of muslin gauze attached to the noseband and covering the external nares. Medical management of head shaking horses is usually ineffective although **fluphenazine** has been used.

Chapter 7

The lower respiratory tract

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Chapter contents

INTRODUCTION

The horse is unique among domestic animals in the demands that are placed on its respiratory system. The cantering and galloping horse has locomotor and respiratory cycles locked in a one-to-one phase. A galloping horse will take over 150 breaths per min (bpm), having <0.5 s to inhale and exhale 12–15 L of air. Minor degrees of respiratory disease in the form of small

increases in mucopus in the airways or minor degrees of airway spasm will quickly take their toll on athletic performance, although horses with minor lower respiratory tract problems may not show overt signs of disease at rest.

Diagnosis has been made easier with the use of the **fiberoptic endoscope and more recently with the videoendoscope**. The covert respiratory problems of the relatively young equine athlete may be precursors of more overt problems later in life in the form of **recurrent airway obstruction (RAO)**, previously known as chronic obstructive pulmonary disease (COPD). Therefore, the diagnosis, treatment and prevention of respiratory problems in young horses have both short- and long-term benefits.

Considerable emphasis has been placed on **environmental factors**. Air quality of stables can affect the incidence and severity of a range of lower respiratory tract problems and in many instances is a valuable adjunct to pharmacologic intervention. The old adage of prevention being better than cure cannot be overemphasized in terms of the respiratory well-being of the stabled horse.

This chapter will review the diagnostic approaches useful in assessing lower respiratory tract disease, therapeutic approaches to some more commonly seen problems and the air hygiene of stables. Exercise-induced pulmonary hemorrhage has been associated with a wide range of equine athletic events and this condition is dealt with separately for this reason.

DIAGNOSTIC APPROACHES TO LOWER RESPIRATORY TRACT DISEASES

INTRODUCTION

The understanding of equine pulmonary disease has greatly increased during the past 25 years due to major advances in veterinary virology, pulmonary pathology, pulmonary function assessments and respiratory endoscopy. The development and application of a wide range of ancillary diagnostic techniques can now enable us to diagnose accurately and monitor objectively pulmonary disease in the horse. Practitioners can readily utilize many of these techniques and their use will greatly enhance the quality of veterinary practice.

CLINICAL EXAMINATION

With gross pulmonary diseases, such as **bacterial pneumonia** in foals (*q.v.*) or advanced **recurrent airway obstruction** (RAO) (*q.v.*) in adult horses, clinical signs of pulmonary disease will be obvious, possibly even on cursory examination.

Clinical signs can include coughing, which may be in bouts (paroxysmal) and which may expectorate large volumes of abnormal **respiratory secretions** (RS) via the oral cavity. Other obvious clinical signs can include bilateral nasal discharge, grossly elevated respiratory rate (i.e. $\geqslant$25 per min in an adult horse), increased respiratory effort (**hyperpnea**) and poor exercise tolerance or even weakness, with severe hypoxemia. Pyrexia and depression may occur in

infectious respiratory diseases and percussion of the ventral chest will reveal dullness in cases of pleural effusion. Cases with such near-pathognomonic signs of pulmonary disease will present no diagnostic challenge.

Additionally, the history and epidemiologic factors such as age, colostral or vaccination status, numbers of animals involved, transport history, history of contact with donkeys and knowledge of the type of forage, bedding and housing used, may enable a specific type of pulmonary disease to be diagnosed.

Limitations of clinical pulmonary examinations

The above examples of gross pulmonary disease are exceptional and in the majority of cases of equine pulmonary disease the clinical signs will not be pathognomonic. Many, if not most, horses with pulmonary disease do not have a nasal discharge, as all excessive RS produced in the lungs are swallowed.

Many horses with pulmonary disease will not have sufficient change in pulmonary function to increase significantly their respiratory rate or effort to an extent that will be clinically apparent and clearly differentiable from changes due to individual variation, breed differences or physiologic changes induced by clinical examination. While many horses with pulmonary disease have insufficient pulmonary inflammation or loss of pulmonary function to enable a clinical diagnosis to be made clearly, they may have sufficient loss to cause a **reduction in exercise performance**, especially in high performance animals such as racehorses.

Auscultation of chest sounds is a very subjective and unreliable procedure in horses with mild or even moderate pulmonary disease, with little agreement between different clinicians in such cases. **Tracheal auscultation** after nasal occlusion or use of a **rebreathing bag** renders auscultation more accurate.

The presence of **coughing** is probably the most reliable clinical indicator of pulmonary disease in the horse. Yet this sign is sometimes inexplicably absent in horses with significant pulmonary disease, even when excessive RS production is present.

Clinical diagnosis of pulmonary disease can thus be unreliable.

ANCILLARY DIAGNOSTIC AIDS

Ancillary diagnostic tests can be used: (1) to confirm the presence of pulmonary disease where clinical signs suggest, but cannot confirm, pulmonary disease; and (2) to examine for the presence of pulmonary disease in horses showing poor exercise performance, without any overt clinical signs of pulmonary disease.

In instances where pulmonary disease has already been diagnosed, diagnostic tests can be used: (1) to identify precisely the specific pulmonary disorder involved; and (2) to assess objectively the degree of pulmonary dysfunction present so that the progress of the disease and/or response to therapy can be monitored.

ENDOSCOPY

Endoscopy is probably the most useful and easily performed diagnostic technique available for equine pulmonary disease investigation. The horse has an **insensitive upper respiratory tract** that readily allows the passage of an endoscope into the trachea. This procedure (**tracheoscopy**) is usually termed bronchoscopy. In the absence of respiratory disease, the equine trachea will contain no endoscopically visible or just tiny flecks of RS.

Most equine pulmonary disorders are associated with increased production of RS, which are usually **mucopurulent** in nature. Purulent RS occur with bacterial pneumonias and secondary bacterial infections. The overproduction of RS is often accompanied by a reduction in the mucociliary clearance mechanisms, and both factors result in an accumulation of RS in the horizontal (thoracic) trachea.

Excessive tracheal RS can be **graded** from 1 to 5 based on **volume**. The endoscopic presence of a pool of RS in the trachea is a most sensitive indicator of the presence of pulmonary disease. In younger horses, excessive RS usually result from viral infections or their sequelae but in older animals are usually due to RAO (*q.v.*). Some animals can perform to a high athletic level despite the presence of grade 1 or 2 tracheal RS. This suggests that, in these animals, insufficient small airways are involved to significantly affect airflow, even during exercise.

Tracheal mucosal inflammation is usually absent in chronic pulmonary diseases unless coughing is present, but bronchial mucosal inflammation will be commonly seen. **Mucosal inflammation** can be recognized as a blunting of the carina and bronchial divisions, along with redness and possibly the presence of prominent mucosal vasculature.

After spraying a few milliliters of local anesthetic (e.g. 0.2% lidocaine) on the carina, it is possible to advance the endoscope to examine the main bronchi. With pulmonary abscessation (*q.v.*) or exercise-induced pulmonary hemorrhage (EIPH) (*q.v.*), it may even be possible to localize the source of pus or blood to a particular lung segment. Rarely a tracheobronchial foreign body may be present and can be removed. With anterior thoracic masses such as mediastinal lymphosarcoma (*q.v.*) or abscessation, a collapsed mainstem bronchus may be observed. In dyspneic horses, a dynamic collapse of the intrathoracic tracheal and bronchial walls may be seen during expiration. With obstructed pulmonary venous return, e.g. with cardiac disease or anterior thoracic masses, prominent veins will be seen on the lateral tracheal wall.

Pleuroscopy, i.e. the insertion of an endoscope through a surgical incision in the chest wall, after drainage of pleural fluid, may be of diagnostic value in horses with pleural effusion. **Ultrasonography** is, however, a less invasive and generally more useful technique for such investigations.

BACTERIOLOGIC EXAMINATIONS

Nasal or nasopharyngeal swabs

If a profuse **bilateral nasal discharge** is present, particularly in the presence of a cough and bilateral submandibular lymphadenitis, this is suggestive of

infectious pulmonary disease. Such nasal discharges will often contain RS from the lower respiratory tract, but also contain variable numbers of upper respiratory tract (URT) bacteria.

Culture of nasal discharge is unreliable in the diagnosis of pulmonary bacterial infections, but is of value in the diagnosis of **strangles** (*q.v.*), a primary URT infection, although culture or polymerase chain reaction (PCR) analysis of guttural pouch lavage fluid is a much more sensitive method of strangles diagnosis. With **chronic unilateral nasal discharges**, which indicate a unilateral URT infection, nasal bacteriology is frequently worthless, as the recovered bacteria are usually secondary to sinusitis or to mycoses of the nasal cavity or guttural pouches. However, the recovery of pure and heavy fungal growths can suggest a URT mycosis (*q.v.*).

Transendoscopic tracheal aspirates

Cultures of RS, aspirated directly from the trachea using a bronchoscope, are more useful than nasal or nasopharyngeal swabs. However, they usually still have bacterial contamination from the URT and/or from the endoscope, even if the greatest care is taken during the nasal, nasopharyngeal and laryngeal passage of the endoscope.

URT contamination can be reduced by sealing the distal end of a sterile transendoscopic catheter with a plug of **sterile agar**, prior to inserting the sterilized endoscope into the trachea. Before RS collection, this plug is flushed out into the trachea, where it is harmless. More complex techniques such as telescopic sheathed catheters and endoscope sheaths have been developed to overcome URT contamination of tracheal aspirates. Contamination of RS by saliva can be reduced by starving the animal for 30 min prior to bronchoscopy and by rapid sample collection.

Direct transendoscopic aspiration of RS from the trachea is more desirable than a tracheal wash as it allows quantitative bacteriology to be performed. Enumeration of the **numbers** of bacteria present is also very important in assessing the significance of recoveries. Isolates $\geqslant 10^6$ colony forming units (CFU)/mL RS are usually significant, particularly if a single type of a potentially pathogenic bacterium is present. Isolates $\leqslant 10^4$ CFU/mL are usually insignificant, especially when a mixed growth is obtained. However, it is essential that **anaerobic** as well as **aerobic** cultures be performed.

Transtracheal aspirates

Transtracheal aspirates constitute the most accurate technique for obtaining pulmonary RS samples for bacteriologic culture. After local anesthesia has been performed on a clipped and prepared distal midline cervical site, a 12–14 G needle or cannula is inserted into the trachea. A sterile catheter is then aseptically inserted through the needle and directed caudally along the floor of the trachea to the thoracic inlet, where RS usually accumulates in the diseased animal.

If RS cannot be directly aspirated after repeated attempts, **20–50 mL sterile saline** can be flushed down the catheter and the resultant "tracheal wash" aspirated. This latter step will, however, preclude quantification of isolates.

Occasionally a **subcutaneous abscess** or **emphysema** (*q.v.*) will develop after tracheal puncture.

Bronchoalveolar lavage fluid (BALF)

Because of inevitable URT contamination and large and variable sample dilution during BALF collection (*q.v.*), cultures of BALF are of limited diagnostic value. With pulmonary abscessation, **transendoscopic** bronchoalveolar lavage of the affected bronchus may be useful.

Pleural fluid

Bacterial pulmonary infections in adult horses are uncommon in the UK, in contrast to the USA where the **pleurisy/pulmonary abscessation syndrome** is common. Such infections are often accompanied by a **massive pleural effusion** that may contain the causative bacteria, which (paradoxically for lung infections) are often **anaerobes**. After routine skin preparation, an 18 G needle is inserted in a caudal intercostal space between the 7th and 10th ribs in the ventral chest. **Thoracocentesis** can confirm the **presence** of and the nature of pleural effusion and can allow the collection of samples for culture and cytology. Concurrent tracheal secretion bacteriology should also be performed in these cases.

VIROLOGIC EXAMINATIONS

Virus isolation is useful only during the **very early febrile stages** of respiratory infections. Nasal or nasopharyngeal swabs should immediately be placed in virus transport medium, cooled and transported within 24 h to a specialized laboratory. If an equine herpesvirus infection (*q.v.*) is suspected, a blood culture is also worthwhile. Because of the short duration of virus shedding and the fragility of such isolates, even with good collection, transport and laboratory techniques, many viral cultures will be negative.

Many immunologic techniques are being developed worldwide that can give rapid diagnosis of viral infections, including an ELISA test for **equine influenza** (*q.v.*) that can give a diagnosis within 24 h, PCR tests for tissue samples for **equine herpesvirus** (*q.v.*), and PCR tests for tissue and semen samples for equine viral arteritis (*q.v.*) that can give results within a couple of days.

Retrospective diagnosis of viral respiratory infections can be obtained by **virus serology**. An initial sample should be taken as early as possible during the course of the disease and a second 2 wk later. The information from such virologic studies may not be available rapidly enough to help the clinical management of individual cases but it can give invaluable information for the development of effective vaccine strategies.

RESPIRATORY TRACT SECRETION CYTOLOGY

RS cytology is a most useful ancillary diagnostic technique, particularly with chronic pulmonary diseases. RS cytology can be performed on tracheal RS or preferably on BALF samples. With pleural effusions, cytology may be used

to diagnose **thoracic neoplasia**, which is commonly due to mediastinal lymphosarcoma (*q.v.*).

Tracheal RS cytology

Tracheal samples are usually collected with a transendoscopic catheter but can also be collected by transtracheal aspiration. Tracheal RS slide preparations usually contain dense mucus clumps, which make cytologic assessment more difficult than BALF cytology. Additionally, tracheal RS cytology does not correlate well with pulmonary histopathology, in contrast to BALF cytology. It appears that different cell populations exist in the trachea and the smaller bronchioles, the latter being the primary site of equine pulmonary disease.

Normal tracheal RS cytology

Tracheal RS cytology from horses without pulmonary disease reveals mainly ciliated epithelial cells and macrophages, with ⩽20% neutrophils in animals kept inside and ⩽5% neutrophils in animals kept outdoors; a few cuboidal epithelial cells and lymphocytes and an occasional eosinophil, mast cell and goblet cell may also be found. If stratified squamous epithelial cells are found in tracheal RS preparations, this indicates **salivary or URT contamination** and such samples should be discarded.

BALF cytology

BALF cytology is easier to examine, enumerate and interpret than tracheal RS cytology. BALF cytology also correlates very well with pulmonary histopathology. The areas lavaged during bronchoalveolar lavage are primarily the distal smaller airways and alveoli. With localized pulmonary disease such as **pulmonary abscessation** (*q.v.*), it is possible to lavage a normal area and so obtain misleading results. BALF cytology is currently considered to be the most sensitive diagnostic technique for the diagnosis of RAO (Table 7.1).

For **transendoscopic BALF collection**, a minimum endoscope working length of 180 cm is required in an adult Thoroughbred, but a 300 cm endoscope is required for BAL of the diaphragmatic lobe. Having entered a main bronchus, the endoscope is then advanced into a secondary or tertiary bronchus until it is wedged. The accessory lobe bronchus, off the right mainstem bronchus, is a convenient site in Thoroughbreds, especially when using a 180 cm endoscope.

Table 7.1 Normal BALF cytology

Neutrophils	<5%
Macrophages (with some containing hemosiderin in horses in hard work)	30–90%
Lymphocytes	30–60%
Eosinophils	<2%
Mast cells	<10%
Epithelial cells	<5%

BALF samples may also be obtained with a proprietary BAL catheter or even with a foal stomach tube. BAL catheters tend to lavage the caudal diaphragmatic areas and so are useful in examinations for EIPH. Unlike transendoscopic BAL, BAL catheters do not permit a specific lung area to be lavaged.

Following wedging, **250 mL lukewarm saline** is quickly infused into the lung and immediately aspirated, approximately 50% usually being recovered. Cytology is best performed on a cytocentrifuge preparation.

BALF cytology in pulmonary disease

Neutrophilia, i.e. the presence of ⩾5% neutrophils in BALF, can occur: (1) permanently in symptomatic RAO, inflammatory airway disease (IAD) (*q.v.*) or summer pasture obstructive pulmonary disease affected horses; (2) for some weeks with viral respiratory infections; and (3) along with high numbers of intracellular bacteria and possibly with toxic neutrophils in bacterial pulmonary infections.

Eosinophilia, i.e. the presence of ⩾3% eosinophils in BALF, can occur: (1) with eosinophilic interstitial pulmonary diseases (*q.v.*); (2) transiently at pasture (due possibly to *Parascaris* migration [*q.v.*]); and (3) in lungworm (*q.v.*) infection.

If the majority of BALF macrophages in horses performing hard work contain hemosiderin, this may indicate that clinically significant EIPH is present. Nearly all horses in hard work have some hemosiderophages in their RS.

PULMONARY FUNCTION EXAMINATIONS

If sufficient pulmonary tissue is diseased, there may be some measurable decrease in lung function. **Pulmonary function measurements** are primarily of value in the diagnosis and monitoring of severe pulmonary disease. Because of the absence of patient cooperation in veterinary medicine, in contrast to human medicine where measurements such as forced expiratory volume are standard tests, lung function tests must be performed at rest, unless treadmill facilities are available. Unless trained, many horses object to face masks and/or pneumotachographs and may react to their presence by breath holding or hyperventilating, both of which will invalidate results. The use of sedation to facilitate pulmonary function measurement can also influence results.

There are **large reserves in lung function**, especially in the smaller airways, where it is estimated that most of the bronchioles must be obstructed before any detectable change in lung function occurs. Consequently, lung function examinations, especially at rest, are **very insensitive** with small airway disease, and will frequently show no abnormalities, even in the presence of moderate bronchiolar disease.

Significant but unexplained short- and long-term variations in pulmonary function values have been found even in normal trained horses examined under ideal conditions. **Pneumotachography**, which is required to derive dynamic compliance or pulmonary resistance values, requires expensive

equipment and expertise for accurate calibration, recording and interpretation of results.

These factors combine to restrict the usefulness of many equine pulmonary function examinations to group studies, using trained experimental animals. Arterial blood gas analysis (normal PaO_2 85–100 mmHg) and maximal intrathoracic pressure measurements (normal $d_{max}P_{pl}$ 1–4 mmHg), if obtained in the relaxed, unsedated horse, are useful examinations that can objectively quantify lung dysfunction. However, they rarely enable pulmonary disease that is not clinically apparent to be diagnosed. Additionally, even when pulmonary function tests indicate dysfunction, they give no indication of etiology.

THORACIC RADIOGRAPHY

Thoracic radiography is of great value for the diagnosis and monitoring of pulmonary disease in foals such as **neonatal or *Rhodococcus* pneumonias** (*q.v.*). In adult horses, due to their large chest mass, thoracic radiography is of limited value.

The majority of adult equine pulmonary diseases, including viral infections, RAO, interstitial diseases and low grade EIPH, result in **diffuse parenchymal lesions** that will not be consistently detected radiographically unless very severe disease is present. Additionally, even minor variations in thoracic radiographic technique in adult horses can cause large perceived differences in chest films. However, major lesions, especially if focal, including severe EIPH, large abscesses or pneumonic lesions, pleural effusions, pneumothorax and diaphragmatic hernias, can be usefully assessed radiographically.

THORACIC ULTRASONOGRAPHY

Ultrasound waves cannot pass through air, limiting the use of ultrasonography in pulmonary investigations to those lesions that extend to the periphery of the lung. However, in cases of pleural effusion and subpleural masses, e.g. abscessation, it is the diagnostic technique of choice.

Ultrasonography can **non-invasively** detect and measure the extent of pleural effusions and can also outline **pleural adhesions** and the presence of particulate matter in these effusions. Most equine pleural effusions are caused by subpleural abscessation. Ultrasonography may detect these abscesses as echoic areas in the peripheral lung field and may even permit ultrasound-guided drainage.

PHARMACOLOGIC APPROACHES TO TREATMENT OF LOWER RESPIRATORY TRACT DISEASES

INTRODUCTION

Viral, hypersensitive and bacterial lower respiratory tract (LRT) diseases generally induce common pathophysiologic changes in the lower respiratory

tract. **Inflammation** is central to these changes and leads to failure in mucociliary clearance, impaired airway and pulmonary defenses and increased susceptibility to airborne environmental irritants (including dusts and noxious gases), allergens, opportunist agents, viral and bacterial pathogens and endotoxin (Gram-negative bacterial lipopolysaccharide and lipo-oligosaccharide).

The pathogenesis of allergic LRT disease is further complicated because many horses progress from *specific* reactivity to allergens to *non-specific* hyperreactivity to a variety of airborne irritants. Maintenance or exacerbation of clinical signs then occurs without exposure to the initiating allergen(s).

The central role of **stable air hygiene** in LRT disease pathogenesis, especially allergic LRT disease, means that pharmacologic approaches represent only one aspect of management. The most important components of successful therapeutic regimens are twofold: (1) **environmental changes** to improve stable air hygiene, and (2) **rest** if severe disease is present. Irrespective of the initial cause of respiratory disease, inhaled environmental challenge must be minimized. The importance of stable air hygiene and its influence on airway and pulmonary function is discussed below. Exercising horses with LRT disease leads to delayed recovery or worsening of the condition, possibly with permanent impairment of pulmonary function, and will occur despite any pharmacologic precautions that are taken to attempt to keep the horse in exercise.

Exercise exacerbates airway and pulmonary inflammation by a variety of mechanisms, principally involving mechanical damage by large tidal flows and high respiratory rates. The stress of exercise also significantly impairs pulmonary defense mechanisms by further compromising mucociliary clearance and decreasing the phagocytic and cytotoxic activity of pulmonary macrophages and lymphocytes.

Common pitfalls in therapy and management regimens include inability or unwillingness of the owner to improve the **air hygiene** of adjacent and communicating airspaces; placing too much reliance on the beneficial effect of soaking hay rather than considering silage/haylage as alternatives; turning out to pasture but using hay and straw in the field shelter; using paper or shavings in stables but as deep litter that allows heavy fungal and mold build-up; failure to use appropriate combinations and doses of drugs, and not choosing the most effective delivery route.

RECURRENT AIRWAY OBSTRUCTION

Recurrent airway obstruction (RAO), also known as heaves and chronic obstructive pulmonary disease (COPD), is one of the most common causes of respiratory disease. However, despite an improved understanding of the etiopathogenesis of RAO and the availability of effective drugs for its therapy, management and prevention, regimens may fail to provide satisfactory control. There are several reasons for the apparent failure of these regimens.

First, although there has usually been an attempt to improve stable air hygiene, environmental improvements are often incompletely carried out so that horses are subjected to continual or intermittently high levels of **airborne antigen** and **irritant challenge**.

Second, there is frequently confusion over which therapies to use, and often a logical therapy sequence is not followed. Bacterial infections are uncommon in symptomatic RAO horses and antibiotics are of little value in most cases. Many drugs are administered at insufficient doses, for insufficient time or by inappropriate routes to produce a significant clinical effect.

Third, partially controlled, long-term symptomatic horses develop a number of more slowly reversible pathophysiologic changes and are less responsive to therapy, thus requiring more determined management.

The pharmacologic management of RAO cases can be divided into three headings:

1. Routine management
2. Prophylaxis and maintenance
3. Crisis management.

Routine management of RAO cases

Therapy for routine RAO cases (i.e. mild to moderately dyspneic and tachypneic horses that are not in crisis) can be represented as a simple tiered pyramid (Figure 7.1). Therapy starts at tier one and if symptoms fail to improve, deteriorate or become more persistent, then tiers two and three are added in turn until satisfactory control is achieved. Once symptoms are controlled and the horse is stabilized, then tiers can be removed from the regimen and the pyramid descended.

Bronchoconstriction and mucus accumulation

Bronchoconstriction and mucus accumulation are central pathophysiologic changes in the development of RAO and are driven by **inflammation**. The critical point of control for RAO cases, therefore, is to block the inflammatory cascade that results in bronchoconstriction and mucus accumulation. While bronchodilators and mucolytics provide symptomatic control of the *effects* of inflammation, these drugs do not control the inflammatory cascade that *causes* these changes.

In some countries, **bronchodilators**, sometimes in combination with mucolytics, have traditionally formed the sole therapeutic approach to RAO. This

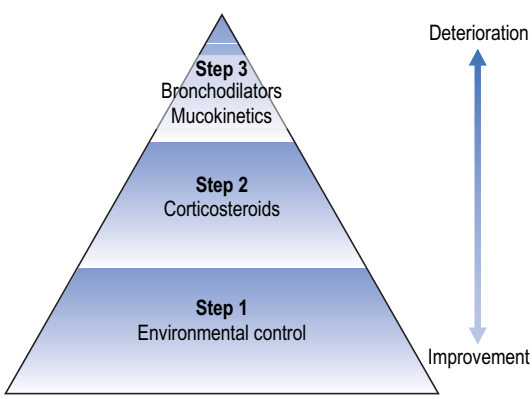

Figure 7.1 RAO therapy objectives (adapted from British Thoracic Society Guidelines).

approach is no longer valid and therapy must control airway inflammation by removing the source of pulmonary allergens and irritants by environmental control, possibly by using **corticosteroids to speed up remission, especially when environmental control is suboptimal**, and then, in cases where there are moderate to severe clinical signs, provide symptomatic relief of bronchoconstriction and mucus hypersecretion using **bronchodilators** and **mucolytics** (*q.v.*).

Step 1: Environmental management

Environmental management is the first and most important component of RAO therapy. The relationship between **stable air hygiene** and RAO is discussed elsewhere (*q.v.*). If adequate environmental improvements are not made, then any therapeutic regimen implemented is unlikely to succeed. **Drug treatments will not compensate for poor air hygiene** and all efforts must be made to impress the pivotal role that environmental management plays in successful disease control.

Drug treatment in the face of inadequate air hygiene improvements will result in temporary, usually partial, symptomatic relief with return of symptoms as soon as therapy ceases. Wherever possible, horses with RAO should be **turned out to pasture** and kept at pasture year-round. Turnout provides the optimum clean air environment; stable air, whatever stable and management modifications are made, will always have poor hygiene in comparison.

Step 2: Block inflammation using corticosteroids

Corticosteroids are highly effective for reduction of airway and pulmonary inflammation but there is a delay of several (3–7) days before clinical signs improve. Horses with mild disease can be managed with corticosteroids alone. Horses with moderate disease, however, should be treated with corticosteroids and bronchodilators/mucolytics to give rapid symptomatic relief.

(a) Systemic corticosteroids. Systemically administered corticosteroids are convenient and cost effective but do carry a slight risk of laminitis, adrenocortical depression and possibly iatrogenic Cushing's syndrome (*q.v.*). However, the traditionally held fears of the risks of laminitis induction by corticosteroid administration appear to be exaggerated, and judicious use reduces these risks to a minimum. Nevertheless, careful thought should be given before administering corticosteroids to animals with a history of laminitis or with Cushing's syndrome. **Dexamethasone** (0.1 mg/kg IV s.i.d.) is highly effective and is regarded as the "gold standard" corticosteroid therapy for RAO.

Clinical signs, airway neutrophilia and pulmonary function, generally improve from day 3 of treatment and are well controlled by day 6–8. In most cases 7–10 days of treatment is sufficient to control clinical signs. **Prednisolone** (0.5–1 mg/kg PO s.i.d.) is widely used and does provide adequate control of clinical signs within 4–7 days of treatment. Improvements in airway neutrophilia and pulmonary function are less consistent than with dexamethasone, which may be due to the shorter duration of prednisolone's anti-inflammatory effect.

Long acting corticosteroid preparations (e.g. **triamcinolone acetonide** 0.1 mg/kg IV single dose and dexamethasone isonicotinate 0.04 mg/kg IM q 72 h) also provide effective control but result in marked adrenocortical suppression (*q.v.*) and, presumably, increased risk of corticosteroid-associated side effects.

(b) Inhaled corticosteroids. Inhalation is a highly effective alternative route for corticosteroid administration that reduces drug dose and the risk of side effects by delivering drug directly to the respiratory tract. This method is more expensive than systemic treatment and does require patient compliance.

Nebulization using jet or ultrasonic units has largely been superseded by the use of **metered dose inhalers** (MDIs). MDIs are quicker and simpler to use than nebulizers and are better tolerated by the horse. There are three equine devices that can be used with MDIs: Equine Aeromask (www.genitrix.co.uk), Equine Haler (www.equinehaler.com) and 3M Equine Inhaler (Boehringer Ingelheim Vetmedica).

Fluticasone (1000–2000 mg b.i.d.) is the most potent (and expensive) corticosteroid MDI. **Beclometasone** (1500–3000 μg b.i.d.) also provides effective symptom control and improves pulmonary function from 24 h of administration. It should be remembered that inhalation reduces, but does not eliminate, the risk of side effects. Corticosteroid inhalation depresses serum cortisol concentrations although adrenal responsiveness to exogenous ACTH administration appears to be less affected. The clinical significance of these observations is not clear but it is sensible to monitor horses treated with inhaled corticosteroids for corticosteroid-associated side effects (*q.v.*).

Step 3: Symptomatic control using bronchodilators and mucolytics

Airway diameter is determined by bronchial wall smooth muscle tone and is a balance between β_2-adrenoceptor-mediated bronchodilatation and muscarinic cholinoceptor-mediated bronchoconstriction.

(a) Systemic bronchodilators. The selective β_2-agonist **clenbuterol** is the most widely utilized bronchodilator for RAO therapy and is initially administered at the rate of 0.8 μg/kg PO b.i.d. or IV. It has minimal α- and β_1-agonist activity and so is relatively free from the unwanted cardiac and peripheral circulatory effects produced by non-selective agonists (e.g. isoprenaline), although transient patchy sweating and muscle tremors may be seen at higher oral doses and following IV injection. There is rapid (within 5–7 days of administration) **tolerance to β_2-agonists** when administered on their own but this effect is reduced when they are co-administered with corticosteroids; this is a further reason why sole therapy with β_2-agonists should not be employed.

Clenbuterol has a more clinically useful duration of action than some other β_2-agonists (e.g. terbutaline and isoproterenol) and requires twice daily administration only. Oral administration provides effective control of symptomatic RAO horses. Clenbuterol can be administered IV to relieve **acute bronchospasm** and produces clinical improvement within 30 min of injection. A further useful property of clenbuterol is that it

improves **mucus removal** from the respiratory tract by stimulating mucociliary clearance.

If the response to the initial dose (0.8 μg/kg b.i.d.) is disappointing, then the dose can be increased by 0.8 μg/kg b.i.d. increments at 3-day intervals (i.e. 0.16, 0.24 up to a maximum of 0.32 μg/kg b.i.d.) until satisfactory response is obtained. Therapy should be maintained at least until clinical improvement is apparent (usually 2–3 wk).

Parasympatholytic anticholinergics produce bronchodilatation by decreasing parasympathetic tone in airway smooth muscle. Parenteral atropine is an effective bronchodilator in RAO-affected horses but has a short duration of action.

Even at low doses of 0.02 mg/kg, atropine has widespread systemic side effects including mydriasis, tachycardia, increased viscosity of respiratory secretions, reduced gut motility and colic, which make it unsuitable for clinical, use.

The phosphodiesterase inhibiting xanthene derivatives theophylline, aminophylline and etamiphyllin (etamiphylline) (all methylxanthines) are moderately effective bronchodilators, but their effect is less profound than that of β_2-agonists and they have a narrower therapeutic index. Xanthines can be administered orally or IV but have a short duration of clinical action of between 2 and 4 h, and side effects, which include tachycardia and sweating, are frequently seen due to their narrow therapeutic margin.

(b) **Inhaled bronchodilators.** The long acting β-adrenergic sympathomimetic **salmeterol** and the atropinic ipratropium bromide require just twice daily administration by MDI using the delivery devices listed above and are therefore potentially practical alternatives to the use of systemic clenbuterol. Inhaled clenbuterol has a short duration of effect (3–6 h), thus requiring q.i.d. administration, making it less practical and cost effective than salmeterol.

(c) **Mucokinetic drugs.** Mucus of increased viscosity and quantity rapidly accumulates in symptomatic RAO horses and its removal is an important component of therapy. This can be partly achieved by improving mucociliary clearance by augmenting ciliary activity via β_2-agonists. The mucolytic drug **dembrexine** (0.3 mg/kg PO b.i.d.) is frequently used in combination with β_2-agonists and this combination provides **effective mucus removal**.

There are a variety of other potential methods of achieving mucokinesis although these have limited application in the field. Sterile water, sterile saline, acetyl cysteine and propylene glycol can be delivered by nebulizer although this is not a convenient method for delivery of large volumes and the technique may induce bronchoconstriction. Large volume administration of sterile saline IV appears to offer few advantages, is expensive and risks cardiac overload and pulmonary edema.

Prophylaxis and maintenance of RAO cases

If exposure to environmental challenge cannot be avoided or symptomatic episodes continue due to constraints on environmental improvements, then

prophylactic therapy or low dose maintenance therapy should be considered. Prophylaxis can be achieved with the mast cell stabilizer **sodium cromoglicate** administered by jet or ultrasonic **nebulizer** or by **MDI**.

Sodium cromoglicate can be given (80 mg/day administered by nebulizer or 200 μg/day by MDI) when the horse is in asymptomatic remission and may provide protection for some time after therapy ceases. In humans, sodium cromoglicate is extensively used to control childhood asthma although inhaled steroids are the more usual approach in adults. Its use in horses has so far been somewhat disappointing although this may reflect historical dosing regimen and delivery apparatus deficiencies.

An alternative approach is to control inflammation using low dose maintenance therapy with **inhaled corticosteroids**, typically 25% of the therapeutic dose, although this varies from horse to horse depending on the level of environmental challenge. Systemic corticosteroids are less suitable for long-term maintenance because, even at reduced doses, systemic side effects will occur.

Crisis management

RAO horses in crisis require **prompt and aggressive management**. The most effective means of achieving rapid and profound bronchodilation is by administration of atropine or, less effectively, of short acting inhaled β-adrenergic sympathomimetics by MDI (or nebulizer). Inhaled **clenbuterol** (0.3–0.6 mg q 1–2 h) or **salbutamol** (360 μg q 30–60 min) are the most suitable choices; the longer acting bronchodilators salmeterol and ipratropium bromide are less suitable because of their delayed onset of action.

If it is not possible to administer bronchodilators by inhalation, IV clenbuterol (0.8 μg/kg) is also suitable although the speed of onset is slower and the maximum effect achieved less than when it is administered by inhalation. Atropine (0.01 mg/kg IV) is a potent bronchodilator and can be used as a single dose for rescue but systemic administration does result in marked systemic effects. Corticosteroids, either by inhalation or systemically, should not be used as front line therapy for horses in crisis because their speed of onset is too low.

Pulmonary ventilation and distribution of inhaled drugs is poor in horses with severe LRT disease and therefore inhaled corticosteroids do not reach the lower airway in sufficient concentration. Corticosteroids can, however, be used to supplement bronchodilator therapy and have the advantage of reducing tolerance to the bronchodilator.

SUMMER PASTURE ASSOCIATED OBSTRUCTIVE PULMONARY DISEASE

The pathogenesis of **summer pasture associated obstructive pulmonary disease (SPAOPD)** is similar to that of RAO (*q.v.*) but the inciting allergens appear to be pollens rather than constituents of stable dust.

Many apparent SPAOPD cases are, in fact, long-term, out-of-control RAO horses that have progressed to a state of non-specific hyperresponsiveness and have such extensive accumulated pathology that there is no longer clinical

improvement, but rather worsening, on turnout. Primary SPAOPD cases present in the **summer months** with clinical signs resembling RAO, although generally they exhibit moderate to severe clinical signs.

Initial therapy of SPAOPD is the same as for moderate to severe RAO (*q.v.*) detailed above using **inhaled bronchodilators** supplemented with **systemic corticosteroids**. Maintenance management is more difficult than for RAO because it is difficult to avoid pollens, although stabling in a scrupulously clean stable air environment may help. Most SPAOPD horses therefore require low dose maintenance therapy with inhaled corticosteroids over the pollen season. In subsequent years **inhaled sodium cromoglicate** can be a useful aid in reducing the severity of clinical signs in response to pollen challenge.

INFLAMMATORY AIRWAY DISEASE

Inflammatory airway disease (IAD) is common in young Thoroughbreds and Standardbreds in training and is probably underdiagnosed in other types of horse.

Clinically, horses affected with IAD are not systemically unwell. The presentation of IAD is variable: it may manifest as **poor performance** or prolonged recovery after exercise or as **more overt respiratory disease** with coughing and nasal discharge. Some horses may also have **subclinical IAD**.

The etiology of IAD is uncertain and probably involves many factors. Bacteria (*Streptococcus zooepidemicus, S. pneumoniae, S. equisimilis; Actinobacillus* spp.; *Klebsiella* spp.) (*q.v.*), respirable endotoxin, viral infection, mycoplasmas, allergens, respirable particulate matter (dusts) and air quality may be involved in causing IAD.

Diagnostically, hematology, blood biochemistry and fibrinogen levels are within normal limits. Airway cytology is less consistent than that for RAO (*q.v.*). **Tracheal aspirates** in horses with IAD contain >20% neutrophils and increased mucus while **bronchoalveolar fluid** has an increased percentage of neutrophils, mast cells or eosinophils.

The **uncertain etiology** of IAD makes rational therapy difficult. In all cases environmental changes should be made as for RAO horses (*q.v.*). Horses with convincing bacterial infection (based on **quantitative bacteriology** of airway lavage samples) are treated with antibiotics (usually penicillin and gentamicin ± metronidazole) although the choice should be driven by the results of bacterial culture and antibiotic sensitivity testing. Airway neutrophilia (in the absence of a bacterial infection) can be managed with **corticosteroids** following the protocols described for RAO (*q.v.*).

Inhaled sodium cromoglicate can be used as adjunct or sole therapy for horses with **increased airway mast cells**. Horses with a mixed inflammatory response are often treated with **immunostimulants** (*q.v.*), although few are licensed for equine use. Popular immunostimulants in the USA include inactivated *Propionibacterium acnes* (EqStim) and mycobacterial cell wall extracts (Equimune). These agents are proposed to act by non-specific upregulation of macrophage and natural killer cell activity and lymphoproliferative responses.

The anthelmintic **levamisole** (*q.v.*) is also empirically used and is believed to upregulate lymphoproliferative responses. There has also been interest in the use of cytokines as immunostimulants. Recombinant human interferon-α

appears to reduce clinical signs in some IAD horses, possibly by increasing lymphoproliferation, T lymphocyte cytotoxicity and macrophage activity.

LOWER RESPIRATORY TRACT INFECTIONS

Bacterial infections

In neonatal foals, common Gram-negative bacteria isolated include *Pasteurella* spp., *Actinobacillus* spp., *E. coli, Klebsiella* spp., *Pseudomonas* spp. and *Bordetella bronchiseptica* (*q.v.*). These are often resistant to commonly used antibiotics.

In foals, *Rhodococcus equi* is a common LRT pathogen in certain regions and is frequently isolated along with other bacteria.

In adult horses, **bacterial infections** of the lung (e.g. pneumonia and pulmonary abscess) and the pleura (e.g. pleuritis and pleuropneumonia) can occur as sequelae to prolonged travel or esophageal obstruction (choke) and occasionally following viral infections and RAO (*q.v.*). *Rhodococcus equi* (*q.v.*) can occur as an endemic disease on certain studs. A wide range of Gram-positive and Gram-negative bacteria can be isolated from horses and foals with LRT bacterial disease.

In adults, the streptococci (*q.v.*), especially *Streptococcus zooepidemicus,* are the most prevalent Gram-positive isolates (others include *S. pneumoniae, S. equisimilis, S. equi*) although other Gram-positive organisms isolated include coagulase positive *Staphylococcus* spp. (including *S. aureus*) and *Enterococcus* spp. However, the presence of bacteria in the airway does not necessarily indicate infection since **resident bacteria** are recovered from the airways of the majority (75%) of normal horses, some of which (10%) are regarded as pathogens (Box 7.1).

Box 7.1 Interpretation of bacterial isolates from tracheal lavage samples

Bacteria regarded as opportunist invaders (commonly isolated from the normal airway but capable of establishing infections):

- Coagulase-negative *Staphylococcus* spp.
- α-Hemolytic streptococci
- *Escherichia coli*
- *Bacteroides fragilis*
- *B. oralis*
- *Enterobacter* spp.

Bacteria regarded as potential pathogens (but may be present in 10% of normal horses):

- *Streptococcus zooepidemicus*
- *Strep. pneumoniae*
- *Pasteurella haemolytica*
- *P. pneumotropica*
- *Klebsiella pneumoniae*
- *Pseudomonas aeruginosa*

It is important that **quantitative bacteriology** to estimate the numbers of bacteria in the airway is carried out to allow more accurate interpretation.

A further complication is that increased numbers of environmental opportunist bacteria (often Gram-negative) that are not involved with the disease process can be recovered from the airway of horses with LRT disease. This is because viral upper respiratory tract infections and most LRT conditions lead to impairment or loss of the **mucociliary escalator** and so the large numbers of bacteria that are inhaled through the equine larynx every day are not removed from the airway. Thus, tracheal lavage results must be interpreted **with caution** and significance can only be attached to bacterial isolates if clinical signs and further investigations (hematology, radiography and ultrasonography) are suggestive of LRT infection. In contrast, **BAL samples** from normal horses are sterile or may contain small numbers of bacteria of low pathogenicity.

Antibiotics are commonly administered to adult horses with respiratory disease but in almost all cases they are not indicated and do not influence the course of the disease. Rest and environmental control are the most appropriate therapy for viral infections. **β_2-Agonists** are a useful adjunct since they promote mucociliary clearance and this effect is enhanced by concurrent administration of a mucolytic drug such as **dembrexine**. β_2-Agonists also control the bronchoconstriction induced by post-viral non-specific airway hyperreactivity.

If antibiotics are employed in the therapy of LRT disease, their use and selection must be based rationally on cytology and bacteriology results from samples obtained by tracheal and bronchoalveolar lavage, and thoracocentesis.

Antibiotic selection

Although the choice of antibiotic for longer term therapy must be based on bacteriology and sensitivity results, it is possible to make rational choices for antibiotic selection before the results of bacteriology and sensitivity on airway or pleural aspirates are known.

Most (≥50%) LRT infections of adult horses involve a mixed Gram-positive and Gram-negative bacterial infection. In approximately 25% of cases, anaerobic bacteria are isolated as well. The principal bacterial species involved are *Streptococcus zooepidemicus* (60% of cases), *Escherichia coli* and *Pasteurella* spp. (36–40% of cases) and *Bacteroides* spp. (Table 7.2).

The selected antibiotic (Table 7.3) should be given for a minimum of 7 days, but therapy should continue for 5 days after clinical remission occurs.

Gram-positive bacteria

Penicillin remains the antibiotic of choice for the streptococci, although penicillin resistance (*q.v.*) is now recognized in an increasing number of *Strep. zooepidemicus* isolates (up to 30% of isolates in some surveys). **Sodium benzylpenicillin** (22 000 units/kg IV) is rapidly eliminated and consequently must be administered every 6 h (q.i.d.). This necessitates IV injection since long-term IM injections at this frequency cause significant injection site reactions. Although this may be a short-term option in practice, it is not suitable for longer term therapy unless the horse can be hospitalized.

Table 7.2 Frequency of isolation of bacteria from pneumonia or pleuropneumonia cases (USA and UK)

Bacterium	Isolation frequency (%)
Aerobes	
Strep. zooepidemicus	60
Pasteurella spp.	40
Escherichia coli	36
Enterobacter spp.	26
Klebsiella spp.	18
Pseudomonas	14
Anaerobes	
Bacteroides spp.	42
Clostridium spp.	28
Fusobacterium	20

Table 7.3 Antibiotics for use in lower respiratory tract infectious disease

Antibiotic	Dose	Route	Frequency[1]
Amikacin	7 mg/kg	IV	t.i.d.
Ampicillin	7.5–10 mg/kg	IM	s.i.d.
Ceftiofur	2 mg/kg	IM	s.i.d.
Enrofloxacin	7. 5 mg/kg	PO, IV	s.i.d.
Gentamicin	6. 6 mg/kg	IV, IM	s.i.d.
Metronidazole	20 mg/kg	PO	b.i.d.
Oxytetracycline	5. 0 mg/kg	IV	s.i.d.
Procaine benzylpenicillin	12 mg/kg	IM	s.i.d.
Sodium benzylpenicillin	22 000 IU/kg	IV	q.i.d.
Rifampicin	5 (10) mg/kg	PO	b.i.d. (s.i.d.)
Trimethoprim–sulfonamide	15 mg/kg	PO	b.i.d.

[1] *Manufacturer's recommendations; in field settings, at their own discretion, practitioners may increase the frequency of use of some antibiotics, e.g. procaine penicillin.*

Procaine benzylpenicillin is cleared more slowly but achieves much lower plasma concentrations. The manufacturers' recommended doses (12 mg/kg s.i.d.) are inadequate to produce effective respiratory tract concentrations. Higher doses of 24 mg/kg IM b.i.d. are required to achieve adequate concentrations in the respiratory tract, necessitating excessively large injection volumes. This, coupled with the lower plasma levels achieved, means that procaine benzylpenicillin is not a viable alternative and is likely only to be effective against highly sensitive Gram-positive bacteria. These problems are shared by ampicillin. The cephalosporin **ceftiofur** (2 mg/kg IM s.i.d.) and the fluoroquinolone **enrofloxacin** (7. 5 mg/kg PO IV s.i.d.) are more expensive than penicillin but are bacteriologically and clinically effective with a broader spectrum of activity than penicillin.

Benzathine benzylpenicillin (a "long-acting" formulation) is poorly absorbed in horses, failing to achieve adequate tissue levels, and should not be used for treatment of respiratory disease.

Gram-negative bacteria

Approximately 90% of Gram-negative respiratory isolates are sensitive to the aminoglycosides **gentamicin** and **amikacin**. Currently, gentamicin is more frequently used, although amikacin may be less nephrotoxic than gentamicin. Gentamicin is now generally administered at a dose of 6. 6 mg/kg IV IM s.i.d. rather than the previous regimen of 2.2 or 4. 4 mg/kg IV or IM t.i.d. or b.i.d. Care must be taken to monitor renal function in compromised horses that may have hypovolemia or endotoxemia.

Anaerobic bacteria

Anaerobes (*Bacteroides* spp. and *Fusobacterium* spp.) are frequently recovered from horses with LRT infections and they appear to be important since their isolation from pleuropneumonia cases is associated with a poor prognosis. Most anaerobes except the β-lactamase-producing *Bacteroides fragilis* are sensitive to penicillin. However, **metronidazole** is the first choice antibiotic because *Bacteroides* spp. are the most frequent anaerobic isolates from pleuropneumonia cases. Clinical cure rates have been reported to be increased when metronidazole is added to the therapeutic regimen. Metronidazole is administered at 20 mg/kg PO b.i.d. (or q.i.d. for more severe infections).

Alternative strategies

Although the sodium benzylpenicillin/gentamicin regimen outlined above is highly effective and provides a potent, broad-spectrum bactericidal effect, it is expensive and the IV route of administration can present practical difficulties in a non-hospital setting. A variety of alternative antibiotics provide possible alternatives. For systemic delivery, **oxytetracyline, ceftiofur** and **enrofloxacin** are all sensible alternatives.

The **potentiated sulfonamides**, trimethoprim and sulfonamide (TMP/S) combinations, are a reasonable alternative to benzylpenicillin/gentamicin regimens and offer a number of potential advantages, including oral administration, although absorption following oral delivery may be less predictable than following systemic administration. They distribute well to the respiratory tract, achieving therapeutic concentrations in the lung and bronchial secretions. They are bactericidal, have a broad spectrum of activity including anaerobes, can be administered both by IV injection and orally at the rate of 30 mg/kg and only need to be given twice daily. Where it may not be possible to achieve the frequent administration required for the penicillins, TMP/S combinations may be the most appropriate first choice antibiotic and should be used along with metronidazole if anaerobic infection is suspected.

Because TMP/S combinations can be administered orally, they are frequently used for longer term therapy. Sulfonamides are absorbed well from the gastrointestinal tract. In contrast, the absorption of trimethoprim is variable since it is degraded by gut flora and its absorption is significantly reduced if it is administered in feed (instead of as a paste independently of feeding). However, it seems that, despite this, adequate trimethoprim–sulfonamide ratios are achieved in the respiratory tract following administration in feed.

Lower respiratory tract infections in foals

LRT bacterial infections are more common in foals than in adults and may occur in association with failure in passive transfer, septicemia, viral upper respiratory infections, stress and specific pathogens, e.g. *Rhodococcus equi* (*q.v.*).

Respiratory and generalized infections in foals should be taken seriously and antibiotics should be used to prevent secondary bacterial infections developing.

A similar range of bacteria are isolated from foals as from adults, although in the first week of life Gram-negative infections (*E. coli, Klebsiella* spp., *Actinobacillus* spp.) predominate.

Sodium benzylpenicillin (22 000 units/kg IV q.i.d.) and **gentamicin** (2 mg/kg IM or IV b.i.d.) used in combination with **metronidazole** (20 mg/kg PO b.i.d.) are suitable for treatment of foals but similar administration difficulties may be encountered as for adults.

The nephrotoxicity of gentamicin may present a significant barrier to its use unless renal function (*q.v.*) is monitored frequently since foals with pneumonias may be dehydrated. Compromised renal function is most accurately monitored by urinalysis for proteinuria and falling specific gravity, and by examination of urinary sediment for casts. Serum creatinine is not a sensitive indicator of renal toxicity since glomerular filtration must be decreased by 75% for serum creatinine to become elevated. **Amikacin** (7 mg/kg IV or IM t.i.d.) may be less nephrotoxic than gentamicin but renal function must still be carefully monitored.

Ampicillin trihydrate can be administered orally (10–20 mg/kg b.i.d.) to foals but is poorly absorbed, achieving low concentrations in the respiratory tract. It is thus only suitable against highly sensitive streptococci and so is of little value in LRT infections.

In view of these difficulties, **potentiated sulfonamides** (30 mg/kg IV or PO b.i.d.) are a good alternative choice of antibiotic and may be the most appropriate first choice in field situations.

Rhodococcus equi

Rhodococcus equi (*q.v.*) is an intracellular organism that causes a **chronic bronchopneumonia** with multiple lung parenchymal abscesses and presents particular therapeutic difficulties. *R. equi* has a **narrow antibiotic sensitivity** and this, combined with **distribution problems** to the affected lung regions, means that the response to most antibiotics is disappointing.

R. equi has 100% sensitivity to a combination of **rifampicin** (5 or 10 mg/kg PO b.i.d. or s.i.d.) and **erythromycin** (25 mg/kg PO b.i.d. or t.i.d.) and this combination is the current treatment of choice. Both drugs distribute well to the lung, pleura and bronchial secretions. Rifampicin is not used alone because of the rapid appearance of resistance. Alternative macrolides (**azithromycin** and **clarithromycin**) have been proposed as alternatives to erythromycin because they have greater bioavailability and decreased side effects in people. In vitro antibiotic sensitivity testing suggests that clarithromycin might be the better choice clinically because its minimum inhibitory concentration (MIC) is 10 times less than that of azithromycin. The potentiated sulfonamides appear to have reasonable activity against *R. equi* and offer an alternative to rifampicin and erythromycin.

Treatment must be continued until **radiographic changes** are no longer present or for 7 days after clinical signs become inapparent. This usually means a regimen of 4–9 wk.

Supportive therapy for lower respiratory tract infections in foals and adults

β_2-Agonists and mucolytics may be useful although in severe pneumonias bronchodilatation may worsen ventilation–perfusion failure by diverting blood flow away from well-ventilated regions.

Corticosteroids should be avoided unless life-threatening pulmonary inflammation is present, in which case short-term or single treatment prednisolone or dexamethasone should be used. NSAIDs, e.g. **flunixin**, may help to decrease pyrexia and improve demeanor and appetite but must be used with care, especially in foals, since they can produce gastric ulceration and are nephrotoxic in dehydrated foals.

Parasitic lung disease

Dictyocaulus arnfieldi (*q.v.*), and migrating larvae of *Parascaris equorum* (*q.v.*) in younger horses, have historically caused clinical disease associated with bronchitis and bronchiolitis, but due to the use of modern anthelmintics rarely occur at present. **Ivermectin** given orally at a single dose of 0. 2 mg/kg is the current treatment of choice and is highly effective against adult *D. arnfieldi* and migrating larvae of *P. equorum*.

There appears to be little advantage in administering ivermectin by the **unlicensed** injectable routes in horses except that plasma levels may be maintained for longer periods. **Mebendazole** at 20 mg/kg PO daily for 5 days (twice the normal dose rate) is also effective against *D. arnfieldi* and *P. equorum* but has a reduced efficacy (75–100%) compared with ivermectin.

AIR HYGIENE OF STABLES

INTRODUCTION

The stabled horse is exposed to a wide range of potential respiratory pathogens. Whether or not the horse succumbs to disease depends upon the pathogenicity of the agent, the level of challenge of pathogen and the horse's susceptibility to disease. The latter two factors are affected by the **air hygiene** of stables, with stable design and management practices being important considerations.

Air hygiene of stables can affect the incidence of cases of respiratory disease in stabled horses as well as the duration and severity of these episodes in individual horses. This occurs in racehorse stables where young horses have been suffering from infectious respiratory disease. **Improved air quality** confers benefits in the time it takes horses to recover and return to full work.

The respiratory pathogens to which stabled horses are exposed include mold spores, noxious gases, parasites, dust mites, plant material, airborne

mycotoxins (including glucans) and endotoxins and infectious agents such as bacteria and viruses. These agents are pathogenic because they possess one or more of the following properties: infectious, allergic, irritant, toxic or mechanically destructive (e.g. migrating parasites). Other than individual pathogens possessing multiple pathogenic abilities, there are interactions between pathogens; for example, irritation caused by a noxious gas can increase the host's susceptibility to infections.

The **environmental prevention** of respiratory disease depends on maintaining pathogen levels below the horse's threshold limiting values for disease. These limits are unknown for horses and, since responses to many inhaled pathogens are graded, it is best to minimize the levels of challenge at all times.

The levels of airborne contaminants depend on their rates of release into the air and their rates of clearance from the air. Release rates and therefore the horse's exposure levels to airborne pathogens can be decreased by paying attention to the selection and management of forage and bedding materials. Clearance rates of airborne pollutants are primarily influenced by **ventilation** or **air change rates** (*q.v.*).

VENTILATION

Paying attention to the ventilation of a stable will lead to decreased levels of airborne contaminants, a decreased likelihood of condensation, and a decreased likelihood of molding of bedding material in situ. The "**open air factor**" is a potent killer of airborne bacteria and viruses.

A target of **six to eight air changes per hour** is ideal in designing new stables or altering existing ones. In most stables, this can be achieved by natural ventilation. There are three forces of natural ventilation:

1. **The stack effect** (rising warm air)
2. **Aspiration** (i.e. wind blowing across the roof of a building sucking air out)
3. **Perflation** (i.e. air blown from side to side and end to end of the building).

The ventilation of a building is best tested in **still air** conditions, i.e. when the only driving force for ventilation is warm air rising off the horse. Thus, theoretical considerations of providing ventilation should be based on the assumption that windless conditions prevail. However, such conditions are rarely maintained for long periods of time and consideration should be made for placing baffles or Netlon over openings in exposed walls to decrease the risk of draughts.

Guidelines for the size of inlets and outlets for some typical stables are presented in Table 7.4. These openings should be well distributed to ensure proper mixing of air. This is especially important for barns. Most box stalls should have inlets in the back and front walls in addition to the stable door that may be shut in poor weather conditions. Boxes with peaked roofs should have a capped chimney or covered ridge to act as an outlet for warm "stale" air.

Table 7.4 shows the benefit of **insulating stables**; by maintaining a slightly greater temperature difference between the inside and the outside of the stable, smaller openings can be used to provide adequate natural ventilation.

Table 7.4 Guidelines for minimum inlet and outlet areas per horse for box stalls and barns (meters)

	Outlet area	Inlet area
Uninsulated box stall[1]	0.34	0.17
Insulated box stall[1]	0.27	0.14
Uninsulated barn[2]	0.46	0.23
Insulated barn[2]	0.38	0.19

[1] *50 m^3 of airspace per horse, 1. 0 m between inlet and outlet.*
[2] *85 m^3 of airspace per horse, 2. 0 m between inlet and outlet.*

Table 7.5 Aerobiology of hays and silages

	Rye (clean)	Rye (dirty)	Alfalfa lucerne (clean)	Alfalfa lucerne (dirty)	Horsehage[3]	Silage[4]
Particle per mg[1]	980 →	65 190	840 →	39 270	44	19
Proportion of particles (%)[2]						
Fungal and actinomycete particles	30	99	55	99	5	5
Plant material	70	ng	45	ng	95	95
Other	ng	1	ng	1	ng	ng

[1] *Assessed using aerodynamic particle sizer.*
[2] *Assessed using a May® impactor.*
[3] *Sealed bags.*
[4] *ng, Negligible.*

MOLD SPORES

Horses in the best-ventilated stables can be exposed to extremely high challenges of **mold spores** from their feed, especially hay, and their bedding, especially straw. These spores cause overt symptoms of respiratory disease in older horses in the form of RAO or heaves and covert respiratory problems such as IAD (*q.v.*), especially in young equine athletes. These covert problems may only be manifest with **poor athletic performance** with no obvious clinical signs when the horse is at rest. Endoscopic examinations are critical in diagnosis.

Forage

Hay is the **single most common source of fungal spores** for the horse (see Table 7.5). Up to 75% of traditionally produced English hay fed to horses has significant mold contamination. The soaking of hay is a time-proven method of minimizing the horse's exposure to fungal spores. However, **feeding soaked, poor quality hay to horses cannot be condoned**. As hay that falls to the floor dries, the spores can again become airborne to be inhaled by the horse or to "seed" clean bedding. Furthermore, even though the spores are not inhaled from soaked hay, they are still ingested along with any

Table 7.6 Aerobiology of fresh bedding materials

	Equibed[3]	Diced[4] newspaper	Shavings (range)		Straw (range)		Tissue[5]
Particle per mg[1]	19	78	148	873	1490	28 100	53
Proportion of particles (%)[2]							
Fungal and actinomycete particles	ng	ng	5	96	90	100	ng
Plant material	ng	ng	95	4	8	trace	ng
Other	100	100	ng	ng	2	trace	100

[1] *Assessed using aerodynamic particle sizer.*
[2] *Assessed using a May® impactor.*
[3] *Equibed®, Melcourt Industries, Tetbury, Glos, UK (absorbent synthetic bedding).*
[4] *Diced newspaper, Shredabed®, Exeter, UK.*
[5] *Tissue bedding, R. H. Lee, Bolton, Greater Manchester, UK.*

mycotoxins present. These toxins can have subclinical effects on performance horses.

Silage and haylages are increasingly being successfully used as alternatives to hay. There have been a small number of deaths due to **botulism** (*q.v.*) associated primarily with big-bale silage. In this context, silage that smells of ammonia or contains dirt should be avoided. When opened, bags of silage or haylage can mold quickly within a matter of days. Opened bags should be used within 2–3 days and damaged bags discarded.

Treated chaffed hay and straw and complete cubed diets also offer alternatives to feeding hay. These products are convenient and are usually effective in minimizing respiratory disease but they do not always offer value for money.

Beddings

Even the cleanest of straws contains significantly more small, respirable fungal spores than alternative beddings such as wood shavings, paper, peat or the new synthetic beddings (see Table 7.6). However, in **poorly ventilated stables** or where deep litter is allowed to develop, significant molding of the plant-based beddings can occur. Deep litter management systems have the added disadvantage of allowing build-up of **noxious gases** such as ammonia, infectious bacteria and the larvae of gastrointestinal parasites.

Feed and bedding storage

Horses can be exposed to significant organic respirable **dust challenges** from feed and bedding storage facilities, especially molds and endotoxins. Haylofts or grain silos are common problem areas for dust generation. Muck heaps in close proximity to stables can also be a significant source of mold spores as well as vermin. Soiled bedding material and manure are best placed in a trailer and removed from close proximity to the stable every 2 or 3 days.

INFECTIOUS AGENTS

Highly infectious agents such as the **equine herpes and influenza viruses** (*q.v.*) are difficult to control by housing and management. Many of these viruses can also be endemic in the horse population and the movement of horses to and from competitive events ensures effective national and international dissemination. Asymptomatic "carriers" exist, and horses can shed bacteria and viruses before they show symptoms of disease. Moreover, it should be remembered that respiratory tract infections can be spread by means other than aerosol dispersal such that, while stable design and management practices are unlikely to affect the incidence of highly contagious respiratory disease, there is clear evidence that attention to the air will help horses recover from such problems. **Sound air hygiene practices** will also decrease the likelihood of low-grade, less contagious infections.

The source for most infectious agents within stables is the **horses themselves**. Most infectious agents only survive a short time once aerosolized. One important exception is the actinomycete *Rhodococcus equi* (*q.v.*). This organism causes severe **bronchopneumonia** in foals. It proliferates in fecal material and soil, and foals are exposed via the aerosol route, especially in dusty conditions. The problem is seen in barns, where the organism proliferates in bedding material, and in fields, especially in warm weather conditions. To avoid this problem, **deep litter management** should be avoided in barns and special attention should be given to the cleaning out of feces.

NOXIOUS GASES

Ammonia is the most commonly encountered noxious gas in horse stables. **Hydrogen sulfide** is also sometimes encountered. The threshold limiting value for ammonia for humans is 5 ppm and for hydrogen sulfide is 20 ppm. Draeger tubes (Oraeger) offer a simple method of assessing the levels of these gases in the field. Problems with noxious gases in stables usually arise because of poor drainage, deep litter management and poor ventilation.

MECHANICAL GADGETRY

A wide range of equipment is increasingly being advocated to improve the air quality of stables. This includes complete mechanical ventilation systems, air filter systems, disinfectant spray systems and ionizers. Owners should be encouraged to improve **natural ventilation** and avoid management practices such as using straw and hay before "investing" in gadgetry.

Most stables and barns can be adequately ventilated without mechanical assistance although fans may be of use in large barns. If mechanical systems are in use, they should be capable of providing **at least six to eight air changes per hour**. Filter systems designed for household and hotel use are usually not of benefit in stables because of their volumetric capacity and the failure of owners to keep filters clean. There is no evidence that justifies the use of ionizers in well-ventilated stables. Equally, spray disinfectant systems that can be of benefit in heavily stocked, poorly ventilated livestock housing are unlikely to be cost effective in a well-ventilated stable.

EXERCISE-INDUCED PULMONARY HEMORRHAGE

INTRODUCTION

Exercise-induced pulmonary hemorrhage (EIPH) (*q.v.*) is defined as the presence of blood in the tracheobronchial tree following athletic exertion. The diagnosis is based on an endoscopic examination. A **grading system** has been established to describe EIPH, categories being based on the thickness of the **streak of blood** in the horse's trachea (Box 7.2).

Surveys of horses have shown that a high percentage of horses that **gallop** suffer EIPH. The incidence is highest in Thoroughbred racehorses with up to 75% of competitors affected. Similar studies of Standardbreds show a lower incidence (approximately 30%). This may relate to the type and level of exertion as well as the different breathing patterns of horses involved in these two types of racing.

Repeated examinations on groups of racehorses show that practically **all racehorses** suffer EIPH. This has been confirmed with "lung wash" studies which show the presence of hemosiderophages coinciding with the beginning of fast work. Repeated examinations on individual horses have also shown that the appearance of blood within the tracheobronchial tree after strenuous exercise is not consistent. A positive diagnosis on one day may be followed by a negative the next. Furthermore, horses with the most severe grade of hemorrhage do not appear to be more likely to bleed subsequently than horses with the less severe grades.

A recent prospective cross-sectional study of Thoroughbred horses competing in flat races in metropolitan Victoria, Australia, has shown that both the presence of EIPH and its severity were **significantly associated with performance**. Horses with EIPH (of grades 2 or higher) were 4.0 times less likely to win, 1.8 times less likely to finish in the top three places and finished 1. 8 m further behind the winner than did unaffected horses. The severity of EIPH was significantly associated with reduced probability of winning, reduced

Box 7.2 Grading of exercise-induced pulmonary hemorrhage

Grade 0:	No blood detected in the pharynx, larynx, trachea, or mainstem bronchi visible from the tracheal bifurcation
Grade 1:	Presence of one or more flecks of blood or $<$2 short (less than one fourth the length of the trachea) narrow ($<$10% of the tracheal surface area) streams of blood in the trachea or mainstem bronchi visible from the tracheal bifurcation
Grade 2:	One long stream of blood (more than half the length of the trachea) or $>$2 short streams occupying less than one third of the tracheal circumference
Grade 3:	Multiple, distinct streams of blood covering more than one third of the tracheal circumference and no blood pooling at the thoracic inlet
Grade 4:	Multiple, coalescing streams of blood covering $>$90% of the tracheal surface with blood pooling at the thoracic inlet

probability of finishing in the top three places, finishing a greater length behind the winner and a lower likelihood of being in the top 10% of money earned.

PATHOPHYSIOLOGY

It is now widely accepted that the hemorrhage observed in the tracheobronchial tree of horses following competitive events mainly arises from the **dorsocaudal region** of the lung. Post mortem studies have identified a systemic neovascularization in this region of the lungs in retired racehorses. Histologic evidence of airway disease and increased amounts of mucus were also observed in these areas.

Given that **EIPH occurs in most horses** from a young age, a cause and effect relationship cannot be deduced from the post mortem findings in retired horses. Endoscopic surveys have not been able to establish a relationship between the presence of mucopus in the tracheobronchial tree and EIPH. It is also noteworthy that the presence of mucopus in horses' airways has been correlated with poor athletic performance. However, small airway disease should be avoided since, even if it is not essential for EIPH to occur, it appears likely to increase the risk of occurrence.

No association has been found between abnormalities of the upper respiratory tract and the occurrence of EIPH. The most recent theory of the hemorrhage in the dorsocaudal lung is that **biomechanical "stresses"** or the transition of shock waves during locomotion to this area of lung lead to the rupture of alveolar capillaries.

DIAGNOSIS

Only a small percentage of horses with EIPH will show **epistaxis** (*q.v.*). Most studies reveal that only 1–2% of horses involved in racing suffer epistaxis although 75% of horses have blood present in the tracheobronchial tree.

While a clear effect on **racing performance** and EIPH has been demonstrated, a thorough clinical examination of all body systems should be carried out on horses suffering poor performance, even when a positive diagnosis of EIPH is made. Radiologic examinations show that a small number of cases ($\leqslant$5%) have a typical radio-opaque lesion in the dorsal caudal region of the diaphragmatic lobes. This change will normally clear within a week. It may be worth noting that horses in which this radiologic change is persistent appear to be the most problematic to treat in practice.

Tracheal washes or bronchoalveolar lavages are worthwhile as cytologic and microbiologic examination of these samples will identify small airway inflammation and/or infectious disease. The site of pulmonary hemorrhage represents an ideal medium for secondary infection to occur.

THERAPY

None of a wide range of therapeutic regimens for EIPH withstands close scrutiny. Early approaches to treating epistaxis assumed that a coagulation defect was the underlying problem and that this could be addressed by using

agents such as estrogens, vitamin K, hesperidin or citrus bioflavonoids. Controlled studies have shown all of these to be ineffective. Similarly, studies using bronchodilators have not shown efficacy in preventing EIPH. However, bronchodilators and mucolytics will be of use in treating small airway problems in such horses. Antibiotics will also be of benefit if infection exists. Care should be taken in using corticosteroids in horses suffering EIPH as this approach could increase the risk of secondary infections developing at the site of hemorrhage.

FUROSEMIDE

Despite the wide use of furosemide (1 mg/kg IV 4 h prior to exercise or racing), there has been a lack of definitive studies that clearly show a beneficial effect in either the prophylaxis or treatment of EIPH. The pharmacologic basis for the use of furosemide in treating EIPH is to decrease pulmonary artery pressure during exercise. Other effects of furosemide that may improve performance have been identified; these include a significant improvement in **lung function** of horses suffering acute attacks of airway obstruction. Another potential explanation of the performance-enhancing effect of furosemide is that it may be little more than a consequence of the reduction of the horse's body weight.

Several studies have failed to show that furosemide affects the **incidence** of EIPH. Likewise, there are no clear benefits in terms of the effect of furosemide on the grades of severity of episodes of EIPH as assessed endoscopically. Data have been generated that show a decrease in the concentration of red cells in the BALF of treated horses. Competitive athletes may have other costs to pay with the use of furosemide including effects on intracellular and extracellular electrolyte levels and thermoregulation.

In summary, careful consideration should be given in assessing the significance of EIPH in individual cases. Full and careful examination should be carried out on all body systems, including the respiratory tract, of a horse with "loss of performance". The latter should include an endoscopic examination and BAL or tracheal wash. Therapeutic regimens should be based on those and other clinical findings.

Chapter 8

The cardiovascular system

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Chapter contents

INTRODUCTION

In horses, the prevalence of cardiovascular disease is low although it can cause **poor performance** (*q.v.*) or cardiac failure and is frequently implicated in sudden death. Cardiovascular diseases can be classified on anatomic, pathologic or functional criteria. A functional approach serves the clinician well as it defines clinical manifestations and, often, appropriate management. A functional classification of equine heart disease is listed in Table 8.1.

Volume overload is the most common type of **heart failure** in the horse and occurs when valvular regurgitation or an intra- or extra-cardiac shunt leads to one or both ventricles receiving excessive quantities of blood. There is activation of the autonomic nervous system and the renin–angiotensin–adrenergic system, progressive ventricular dilatation and, in response, ventricular hypertrophy. Ultimately cardiac dysfunction and irreversible changes within the myocardium ensue.

Table 8.1 Equine heart disease

Problem	Etiology
Volume overload	Acquired valvular disease (degenerative or inflammatory) Congenital defects (intra- or extra-cardiac shunts, valvular malformations)
Pressure overload	Congenital valvular defects (stenosis)
Myocardial failure	Primary myocardial disease (toxic, nutritional, viral, immune-mediated) Secondary myocardial disease (toxic, drug-induced, hypoxia, endotoxemia, septicemia, electrolyte or metabolic disturbances)
Arrhythmias	Primary myocardial disease (toxic, nutritional, viral, immune-mediated) Secondary myocardial disease (toxic, drug-induced, hypoxia, endotoxemia, septicemia, electrolyte or metabolic disturbances)
Diastolic failure	Pericardial disease (effusive or constrictive)

Pressure overload occurs when there is an anatomic or physiologic obstruction impeding ventricular ejection. In response to increased afterload, the myocardial cells in the affected ventricle increase in diameter as myofibrils are laid down in parallel within them. **Myocardial failure** occurs as cellular function deteriorates. Lesions resulting in pressure overload such as aortic or pulmonic stenosis are uncommon in horses and this form of heart failure is rare.

Both volume and pressure overload ultimately lead to failure of the affected ventricle. Accumulation of fluid and congestion in the vascular compartments develops "upstream" to the affected ventricle. **Left-sided heart failure** leads to congestion in the pulmonary circulation, pulmonary edema and respiratory signs (Box 8.1). **Right-sided heart failure** leads to fluid accumulation in the systemic circulation, signs of venous distension and ventral edema. There can be effusions in the pleural and peritoneal cavities and, rarely, bowel edema and diarrhea (Box 8.1). Usually, failure of one ventricle will lead to failure of the other, so that **biventricular failure** ensues and the clinical presentation includes both left- and right-sided signs (Box 8.1).

Primary myocardial (pump) failure implies that there is a primary defect in myocardial contractility leading to a reduction in stroke volume. The low cardiac output reduces perfusion and can lead to **multiple organ dysfunction** (see Box 8.1). This is seen in association with severe cardiomyopathies. Clinical signs produced by low cardiac output will also occur as myocardial failure develops in volume or pressure overload. Where the venous return is severely compromised, e.g. by **effusive pericarditis** (*q.v.*), low output heart failure also occurs.

CLINICAL EVALUATION OF THE CARDIOVASCULAR SYSTEM

THE CIRCULATORY SYSTEM

Physical examination including visual inspection and palpation provides a useful guide to **hydration status**, circulating volume and the efficiency of

Box 8.1 Clinical signs associated with cardiac diseases in the horse

Left-sided heart failure*
- Exercise intolerance
- Tachypnea
- Moist bronchovesicular sounds (±crackles and/or wheezes)
- Coughing
- Frothy nasal discharge
- Bounding arterial pulses (aortic insufficiency/patent ductus arteriosus)
- Atrial fibrillation

Right-sided heart failure*
- Jugular distension and pulsation
- Ventral edema
- Fluid line on auscultation and/or percussion of the thorax (pleural effusion)
- Diarrhea
- Atrial fibrillation

Low output failure
- Lethargy
- Weakness
- Depression
- Syncope
- Weak pulses
- Renal failure

**Biventricular failure produces a combination of right- and left-sided signs.*

perfusion. The skin turgor, venous filling and moistness of the mucous membranes reflect total body water, while the color of the membranes, the capillary refill time, the temperature of the extremities and the pulse volume are indicators of circulating volume and perfusion.

The **arterial pulses** are palpable at the facial, submandibular, carotid, radial, digital, saphenous and coccygeal arteries. The normal arterial pulse has a symmetrical profile. The rate, volume and quality should be assessed by palpation. A pulsation can be seen and felt in the jugular vein in the distal third of the neck in normal horses.

THE HEART

The horse has four **heart sounds**, although in some horses only two or three may be audible.

The **first heart sound** occurs when the left and right atrioventricular valves close at the onset of mechanical systole. It is a loud and low-pitched sound, audible throughout the cardiac silhouette, on both sides of the thorax. Its point of maximal intensity is over the left apex and it is followed immediately by the arterial pulse. Splitting of the first heart sound occurs uncommonly in normal horses.

The **second heart sound** is coincident with closure of the semilunar valves and reversal of blood flow in the great arteries at the conclusion of ventricular systole. The aortic and pulmonic valves may not close synchronously and physiologic splitting of the second heart sound is often found.

The **third heart sound** is not present in every horse. It is associated with termination of rapid ventricular filling, and it is usually heard best around the left atrioventricular (AV) valve area.

The **fourth, or atrial, sound** is almost always audible. It is produced by atrial systole with flow of blood from the atrium to the ventricle. It is usually heard best dorsally over the heart base on the left side. The fourth heart sound occurs immediately before the first heart sound so that it can be mistaken for splitting of the first sound.

The horse's heart is almost totally located under the muscles of the shoulder in the third, fourth and fifth intercostal spaces. The **left AV valve** is auscultated in the left fifth intercostal space, at the caudal border of the triceps muscle and midway between the points of the shoulder and the elbow; sounds associated with the aortic valve are heard in the left fourth intercostal space deep to the triceps muscle just ventral to the point of the shoulder; and sounds associated with the pulmonic valve are in the left third intercostal space at the level of the point of the elbow and deep to the triceps muscle. In the right hemithorax, the **right AV valve** is auscultated in the fourth intercostal space at the midpoint between the shoulder and the sternum.

CARDIAC MURMURS

Cardiac murmurs are found in **up to 80% of normal Thoroughbreds**, and are also frequently auscultated in other breeds of horses and ponies. They are prolonged sounds occurring during periods of the cardiac cycle that are usually silent. Murmurs arise when normal laminar flow is disrupted. **Physiologic (functional) murmurs** are present where there is no cardiac pathology, particularly associated with left ventricular ejection. Although often found in normal horses, they also occur if blood viscosity is lowered in anemia or hypoproteinemia. However, because cardiac murmurs can accompany congenital cardiac disease or valvular insufficiency, it is important that physiologic murmurs are distinguished from pathologic murmurs.

The criteria used to describe murmurs are described in Box 8.2. If all five characteristics of a murmur are considered carefully, the clinician is usually able to formulate a differential diagnosis and differentiate those murmurs that are physiologic (functional) from those that indicate that there is cardiac pathology and justify further diagnostic evaluation.

Functional murmurs are quieter (grade 3 or less), soft and localized, do not have precordial thrills and do not obscure the heart sounds. Functional murmurs in **systole** caused by ventricular ejection are localized to the heart base in the third or fourth intercostal space; they are usually grade 3 or less and have a soft, blowing quality. Functional **diastolic murmurs** occur in early or mid diastole, are frequently musical or squeaky, and are auscultated over the left heart base or left AV valve area. The characteristics of functional murmurs and those associated with a variety of forms of cardiac pathology are compared in Table 8.2.

Box 8.2 Parameters used to describe and classify cardiac murmurs in the horse

1. Timing
Systolic: Between the first and second heart sounds
Diastolic: Between the second and first heart sounds
Pan: Obscuring the heart sounds
Holo: Begins/ends immediately after/before the heart sounds
Early or mid: Distinct from the heart sounds

2. Intensity
Grade 1: A soft murmur audible only after careful auscultation in a localized area of the thorax
Grade 2: A soft murmur that is clearly audible after a few seconds of auscultation
Grade 3: A moderately loud murmur that is audible over a wide area of the thorax, with no precordial thrill
Grade 4: A loud murmur that is immediately audible and heard over a wide area of the thorax, with no precordial thrill
Grade 5: The loudest murmur that becomes inaudible when the stethoscope is removed from direct contact with the thorax, which is always accompanied by a precordial thrill
Grade 6: A loud murmur that can still be heard when the stethoscope is removed from direct contact with the thoracic wall and is always accompanied by a precordial thrill

3. Quality
Frequency, e.g. harsh, coarse, soft, musical or honking
Shape, e.g. band-shaped, crescendo–decrescendo, decrescendo or machinery

4. Point of maximal intensity
Left AV valve: Left fifth intercostal space, midway between the levels of the points of the shoulder and elbow
Aortic valve: Left fourth intercostal space, at the level of the point of the shoulder
Pulmonic valve: Left third intercostal space, at the level of the point of the elbow
Right AV valve: Right fourth intercostal space, midway between the levels of the point of the shoulder and elbow

5. Radiation
Dorsal, caudo-dorsal, etc.: The direction of radiation corresponds to the direction of turbulent blood flow

Note: The caudal border of the triceps muscle overlies the fifth intercostal space.

Table 8.2 Cardiac murmurs and their causes

	Timing	Location	
		Point of maximal intensity[1]	Radiation
Physiologic			
Aortic ejection	Mid/holo systolic	LIC4	Localized
Diastole squeak	Early diastolic	L or RIC4	Localized
Valvular insufficiency			
Left AV valvular regurgitation	Holo/pan systolic	LIC5	Caudodorsally
Aortic regurgitation	Early, mid, holo or pan diastolic	LIC4	Ventrally
Pulmonic regurgitation	Early, mid, holo or pan diastolic	LIC3	Ventrally
Right AV valvular regurgitation	Holo/pan systolic	RIC4	Cranially
Congenital defects			
Ventricular septal defect (VSD)	(1) Pan/holo systolic	RIC4	Widespread
with functional pulmonic stenosis[2]	(2) Pan/holo systolic	LIC3	Widespread
Patent ductus arteriosus	Continuous or pan/holo systolic	LIC3 or 4	Localized

	Grade	Quality	
		Frequency	Shape
Physiologic			
Aortic ejection	1–3	Soft, blowing	Crescendo–decrescendo
Diastole squeak	1–3	Squeaky	Decrescendo
Valvular insufficiency			
Left AV valvular regurgitation	3–6	Coarse or honking	Band
Aortic regurgitation	2–6	Coarse or honking	Band, decrescendo
Pulmonic regurgitation	2–6	Coarse or honking	Band, decrescendo
Right AV valvular regurgitation	3–6	Coarse or soft	Band, decrescendo, crescendo–decrescendo
Congenital defects			
Ventricular septal defect (VSD)	4–6	Coarse	Band
with functional pulmonic stenosis[2]	3–6	Coarse or blowing	Crescendo–decrescendo
Patent ductus arteriosus	3–6	Coarse	Machinery

[1] *L, left; R, right; IC, intercostal space.*
[2] *VSD is frequently also accompanied by aortic regurgitation with an additional, diastolic murmur.*

DIAGNOSTIC AIDS IN EQUINE CARDIOLOGY

There are a wide variety of diagnostic aids available for use in the evaluation of equine cardiovascular disease. The selection of appropriate diagnostic procedures depends on the clinical presentation and the differential diagnosis. Table 8.3 summarizes some of the diagnostic techniques that are used in equine cardiology. **Echocardiography** is the principal means of evaluation of horses with cardiac murmurs where valvular pathology or congenital cardiac diseases are suspected. Normal values for various M mode echocardiographic parameters are listed in Table 8.4.

Electrocardiography, including radiotelemetric and ambulatory electrocardiography, is the principal means of investigation of arrhythmias. Non-specific

Table 8.3 Summary of diagnostic techniques in equine cardiology

Clinical presentation: Cardiac murmurs	
2-Dimensional and M mode echocardiography	Identification of specific anatomic lesions; assessment of cardiac size, dilation, hypertrophy and ventricular contractility; regurgitant jets may cause abnormal valvular motion
Doppler echocardiography	Identification of regurgitant jets or intracardiac shunts; mapping of their extent and location; calculation of pressure gradients between chambers
Angiography	Demonstration of intracardiac shunts in foals
Phonocardiography	Confirmation and characterization of murmurs
Cardiac catheterization	Identification of pressure and PO_2 changes localizes lesions and determines hemodynamic effects of shunts or valvular regurgitation
Clinical presentation: Arrhythmias	
Electrocardiography (ECG)	Identification and localization of arrhythmias and conduction abnormalities
Radiotelemetric ECG	Identification of arrhythmias during exercise
24 h ambulatory ECG	Documentation of the frequency of occurrence of arrhythmias at rest and during exercise
Cardiac troponins, LDH and CK isoenzymes	Confirmation of the presence of acute myocardial necrosis
Echocardiography	Identification of ventricular dilation, reduced ventricular function and concurrent valvular disease
Non-specific aids	
Radiography	Subjective assessment of cardiac size and demonstration of pulmonary edema
Hematology, biochemistry, blood culture and serology	Elucidation of the underlying cause of valvular or myocardial pathology. Determination of the multisystemic effects of cardiac dysfunction

Modified with permission from Marr, C.M. (1990) Ancillary aids in equine cardiology, Equine Veterinary Education 2: 18–21.

Table 8.4 Normal M mode echocardiographic values for adult horses

	Range (mean)
Right ventricle: diastole	32–52 (38.6) mm
Ventricular septal thickness: diastole	19–43 (30.6) mm
Ventricular septal thickness: systole	35–62 (48.1) mm
Left ventricular internal dimension: diastole	80–130 (110.6) mm
Left ventricular internal dimension: systole	43–79 (61.1) mm
Left ventricular wall thickness: diastole	20–40 (29.2) mm
Left ventricular wall thickness: systole	32–56 (44.5) mm
Left ventricular fractional shortening	32–55 (44.1) %[1]
Septal-left AV valve E point separation	$<$10 mm
Left auricular dimension	35–75 (56.4) mm
Aortic root dimension	55–90 (73.1) mm
Left ventricular ejection time	$<$0.45 s[2]

[1] *The left ventricular fractional shortening is normally* $\leqslant$ *40% at heart rates of less than 50 bpm.*
[2] *At heart rates of less than 50 bpm.*
Reproduced with permission from Bongura et al. (1985) Veterinary Clinics of North America 1: 311–333.

aids are used to investigate the etiology of certain cardiac diseases and to assess the other body systems that may be affected secondary to cardiac disease.

MYOCARDIAL DISEASE

There are few known causes of primary myocardial disease (cardiomyopathy) in the horse. The **ionophore antibiotics** (monensin, salinomycin), common additives in cattle and poultry feed, produce **myocardial necrosis** in the horse. Other proposed etiologies include viral and immune-mediated myocarditis. Nutritional deficiencies are common causes of cardiomyopathy in other species and, in the horse, vitamin E–selenium deficiency produces **cardiomyopathy** as well as **skeletal muscle disease** (white muscle disease) (*q.v.*).

Myocardial dysfunction is often secondary, resulting from extracardiac systemic disease or drug reactions. Significant reductions in myocardial contractility have been noted in horses with lymphosarcoma (*q.v.*) (without cardiac infiltration), electrolyte disturbances, severe metabolic derangements, endotoxemia and septicemia.

Myocardial disease is characterized by cardiac arrhythmias and/or ventricular dysfunction with ventricular dilatation and reduced myocardial contractility. The presenting signs depend on the severity of myocardial dysfunction and range from varying degrees of **exercise intolerance** to signs of congestive or low output heart failure in severe cases (see Box 8.1).

The **diagnostic procedures** that are useful in investigation of myocardial disease are listed in Table 8.3. Echocardiography is used to assess ventricular function while electrocardiography is used to categorize arrhythmias and can reveal S-T segment changes or changes in the duration of complexes. Prolongation of ECG intervals may be associated with **primary myocardial disease**, however this should alert the clinician to the possibility of electrolyte or metabolic imbalances.

Measurement of serum concentrations of **cardiac troponins** and CK-MB and HBDH (cardiac isoenzymes of creatinine kinase [CK] and lactate dehydrogenase [LDH], respectively) can be helpful as increases indicate active or recent myocardial damage. However, normal results have been found in horses with significant myocardial necrosis and in chronic myocardial disease. In addition, concurrent damage to other organ systems must be taken into consideration because CK-MB and HBDH are not cardiac-specific in the horse.

Feed analysis for ionophore antibiotics, assessment of acute and convalescent viral titers (e.g. influenza, herpesvirus [*q.v.*]) or virus isolation is appropriate for determining the etiology of myocarditis in individual cases. Myocardial biopsy has not been attempted successfully in the horse.

Appropriate **therapy** depends on the presence and significance of any arrhythmias, and the degree of myocardial dysfunction. Certainly, any **electrolyte or metabolic imbalances**, or systemic disease should be corrected or excluded as a cause of myocardial disease (*q.v.* arrhythmias for further details of management of those horses with clinically significant arrhythmias).

Therapy for myocardial dysfunction includes rest, diuretics (**furosemide**) and, if the horse is showing signs of heart failure, positive inotropic agents such as **digoxin** or, in emergency situations, **dobutamine**. Digoxin is contraindicated in ionophore poisoning. Activated charcoal or mineral oil may be beneficial in horses that are known to have ingested ionophore very recently.

The **prognosis** for myocardial disease varies, and is based on the severity of the myocardial insult, the extent of irreversible changes and the degree of ventricular dilatation. Although horses with arrhythmias are often tentatively diagnosed as suffering from "myocarditis" or "myocardial disease", these horses can have very **localized inflammation** of the conducting tissue alone. Horses with a pathologic arrhythmia as the only abnormality have a better prognosis than those with accompanying myocardial dysfunction and ventricular dilatation. Thus, **echocardiographic assessment** of ventricular function is the most accurate means of formulating a prognosis.

Horses with recent onset of myocardial dysfunction, including those with ionophore poisoning, may recover completely and return to their previous level of performance. However, if the damage is extensive, irreversible **myocardial fibrosis** will ensue. These horses may survive the cardiac disease, but their **athletic capability** can be markedly reduced. In other cases, cardiac dilatation progresses over weeks to years and the animal eventually dies of congestive heart failure.

CARDIAC ARRHYTHMIAS

Cardiac arrhythmias are common in horses, both at rest and during exercise. They are often physiologic in nature, produced by normal neurohumoral mechanisms as a means of regulating the heart rate and modifying blood pressure. However, arrhythmias can also be pathologic, signifying **myocardial disease**. The equine clinician is frequently required to determine the significance of arrhythmias. A methodical approach allows precise characterization of the rhythm disturbance and its origin and thus provides the basis for assessment of the importance of the arrhythmia.

Diagnosis of arrhythmias

Careful **cardiac auscultation** will enable the detection of most cardiac arrhythmias in the horse and in some instances a tentative diagnosis can be made from auscultation alone. However, an **ECG** is required to diagnose definitively the type of arrhythmia present, and should always be performed if a pathologic arrhythmia is suspected (see Table 8.3). The base-apex lead is used routinely in the horse for assessment of the heart rate and rhythm because movement artifacts are minimized and waveforms are easily visualized.

For the base-apex lead placement is as follows:

1. The negative ("right arm") electrode is sited dorsal to the right scapula, or in the right jugular groove, two thirds of the way down the neck.

Table 8.5 Normal interval durations in the equine ECG (lead II)

Interval	Duration
P–R	0.22–0.56 s
QRS	0.08–0.17 s
Q–T	0.32–0.64 s

2. The positive ("left arm") electrode is sited over the cardiac apex (just above the point of the elbow in the sixth intercostal space on the left side).
3. The ground ("right leg") electrode is sited anywhere on the body, remote from the heart.

Multiple leads can be necessary for the accurate diagnosis of some complex arrhythmias and the standard limb leads used in other species are adequate in the horse. PR, QRS and QT interval determinations are most commonly calculated from lead II (Table 8.5).

ECGs can be obtained during exercise using radiotelemetry or digital ambulatory systems. These techniques are particularly valuable in the horse because arrhythmias that are not present at rest can occur during **exercise**. Equally, arrhythmias that are present at resting heart rates can disappear during exercise. Twenty-four hour ambulatory (Holter) ECG monitoring is a method by which an ECG is recorded **continuously** on magnetic tape or using digital recorders, for prolonged periods. It allows a more accurate assessment of the frequency of occurrence of arrhythmias, and the horse can be left unattended, removing environmental influences that induce or abolish arrhythmias by modification of autonomic tone.

Physiologic arrhythmias

Physiologic arrhythmias are extremely common in normal horses. These are **bradyarrhythmias** associated with parasympathetic activity and occur at resting heart rates, generally <40 bpm. Reduction of vagal tone with exercise, excitement or vagolytic drugs (e.g. **atropine sulfate** or **glycopyrrolate**, see Table 8.6) will remove these arrhythmias. These arrhythmias are not indicative of cardiac disease unless the arrhythmia persists at high heart rates or the animal exhibits syncope during the arrhythmia. Table 8.7 lists and describes the physiologic arrhythmias.

First and second degree atrioventricular block are the most common. Second degree atrioventricular block may occur as often as one beat in three. Generally beats are dropped singly, but occasionally, in normal horses, two beats may be dropped in succession. The other bradyarrhythmias are seen sporadically in normal horses.

Pathologic arrhythmias

Pathologic arrhythmias can be associated with primary or secondary myocardial disease, non-cardiac systemic disease, toxins such as monensin, hypoxia,

Table 8.6 Dosages of drugs used for management of cardiac arrhythmias in the horse

Drug	Dose
Atropine	IV: 0.005–0.01 mg/kg
Digoxin	IV: 0.002 mg/kg b.i.d. PO: 0.01 mg/kg b.i.d.
Glycopyrrolate	IV: 0.005–0.01 mg/kg
Lidocaine	IV: 0.5 mg/kg IV bolus every 5 min to 2.0–4.0 mg/kg total
Magnesium sulfate	IV: 2.2–5.5 mg/kg every 5 min to 55 mg/kg total
Procainamide	IV: 1 mg/kg/min to 20 mg/kg total PO: 25–35 mg/kg t.i.d.
Propranolol	PO: 0.38–0.78 mg/kg t.i.d. IV: 0.05–0.16 mg/kg b.i.d.
Phenytoin	PO: 10–22 mg/kg b.i.d.
Quinidine	PO: 22 mg/kg every 2–6 h (quinidine sulfate) IV: 2.2 mg/kg bolus every 10 min to 8–10 mg/kg total IV drip: 0.064% solution,[1] 0.7–3 mg/kg/h (1.2–2 L/h/450 kg) (quinidine gluconate)

[1] *A 0.064% solution of quinidine gluconate may be made by mixing 3.2 g of quinidine gluconate (four 800 mg vials) in 5 L of isotonic IV fluids.*

Table 8.7 Physiologic arrhythmias in the horse

Arrhythmia	Auscultation	ECG
First degree AV block[1]	Low to normal resting heart rate; regular rhythm	Prolonged (>0.5 s) P-R interval
Second degree AV block	Low to normal resting heart rate; regular rhythm with occasional pauses; isolated 4th heart sound during pauses	Occasional P waves not followed by a QRS-T Mobitz type I (Wenckebach): progressive lengthening of P-R intervals preceding the dropped beat Mobitz type II: constant P-R interval
Wandering atrial pacemaker[1]	Low to normal resting heart rate; regular or slightly irregular rhythm	Variable P wave morphology; constant or variable P-P intervals
Sinus arrhythmia	Low to normal resting heart rate; slightly irregular rhythm ± associated with respiration	Variable P-P and P-R intervals
Sinoatrial block[1]	Low to normal resting heart rate; regular rhythm with pauses	Absence of P waves during pauses of less than or equal to two P-P intervals
Sinoatrial arrest	Low to normal resting heart rate; regular rhythm with long pauses	Absence of P waves for greater than two P-P intervals

[1] *May occur in association with other physiologic arrhythmias.*

and metabolic or electrolyte imbalances. A history of, or concurrent, **respiratory viral infection** or fever may be indicative of viral myocarditis. However, the underlying cause of the arrhythmias is often not apparent.

Arrhythmias induced by **exercise**, particularly those immediately after exercise as the heart begins to slow down, are thought to be the result of **autonomic imbalance**. Circulating catecholamines and other hormones released in large quantities during exercise may promote electrophysiologic instability and result in rhythm disturbances during or after exercise.

Exercise-induced arrhythmias can be of no clinical significance, particularly isolated infrequent premature beats occurring during the recovery phase. Exercise-induced arrhythmias have been associated with dynamic upper airway lesions and therefore this possibility should be considered if exercise-induced arrhythmias are noted. Sustained or paroxysmal tachyarrhythmias compromise cardiac function and result in poor performance.

The importance of arrhythmias in the etiology of **sudden death during exercise** is unknown. There is no concrete evidence, but there is considerable speculation that arrhythmias are a major cause. Auscultatory findings indicative of pathologic arrhythmias include premature beats, erratic rhythms, inappropriate tachycardia, and inappropriate or symptomatic bradycardia.

Arrhythmias can arise from any location within the heart. They are classified according to their origin as **supraventricular** (originating in the sinoatrial node, atrial myocardium, the atrioventricular node or junctional conduction tissue), or **ventricular**. An **ECG** is necessary to differentiate supraventricular and ventricular arrhythmias. Table 8.8 describes the auscultatory and electrocardiographic findings in the pathologic arrhythmias that are seen frequently in horses.

Supraventricular tachyarrhythmias

Supraventricular premature depolarizations

Supraventricular premature depolarizations (SVPDs) are unlikely to affect performance unless they occur frequently during exercise. Isolated SVPDs immediately after exercise during the heart rate recovery phase are not usually clinically significant. If these are documented with radiotelemetric ECG, it is usually possible to offer a good prognosis provided they are not occurring during exercise or very frequently. However, in some horses SVPDs may reflect the presence of **atrial myocardial disease**, which itself can predispose the horse to the development of atrial fibrillation. The presence of underlying electrolyte or metabolic imbalances or systemic diseases should be investigated and, where possible, corrected.

Rest (stall rest with turnout in a small paddock) for 1–2 mo can result in resolution in some cases. **Corticosteroids** (for example prednisolone and dexamethasone) are indicated if an immune-mediated post-viral myocarditis is suspected; however, they are **contraindicated in the presence of active viral infection** due to their potential for immunosuppression. Prednisolone and dexamethasone are given in decreasing dosage regimens, starting at 1 mg/kg and 0.1 mg/kg, respectively. Prednisolone is often used on alternate days whereas dexamethasone can be given at 2–4-day intervals. Clear evidence to favor one specific drug or dosage regimen is currently lacking.

Table 8.8 Supraventricular and ventricular arrhythmias in the horse

Arrhythmia	Auscultation	ECG
Atrial premature complexes	Premature beat ± compensatory pause	Premature P wave; may or may not be followed by a normal QRS-T
Supraventricular tachycardia	Inappropriately rapid regular rhythm; paroxysmal or sustained; abrupt onset and offset; irregularly irregular if accompanied by variable first and second degree AV block	Atrial: rapid atrial rate P waves may or may not differ from sinus P waves constant, normal QRS-T morphology ± variable first and second degree AV block Junctional: rapid succession of normal QRS-Ts unassociated with sinus P waves
Atrial fibrillation	Normal resting heart rate (elevated if myocardial dysfunction or congestive heart failure is present); irregularly irregular rhythm; variable intensity heart sounds	Irregular R-R intervals; absence of "P" waves; "f" fibrillation waves
Pre-excitation	Normal	Shortened P-R interval ± abnormal QRS configuration
Advanced second or third degree AV block	Very low to normal resting heart rate; little to no increase in heart rate with excitement/exercise/atropine Third degree and repetitive second degree: regular rhythm Second degree: slightly irregular	Second degree: frequent P waves not followed by QRS-T occasional conduction Third degree: no evidence of conduction (AV dissociation) junctional or ventricular escape rhythm (third degree and second degree)
Ventricular premature contractions	Premature beat ± compensatory pause	Premature QRS-T not preceded by a P wave; VPC differs in morphology from sinus QRS; T wave of VPC oriented in opposite direction of its QRS; ±increased duration of the premature QRS
Accelerated idioventricular rhythm	Normal to slightly elevated heart rate ± regular rhythm	"Slow" ventricular tachycardia (⩽50/min) (see ventricular tachycardia)
Ventricular tachycardia	Rapid inappropriate rate ± regular rhythm	Four or more successive VPCs Uniform VT: single VPC morphology Multiform VT: more than one VPC morphology

Digoxin and **phenytoin** may be successful in suppressing SVPDs (see Table 8.6), but this is not usually necessary unless there is a rapid ventricular response rate and the arrhythmia is accompanied by signs of low cardiac output (see Box 8.1).

Unfortunately, the SVPDs usually **recur** following discontinuation of the anti-arrhythmic agent. Twenty-four hour ambulatory and radiotelemetric ECG recordings obtained before and after treatment are useful to assess the response to treatment.

Supraventricular tachycardia

Supraventricular tachycardia (SVT) can originate in either an ectopic atrial focus (**atrial tachycardia**) or the AV junction (**junctional tachycardia**). Differentiation from sinus tachycardia may be difficult, but is based on the following:

1. With SVT the heart rate is inappropriately high for the horse's clinical condition, whereas with sinus tachycardia the cause is often evident, for example exercise, excitement, pain, systemic disease, or compromised hemodynamic status.
2. With SVT the onset and offset of tachycardia is often abrupt, while the onset and offset of sinus tachycardia is somewhat gradual.
3. Vagal maneuvers: AVT may be suppressed with vagal stimulation, while sinus tachycardia persists.

Anti-arrhythmics are used in the treatment of supraventricular tachycardia only if the ventricular rate is high and/or there are signs of low output cardiac failure (see Box 8.1). **Digoxin** is used to slow the ventricular response rate (see Table 8.6). **Quinidine** (sulfate or gluconate) and **procainamide** can be used as specific anti-arrhythmics in SVT (see Table 8.6).

Atrial fibrillation

Atrial fibrillation (AF) is the most common, and the most clinically significant, pathologic arrhythmia in the horse. It can occur in the absence of myocardial pathology, in association with atrial myocardial disease (myocarditis), or in the presence of **atrial enlargement** due to acquired valvular or congenital cardiac disease.

The clinical signs vary, depending on the **athletic use** of the horse and the presence or absence of **underlying heart disease**. Racehorses often exhibit a marked reduction in performance and, on occasion, have marked exercise-induced pulmonary hemorrhage (*q.v.*) or appear to tie up (*q.v.*). Horses used for less demanding sports may be asymptomatic.

Congestive heart failure (*q.v.*) is often accompanied by AF, in which case the clinical signs (increased resting heart rate, severe exercise intolerance, pulmonary edema and/or ventral edema, see Box 8.1) reflect the congestive heart failure rather than the AF. **AF is a consequence of, and not a cause of, congestive cardiac failure**. Negative prognostic indicators for horses with AF are presented in Box 8.3. The prognosis for successful treatment of AF is good if there is no underlying heart disease, but extremely poor if congestive heart failure is present.

The recommended **treatment** for AF is dependent on the presence or absence of **underlying heart disease** and the **athletic performance required** of the horse. In some horses in which AF is detected as an incidental finding, which are asymptomatic and performing to their owners' expectations and in which the history suggests that the AF may have been present for some time, it is not necessary to treat the horse unless the owner so wishes. These horses are unlikely to collapse or otherwise represent a danger to their riders. In horses with congestive heart failure and AF, therapy should be aimed at reducing

Box 8.3 Negative prognostic indicators for horses with atrial fibrillation

1. Increased resting heart rate (>60 bpm)
2. Grade III or louder murmurs of left or right atrioventricular valvular insufficiency, particularly if atrial dilatation is detected on echocardiographic examination
3. Prolonged (>6–12 mo) duration of AF (the duration may be inferred from the horse's performance history). Horses with prolonged duration of AF require larger quantities of quinidine sulfate to effect conversion, and are at greater risk of recurrence
4. Development of atrial tachycardia with variable first and second degree block during the course of treatment
5. Supraventricular premature depolarizations (SVPDs) following conversion to sinus rhythm (this may indicate underlying atrial myocardial disease, or the SVPDs may result in atrial fibrillation)

congestion with **furosemide** and slowing the ventricular rate with **digoxin** (see Table 8.6) (see congestive heart failure [*q.v.*]). **Quinidine sulfate is contraindicated** in these horses.

In horses with **symptomatic AF but no underlying heart disease**, quinidine sulfate is the drug of choice. Quinidine prolongs the effective refractory period of the atrial myocardium, suppressing the fibrillation waves and allowing sinus rhythm to be restored. The standard protocol for the use of quinidine sulfate is given in Box 8.4.

The **adverse effects** of quinidine include depression and anorexia, diarrhea and abdominal pain. Occasionally, some horses have idiosyncratic reactions, which may include ataxia, sudden death, nasal mucosal edema and urticaria. Quinidine has profound hypotensive and positive chronotropic effects, and horses should not be stressed or moved out of their stalls during treatment. Quinidine also has pro-arrhythmic effects.

Continuous **ECG monitoring** is advisable in order to detect severe arrhythmias during treatment of AF. If persistent **ventricular tachycardia** occurs, magnesium sulfate is the drug of first choice while **propranolol** can also be useful (see Table 8.6). Procainamide should be avoided as it is similar in action to quinidine.

Supraventricular tachycardia with variable first and second degree heart block is frequently seen during treatment with quinidine sulfate and is a poor prognostic indicator. Severe supraventricular tachycardia (200–300 bpm) has been observed in some horses undergoing treatment with quinidine for atrial fibrillation. This arrhythmia, in combination with the hypotensive effects of quinidine, could result in death. If SVT occurs, the measures listed in Box 8.5 should be undertaken.

In most cases, once sinus rhythm has been restored, the horse can resume training immediately unless **active myocardial disease** is suspected, significant adverse effects of quinidine were noted during treatment, or there was a recent history of pronounced **exercise-induced pulmonary hemorrhage** (*q.v.*)

Box 8.4 Treatment regimen for atrial fibrillation using quinidine sulfate

1. Monitor the ECG continuously during treatment if possible
2. Do not move the horse from its stall during treatment
3. 22 mg/kg (10 g/450 kg) quinidine sulfate via stomach tube q 2 h*
4. Obtain ECG prior to each dose and assess for widening of QRS by more than 25% of pre-treatment value; discontinue quinidine if this occurs as quinidine concentrations are likely to be in the toxic range
5. Discontinue if toxicity develops (prolongation of the QRS by 25% of pre-treatment duration, diarrhea, ataxia, nasal mucosal edema or significant tachycardia)
6. If sinus rhythm is not restored after 5–6 treatments have been given, options include:
   (a) Continue the administration of quinidine, changing to 6 h dosing interval (one half-life of quinidine) to attain a constant plasma quinidine concentration until sinus rhythm is restored or signs of toxicity appear
   (b) Monitor serum quinidine concentrations to ensure that therapeutic levels are being achieved
   (c) Digitalization should be strongly considered in horses with supraventricular tachycardia (ventricular rate of 100 per min). Anecdotally, digitalization has also been beneficial in horses that appear to be refractory to quinidine alone. Although digoxin toxicity can occur when quinidine and digoxin are administered together, short-term simultaneous drug administration appears to be safe

** Previously a test dose was recommended, however the majority of quinidine's toxic effects are dose dependent and the first dose in this regimen serves as a test dose for idiopathic anaphylactic reactions.*

Box 8.5 Protocol for the emergency treatment of rapid supraventricular tachycardia induced by quinidine sulfate

1. Digoxin (0.002 mg/kg IV) to slow ventricular response rate
2. Intravenous fluids (large volumes of isotonic fluids, or 4 mL/kg of hypertonic saline) to increase blood pressure
3. Bicarbonate (1 mg/kg IV) to increase protein binding of quinidine and decrease the concentration of free drug
4. Phenylephrine (10 mg in 500 mL of 0.9% saline) in a fast drip to effect vasoconstriction and increase blood pressure
5. Activated charcoal or oil to limit further absorption of quinidine from gastrointestinal tract

or myositis associated with AF. In such cases, an additional period of rest may be warranted. After the horse returns to training, the heart rhythm should be monitored periodically to ensure that AF has not recurred. Most owners can be taught to do this regularly.

Ventricular tachyarrhythmias

Ventricular premature depolarizations

Ventricular premature depolarizations (VPDs) are seen in the same clinical circumstances as those described for SVPDs. Isolated VPDs can be detected after exercise as the heart rate slows, and if they can be shown to be isolated and infrequent they can be considered to be insignificant. Similarly, the treatment for VPDs is that also recommended for SVPDs (stall rest, corticosteroids). VPDs should be more aggressively managed if they are multiform, frequent or the coupling interval is very short (R-on-T phenomenon).

Accelerated idioventricular rhythm

Accelerated idioventricular rhythm is defined as four or more successive VPDs occurring at intervals similar to the sinus R-R interval (i.e. a **sustained accelerated idioventricular rhythm** would occur at a rate of 30–50 bpm). This arrhythmia is seen most often in the presence of non-cardiac disease, particularly gastrointestinal disease. In the majority of horses, the arrhythmia will resolve without specific anti-arrhythmic therapy.

Ventricular tachycardia

Ventricular tachycardia (VT) is defined as four or more successive VPDs occurring at a rapid rate (⩾50/min). Again, this arrhythmia is most frequently seen in association with non-cardiac disease, particularly gastrointestinal disorders. In addition to the correction of any underlying disorders, anti-arrhythmic therapy should be considered if the rate is rapid (⩾100/min), multiform VPDs are present, or very short coupling intervals (R-on-T phenomenon) are noted. In some instances, the arrhythmia needs to be treated even if none of these criteria applies: a systemically ill horse, particularly one that is hypovolemic, will be much less able to tolerate ventricular tachycardia than an otherwise healthy horse, and signs of low output failure may be present (see Box 8.1).

Evidence on the efficacy and safety of anti-arrhythmic agents in horses is lacking. **Procainamide, lidocaine** or **quinidine** may be selected for the initial treatment of VT (see Table 8.6). However, the clinician should be familiar with the following disadvantages:

1. **Lidocaine:** CNS excitability—use with caution; may be preferred over quinidine in an emergency situation or in horses with myocardial dysfunction.
2. **Quinidine:** Hypotension—hypotensive effects may be minimized by administration as a drip, however therapeutic concentrations may not be achieved for several hours.

Magnesium sulfate, phenytoin and **propranolol** have been used successfully for the treatment of VT in some horses (see Table 8.6).

Conduction disorders

Pre-excitation

Pre-excitation is a conduction abnormality that has been reported infrequently (**Wolff–Parkinson–White syndrome**), usually as an incidental ECG finding,

without a documented adverse effect on performance. Affected horses can present with SVT that is responsive to therapy with procainamide. However, further episodes may occur due to the presence of an aberrant pathway between the atria and ventricles.

Advanced second degree and third degree atrioventricular block

These are uncommon arrhythmias in the horse and are caused by inflammation or fibrosis at the atrioventricular node. Corticosteroids may be of benefit in the short term. However, cardiac pacemaker implantation is the definitive treatment for pathologic atrioventricular blocks. Vagolytic drugs (**atropine sulfate** 0.01 mg/kg IV, **glycopyrrolate** 0.005 mg/kg IV, see Table 8.6) or β1-adrenergic drugs (**dobutamine** 0.5–5 μg/kg/min IV) are indicated if advanced atrioventricular blocks develop under anesthesia.

CONGENITAL CARDIAC DISEASES

Many congenital cardiac diseases have been reported in horses (Box 8.6); however, the majority of these are **extremely uncommon**, and single case reports or small series are often all that are described in the literature. Complex cardiovascular defects usually become apparent within a short period after birth. Foals may be presented with stunting, weakness, lethargy and signs of congestive heart failure (see Box 8.1). Anatomic defects result in disturbances of blood flow, and thus cardiac murmurs are present. The characteristics of these murmurs depend on the specific defect (or defects) present.

Echocardiographic examination is the technique of choice for the evaluation of congenital defects (see Table 8.3). A segmental approach to examination is

Box 8.6 Congenital cardiac defects in the horse

Intracardiac defects
- Ventricular septal defect
- Atrial septal defect
- Atresia of the right atrioventricular orifice
- Tetralogy of Fallot
- Hypoplastic left ventricle
- Common ventricle
- Semilunar valvular anomalies

Extracardiac defects
- Patent ductus arteriosus
- Persistent truncus arteriosus
- Transposition of the great vessels
- Sinus of Valsalva aneurysm
- Coarctation of the aorta
- Persistent right aortic arch
- Miscellaneous anomalies of the great vessels and their branches

necessary. Each cardiac structure is identified separately and its relative position to other structures is assessed. Doppler echocardiography is used to confirm the existence of aberrant blood flow (intra- or extra-cardiac shunts). Angiography may be used as a diagnostic aid in foals and small weanlings, but body size usually precludes its use in older animals. Cardiac catheterization can be helpful in some cases.

VENTRICULAR SEPTAL DEFECT

Ventricular septal defect (VSD) is the most common congenital cardiac disease in the horse. It is usually located in the non-muscular septum, immediately beneath the aortic valve. Occasionally, defects occur in the muscular septum. The shunt through the VSD is from left to right; however, it causes left ventricular volume overload as the extra blood enters the right ventricular outflow tract, over-perfuses the pulmonary circulation and then enters the left heart. Increased right ventricular pressure may be present with large shunts.

The hemodynamic effects and clinical significance of VSDs are dependent on their size. Large defects produce signs of left-sided and, ultimately, biventricular failure (see Box 8.1). More typically, horses with a VSD show signs of **poor performance** or **exercise intolerance** associated with smaller defects. The signs generally become apparent in 2 or 3 yr old horses beginning training. If the defect is extremely small ($\leqslant$2 cm diameter) there may be little or no effect on athletic capability. The prognosis for continuing performance at the same level is good and life expectancy is unaffected. In ponies, it is helpful to compare the size of the VSD with that of the aortic root: a small VSD, $\leqslant \{1/3\}$ the diameter of the aortic root warrants a favorable prognosis.

The pattern of blood flow accounts for the typical murmurs associated with VSDs (see Table 8.2). The intracardiac shunt within the VSD produces a systolic murmur that is loudest on the right side. This is frequently accompanied by a systolic murmur on the left side over the pulmonic valve because the extra right ventricular ejection produces a relative pulmonic stenosis. The location of the VSD beneath the aortic valve may compromise the right coronary cusp, which prolapses into the VSD. There is, therefore, often aortic regurgitation and a diastolic murmur.

Echocardiography is the method of choice for the diagnosis of VSDs, which are readily visualized in the horse. The prognosis is also based on echocardiographic findings: the diameter of the VSD can be measured and signs of left ventricular volume overload or right ventricular pressure overload can be detected. In many cases the horse can be allowed to continue work.

PATENT DUCTUS ARTERIOSUS

The ductus arteriosus generally closes within the first four days of life, and is considered abnormal if patency persists beyond 1 wk of age. Patent ductus arteriosus (PDA) is **uncommon** in horses. When it does occur, the shunt is from left to right from the descending aorta to the pulmonary artery. As in VSD, the increased blood flow to the lungs returns to the left side of the heart

and leads to left ventricular volume overload. Blood flow in the PDA is continuous, thus there may be a continuous "machinery" murmur (see Table 8.2). However, often the murmur is heard in systole only, particularly as pulmonary hypertension increases and the diastolic component of the shunt decreases. The arterial pulses are usually bounding in quality (water hammer) due to the rapid fall in diastolic pressure as blood leaves the left side via the shunt.

Horses with PDA may be presented within the first year of life with stunting, ill-thrift and signs of left-sided or congestive heart failure (see Box 8.1). However, PDA has been detected as an incidental finding on post mortem examination. The diagnosis of PDA can be difficult. It cannot be visualized easily with echocardiography because the lung often obscures the descending aorta. Retrograde blood flow in the pulmonary artery may be apparent on Doppler echocardiographic examination. Cardiac catheterization may be of benefit. Surgical closure of PDA has not been reported in horses. Short-term management of congestive heart failure with digoxin, furosemide and vasodilators may be instituted in some cases (see congestive heart failure [*q.v.*]).

ACQUIRED VALVULAR HEART DISEASES

Valvular lesions are the most common pathologic cause of cardiac murmurs in the horse. They are usually acquired and degenerative or inflammatory in nature. **Valvular stenosis**, which is common in other species, is extremely uncommon in the horse, although reports of congenital valvular malformations have appeared in the literature. Inflammation of the endocardium is most frequently associated with bacterial infection (**bacterial endocarditis** [*q.v.*]). In this disease, the lesions may not be confined to the valves, and may also affect the mural endocardium and the myocardium.

Rupture of the chordae tendineae of the left or right AV valve may occur spontaneously or following degenerative or inflammatory changes in the chordae. The right accessory leaflet of the left AV valve is affected most commonly, but any leaflet may be affected. Rupture of the chordae tendineae produces acute regurgitation, which is usually severe, leading to left- or right-sided heart failure, depending on which valve is affected. Tearing of a semilunar valve cusp can also occur spontaneously and this also results in acute severe valvular insufficiency.

DEGENERATIVE VALVULAR DISEASE

Degenerative lesions include generalized or nodular **fibrosis** and distortion of the **valve cusps**. The precise etiology and pathogenesis of degenerative valvular lesions in the horse is unknown. They are detected most often in middle-aged or older horses but can be seen in horses of any age.

The clinical presentation and prognosis in degenerative valvular heart disease varies according to which particular valve is involved. Careful auscultation allows the identification of murmurs and their characterization. On this basis a differential diagnosis and, frequently, a tentative diagnosis can be formed. The characteristics of physiologic murmurs, and the murmurs typical of each type of valvular insufficiency are listed in Table 8.2.

Table 8.9 Echocardiographic findings in acquired valvular heart disease in the horse

Left ventricular volume overload	
B mode	Globoid, enlarged LV; hyperkinetic LV
M mode	Increased LVD, LVS, FS% and SEP; "swinging" septal motion
Pulmonary hypertension	
B mode	Pulmonary artery dilatation[1]
Right ventricular volume overload	
B mode	Globoid, enlarged RV
M mode	Paradoxical septal motion
Left atrioventricular valvular insufficiency	
B mode	LAV valve thickening or nodules; flail cusp (ruptured chordae tendineae); valvular prolapse;[2] LA enlargement; signs of LV volume overload; pulmonary artery dilatation[1]
M mode	Valve thickening; signs of LV volume overload
Doppler	Regurgitant (high speed, turbulent retrograde) blood flow in the LA
Right atrioventricular valvular insufficiency	
B mode	RAV valve thickening or nodules; flail cusp (ruptured chordae tendineae); valvular prolapse;[2] RA enlargement
M mode	Signs of RV volume overload
Doppler	Regurgitant (high speed, turbulent retrograde) blood flow in the RA
Aortic valvular insufficiency	
B mode	Valve thickening or nodules; flail valve (torn cusp); valvular prolapse;[2] signs of LV volume overload
M mode	Diastolic vibrations on the LAV valve; early diastolic closure of the LAV valve; aortic valve thickening; signs of LV volume overload
Doppler	Regurgitant (high speed, turbulent retrograde) blood flow in the LV
Pulmonic valvular insufficiency	
B mode	Valve thickening or nodules; signs of RV volume overload
M mode	Signs of RV volume overload
Doppler	Retrograde (high speed, turbulent, retrograde) blood flow in RV

[1] Pulmonary artery dilatation is a poor prognostic indicator as pulmonary artery rupture and sudden death may follow.
[2] Valvular prolapse is a common echocardiographic finding but usually it is not accompanied by significant regurgitation.
LV, left ventricle; LVD, diameter of the left ventricular lumen in diastole; LVS, diameter of the left ventricular lumen in systole; FS%, fractional shortening:

$$\frac{LVD - LVS}{LVD} \times 100$$

SEP, maximal excursion in diastole of the distance between the interventricular septum and the mitral E point; RV, right ventricle; LAV, left atrioventricular valve; LA, left atrium; RAV, right atrioventricular valve; RA, right atrium.

Echocardiographic examination allows confirmation of regurgitation and assessment of the hemodynamic effects of lesions (see Table 8.3). The echocardiographic changes that may be associated with valvular lesions are listed in Table 8.9.

BACTERIAL ENDOCARDITIS

Bacterial endocarditis is an important cause of **fever of unknown origin**. The specific cardiovascular signs depend on which valve or valves are involved

(see Box 8.1 and Table 8.2). The signs are accompanied by depression and occasionally shifting leg lameness and limb swelling. Hyperfibrinogenemia and neutrophilia reflect the inflammatory response.

Streptococcus spp., *Actinobacillus equuli*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Rhodococcus equi*, *Erysipelothrix rhusiopathiae* and *Candida parapsilosis* have all been reported as causes of bacterial endocarditis. Blood culture is helpful as antimicrobial sensitivity can be established, but a negative blood culture does not exclude the diagnosis of bacterial endocarditis. Broad-spectrum antibiotics (e.g. **benzylpenicillin sodium** 20 000–40 000 IU/kg IV q.i.d. and **gentamicin** 6.6 mg/kg IV s.i.d.) should be administered, pending blood culture results. The long-term prognosis depends on the degree of residual damage to the valve and the associated valvular regurgitation.

CLINICAL FINDINGS IN VALVULAR DISEASE

Left atrioventricular valvular insufficiency

The left AV valve is the second most common site for valvular pathology in the horse. However, left AV valvular insufficiency is the most important form of acquired valvular heart disease, as it carries a **poor prognosis**. Thus, echocardiographic examination should be considered in all horses with murmurs associated with the left AV valve.

The clinical presentation is dependent on the severity of regurgitation and the speed of progression of the lesion (see Box 8.1 and Table 8.2). **Atrial fibrillation** (*q.v.*) often accompanies moderate or severe left AV valvular regurgitation. Pulmonary hypertension produces pulmonary edema and signs of respiratory dysfunction, and fatal rupture of the pulmonary artery may occur. Periodic echocardiographic assessment is the best means of determining the speed of progression of valvular lesions to provide an accurate prognosis.

Right atrioventricular valvular insufficiency

Right AV valvular insufficiency is present in many **normal horses** in the absence of valvular pathology (see Table 8.2). Consequently, right AV murmurs associated with mild or moderate valvular regurgitation are often detected in horses showing no clinical signs, and these horses generally have no associated performance problems. These horses often have loud grade 3 or 4–6 holosystolic murmurs audible in the right fourth intercostal space.

Clinical signs of right AV valvular insufficiency, if they do occur, are most often seen accompanying **congestive heart failure** (*q.v.*). Rarely, horses are presented with signs of right-sided heart failure following rupture of the chordae tendineae or other right AV valvular lesions (see Box 8.1). Murmurs of right AV valvular insufficiency that are grade 4–6 or greater and/or the presence of an increased jugular pulse indicating severe right AV valvular regurgitation should prompt **further diagnostic evaluation**.

Aortic insufficiency

Degenerative lesions are frequently found on the aortic valve, particularly in middle-aged or older horses. The murmur of aortic insufficiency is a common

incidental finding in these horses (see Table 8.2). The horse can tolerate aortic insufficiency very well and it rarely produces signs of cardiac failure. Hemodynamically significant **aortic insufficiency** produces bounding or tapping pulses, indicating left ventricular volume overload with a rapid fall in diastolic pressure. If these are detected, further diagnostic evaluation is warranted. In the majority of horses, aortic insufficiency progresses slowly and aortic insufficiency alone rarely results in poor performance or cardiac failure.

Left ventricular dilatation secondary to aortic insufficiency can eventually progress to the stage where the left AV valve annulus becomes stretched, with **left AV valvular insufficiency** and more severe clinical signs. The clinician should be alert to this possibility and should evaluate the left AV valve area carefully in horses with murmurs of aortic insufficiency.

Horses with aortic insufficiency and concurrent ventricular arrhythmias appear to be more likely to have **progressive heart disease**, therefore ambulatory and exercising ECG studies are helpful in identifying these individuals.

Pulmonic insufficiency

The pulmonic valve is an uncommon site for valvular pathology. Horses with severe pulmonic insufficiency have a diastolic murmur (see Table 8.2) and signs of right-sided heart failure (see Box 8.1).

TREATMENT OF CONGESTIVE CARDIAC FAILURE

Long-term management of horses with congestive heart failure is rarely necessary. However, short- or mid-term management may be appropriate. Drugs used for the treatment of congestive heart failure are listed in Table 8.10. Regardless of the underlying cause, the goals of therapy in cardiac failure are to **reduce congestion** and to **increase cardiac output**. Diuretics, principally **furosemide**, are used to decrease fluid accumulation, and a **salt-restricted diet** may be beneficial.

Digoxin is used in the hope of increasing cardiac output. Its negative chronotropic effect allows more efficient diastolic filling and consequently increases stroke volume. Digoxin also increases cardiac contractility.

Vasodilators are widely used in the management of cardiac failure in other species. Their efficacy in horses has yet to be evaluated. Angiotensin-converting enzyme inhibitors such as **enalapril** (*q.v.*) are widely used in other species and have been shown to be safe in normal horses (see Table 8.10). They are being

Table 8.10 Drugs used for the management of congestive heart failure in horses

Drug	Dose
Acepromazine	0.04–0.1 mg/kg b.i.d. or t.i.d.
Digoxin	0.01 mg/kg IV b.i.d.
Enalapril	0.5 mg/kg PO b.i.d.
Promazine	0.4–1 mg/kg PO b.i.d. or t.i.d.
Nitroglycerin ointment	Not known

used increasingly in the treatment of horses with congestive heart failure. **Acepromazine, promazine (arterial) and nitroglycerin ointment** (venous) may potentially be used as vasodilators (see Table 8.9). Again, there is no information on their efficacy in congestive heart failure.

DETERMINATION OF THE PROGNOSIS IN VALVULAR DISEASE

The prognosis in equine valvular disease is dependent on its site and the precise type of pathology involved, the speed of onset of the lesion and severity of the regurgitant fraction, the degree of associated ventricular volume overload and the presence of complications and sequelae such as pulmonary hypertension, pulmonary artery dilatation and atrial fibrillation (*q.v.*). Left AV valvular insufficiency is more likely to limit performance and shorten life expectancy than aortic or right AV valvular insufficiency.

Degenerative lesions that are slowly progressive are less significant than acute, severe lesions such as ruptured chordae tendineae, torn semilunar cusp and bacterial endocarditis (*q.v.*). The rate of progression of lesions can be determined most accurately by repeated echocardiographic evaluation. Thus a **precise diagnosis** and **detailed cardiovascular work-up** are required for the purposes of forming a prognosis and assessing the horse's safety for riding or insurance purposes (*q.v.*). It should be noted that although valvular insufficiencies can be fatal they are not likely to result in sudden death without preceding signs of congestive heart failure.

PERICARDIAL DISEASES

Pericarditis is categorized as effusive or constrictive, and also on the basis of its fluid characteristics, which may be fibrinous, septic, inflammatory or hemorrhagic. The etiologies of pericardial disease include bacterial or viral infections, penetrating wounds and, rarely, neoplasia. However, the majority of cases appear to be **idiopathic**. Increased numbers of pericarditis cases have been documented to occur during outbreaks of **mare reproductive loss syndrome**, a syndrome of fetal loss that has been linked to exposure to the Eastern Tent caterpillar (*q.v.*), but the precise mechanism by which pericarditis is induced in the syndrome is unknown.

EFFUSIVE PERICARDITIS

Effusive fibrinous pericarditis is the most common pericardial disease seen in horses. The hemodynamic effects of the pericardial effusion depend on the rate and amount of fluid accumulation and the physical characteristics (stretch) of the pericardium. When the pericardial effusion increases, the pressure within the pericardial sac can rise to equal the right atrial and ventricular diastolic pressures. Consequently, ventricular diastolic filling is impaired and in turn stroke volume declines (**cardiac tamponade**).

The clinical signs reflect right-sided, low output heart failure and include lethargy and weakness, jugular venous pulsations or distension, ventral

edema, weak arterial pulses and dyspnea (see Box 8.1). Typically, auscultation reveals tachycardia with muffled heart sounds. However, pleural effusion and obesity can also produce muffled heart sounds. In **fibrinous pericarditis**, pericardial friction rubs can be detected, although rubs are often absent in cases of effusive fibrinous pericarditis.

Echocardiography is used to confirm the diagnosis of pericardial disease and to characterize the pericardial fluid. The electrocardiogram may reveal diminished QRS voltage; however, this finding is not specific for pericardial effusion as it may also be seen in obese animals and in animals with pleural effusion. Electrical alternans (cyclical variation in the QRS configuration due to cardiac movement) is occasionally seen. This is most easily detected in one of the limb leads rather than the base-apex lead. Radiographs reveal an enlarged cardiac silhouette. However, if a **pleural effusion** accompanies the **pericardial effusion** this will obscure the cardiac silhouette. Ideally, a sample of **pericardial fluid** should be obtained (Box 8.7). The nucleated cell count, protein content, cytologic evaluation and bacterial culture are of value in determining the etiology and in selecting a therapeutic regimen.

In recent years, reports have indicated that, if effusive fibrinous pericarditis is treated early and aggressively, the prognosis for return to previous athletic performance is good. **Pericardiocentesis** is the procedure of choice for the treatment of horses with effusive pericarditis. The indications include clinical signs of right-side heart failure, cardiac tamponade, and echocardiographic evidence of right atrial collapse. A technique for pericardiocentesis is described in Box 8.7. Removal of the pericardial effusion produces a rapid improvement in the horse's clinical status because cardiac tamponade is reduced and right

Box 8.7 Technique for pericardiocentesis

Location
Left 4–6 intercostal spaces, 6 cm ventral to point of shoulder. Selection of site is facilitated by the use of diagnostic ultrasound.

Sedation
May not be necessary, depending on the horse's clinical status. If necessary, use with caution; these drugs may exacerbate cardiovascular compromise.

ECG monitoring
Have appropriate doses of procainamide, quinidine or lidocaine at hand. If ventricular arrhythmias occur, the needle should be retracted; if this fails, anti-arrhythmic drugs may be necessary.

Site preparation
Clip; surgical scrub; infiltration of lidocaine in skin, subcutaneous layers and intercostal muscles; stab incision.

Catheter selection
Over-the-needle IV catheters (14 G, 13 cm), or chest drains (16 to 20 French) (withdraw trocar once pericardial sac has been penetrated).

ventricular function improves. Potential complications include laceration of a coronary artery or intercostal artery, fatal ventricular arrhythmias and cardiac puncture.

Specific treatment of effusive pericarditis depends upon the suspected etiology. **Broad-spectrum antimicrobials** (for example **benzylpenicillin sodium** 20 000–40 000 IU/kg IV q.i.d. and **gentamicin** 6.6 mg/kg IV s.i.d.) are indicated in septic pericarditis or in those cases in which pericardial disease occurs in conjunction with a systemic septic process such as pleuropneumonia. Non-steroidal anti-inflammatory drugs (for example flunixin meglumine 1.1 mg/kg IV b.i.d.) may be of additional benefit.

Corticosteroids appear to be very useful in horses with idiopathic effusive fibrinous pericarditis but should be avoided when a bacterial or viral etiology is suspected due to their potential for immunosuppression. Prednisolone and dexamethasone are given in decreasing dosage regimens, starting at 1 mg/kg and 0.1 mg/kg, respectively. Prednisolone is often used on alternate days whereas dexamethasone can be given at 2–4-day intervals. Clear evidence to favor one specific drug or dosage regimen is currently lacking.

An indwelling **pericardial drain** may be necessary for cases in which the effusion is septic and/or recurrent. A catheter or drain (e.g. 16 to 20 French chest drain) may be inserted as described in Box 8.7. This can be sutured in place and sealed with a one-way stopcock. An indwelling catheter allows for twice daily lavage of the pericardial sac, with instillation of antimicrobials.

CONSTRICTIVE PERICARDITIS

Constrictive pericarditis is very rare in the horse. It can be idiopathic or, more commonly, a sequel to effusive and/or fibrinous pericarditis. In this condition, inflammation and fibrosis thicken the pericardium and it becomes **inelastic**.

The clinical signs in constrictive pericarditis are similar to those described above for effusive pericarditis (*q.v.*), although **pericardial friction rubs** may be present. Differentiation of constrictive pericarditis from pericardial effusion can be difficult, even with echocardiography. In some cases of constrictive pericarditis there is no effusion but echocardiography reveals a thickened pericardium, measuring approximately 5–7 mm. However, constrictive pericarditis can be accompanied by a fibrinous effusion.

Compression of the right atrium confirms the presence of **cardiac tamponade**. Cardiac catheterization is the best means of differentiating effusive from constrictive pericarditis. In constrictive pericarditis, ventricular filling is limited to early diastole, with abrupt cessation of filling in mid diastole. In contrast, effusive pericarditis interferes with ventricular filling throughout diastole.

Treatment of constrictive pericarditis requires the **surgical resection** of the affected pericardium. **Partial pericardectomy** has been attempted in the horse with limited success. The prognosis is guarded as partial pericardectomy may not be sufficient to improve the horse's hemodynamic status, involvement of the epicardium may result in further restrictive pathology,

and extension of the inflammatory process may produce myocardial atrophy or fibrosis.

VASCULAR DISEASES

JUGULAR THROMBOSIS

Jugular thrombosis can be septic or non-septic. It occurs most frequently as a sequel to **vessel trauma** by IV catheterization or injection, particularly in endotoxemic (*q.v.*) horses or when inadvertent perivascular infiltration of irritant substances occurs. It may also be seen in horses with coagulopathies, notably **disseminated intravascular coagulation** (*q.v.*).

The thrombosed vein is swollen and firm and is hot and painful on palpation if it is infected. In chronic cases it may feel cord-like. In septic thrombosis the horse may be febrile. There are varying degrees of occlusion. **Acute complete obstruction** of venous drainage leads to swelling of the facial structures of the affected side, particularly the cheek and supraorbital fossa. If occlusion is **bilateral**, the swelling can be sufficient to cause obstruction of the airways, stertorous breathing and dyspnea. There may be distension of the superficial veins of the head in horses with long-standing jugular occlusion.

The diagnosis of jugular thrombosis is based on the clinical findings. However, it is important to differentiate septic from non-septic thrombosis. Neutrophilia and hyperfibrinogenemia are present in **septic thrombosis**. The definitive diagnosis of infection is provided by aspiration and culture and allows antimicrobial sensitivity to be performed. **Ultrasonographic examination** is useful for the identification of fluid pockets within a thrombus, which is strongly suggestive of sepsis and is a guide to the best site of aspiration. Gas echoes within a thrombus suggest **anaerobic infection**.

The goals of therapy are to eradicate infection, reduce local swelling, and minimize the effects of venous occlusion. The choice of antimicrobials should be based on the results of bacterial culture and sensitivity. Broad-spectrum antimicrobial treatment should be provided pending these results. Surveys have shown that **penicillin–gentamicin** and **penicillin–amikacin** combinations (benzylpenicillin sodium 20 000–40 000 IU/kg IV q.i.d., gentamicin 6.6 mg/kg IV s.i.d., amikacin 3.5 mg/kg IV q.i.d.) are most successful. **Metronidazole** (15 mg/kg PO q.i.d.) should be administered if anaerobic infection is suspected. Additional measures include aspirin (15 mg/kg PO every other day) and other **non-steroidal anti-inflammatory drugs**, hot packs, poultices and topical anti-inflammatory ointments containing dimethyl sulfoxide to reduce local swelling. The head should be raised and cross-tied if extensive head swelling occurs. **Emergency tracheostomy** may be necessary with severe dyspnea in acute, bilateral jugular thrombosis.

In **septic jugular thrombosis** the prognosis is variable. Potential complications include embolic pneumonia and endocarditis. In **non-septic thrombosis**, the prognosis is better and the affected vein will often recanalize in time. However, long-standing jugular thrombosis has been associated with exercise intolerance. A surgical procedure to replace the occluded vein with a vascular graft has been successfully performed.

AORTO-ILIAC THROMBOSIS

Aorto-iliac thrombosis is an **acquired progressive disorder** affecting the aortic quadrification and its branches. The etiology is unknown. Although some authors have suggested that migrating parasites may be contributory, there is little substantial evidence to support this. Its clinical presentation is related to disruption of blood supply to the hindlimbs. Affected horses show **vague hindlimb lameness**, which is exacerbated by exercise. The digital pulses in the affected limb may be weak or absent and the limb is cooler than the contralateral one.

Successful treatment has been reported using anthelmintics (**ivermectin** 0.2 mg/kg PO) and non-steroidal anti-inflammatory drugs (e.g. **phenylbutazone** 2–4.4 mg/kg PO or IV s.i.d. or b.i.d.). **Aspirin** (15 mg/kg PO every other day) may be beneficial as it inhibits the local vasoconstriction induced by release of thromboxane from platelets within the thrombus. Some horses will recover if they are kept in work, which is believed to promote the development of a collateral circulation. However, the prognosis in aorto-iliac thrombosis is guarded.

AORTIC ANEURYSMS

Aortic aneurysms can involve either the thoracic or abdominal portions of the aorta. In many anatomic locations, the diagnosis of aortic aneurysms is difficult and they are usually first discovered at post mortem examination, following rupture and fatal hemorrhage. However, **sinus of Valsalva aneurysm** has been detected echocardiographically and aneurysms of the terminal aorta may be palpable per rectum. Erosion of an intra-abdominal aneurysm through the **ureter** leading to **hematuria** (*q.v.*) has been reported. The prognosis for aortic aneurysm is guarded regardless of the site as fatal hemorrhage is likely to occur at any time.

VASCULAR RUPTURE

Rupture of major blood vessels is the **most common cause of sudden death** in horses, particularly those that die during exercise. Major vessels can be traumatized or lacerated by long bone fractures, but in most cases the ruptures occur **spontaneously** and unexpectedly. Aneurysms, vessel wall damage and medial necrosis (*q.v.*) can predispose the vessel to rupture. Rupture of a wide variety of blood vessels has been reported, but **severe pulmonary hemorrhage** has been recognized most frequently in horses that die during exercise.

Aortic ring rupture is associated with sudden death during **breeding** in middle-aged or older breeding stallions. The pathogenesis is unknown, although **acquired medial necrosis** or **congenital sinus of Valsalva aneurysms** may be predisposing factors (*q.v.*). The aorta may rupture either into the right ventricle, causing **acute right-sided heart failure**, or produce a **subendocardial hematoma** within the interventricular septum, disrupting the conduction system and leading to **ventricular arrhythmias**. If the horse survives the initial crisis, it may present with signs of distress, thoracic pain, a rumbling continuous

murmur loudest on the right hemithorax and rapid heart rate due to ventricular tachycardia.

In middle-aged, multiparous mares, rupture of the **middle uterine artery** or its branches occurs in **late pregnancy** or the weeks **immediately after foaling**. These mares may be found suddenly dead, or be presented with signs of hemorrhagic shock and collapse. Location of the ruptured vessel at exploratory laparotomy is unlikely to be successful, thus surgery is not recommended. Supportive therapy, including blood transfusion, is indicated. The prognosis for life is guarded; some mares can recover, although their future breeding potential may be jeopardized.

Chapter 9

The hemolymphatic system

D. D. Morris (Consultant Editor)

Chapter contents

INTRODUCTION

Diseases of the hemolymphatic system are generally due to abnormal quantity and/or function of the normal cellular and humoral components of blood. In order to understand fully hemolymphatic diseases, a basic knowledge of normal blood production (hematopoiesis) and the hemostatic mechanism is necessary.

HEMATOPOIESIS

During postnatal life, hematopoiesis occurs in the **bone marrow**. Maturation is attended by recession of hematopoiesis from the shafts of the long bones and

the replacement of red marrow by resting yellow marrow; however, active hematopoiesis continues throughout life in the epiphyses of long bones and in the flat bones of the skull, vertebrae, sternum, ribs and pelvis. Transition from yellow to red marrow can occur in response to increasing demand for erythrocytes via the glycoprotein hormone **erythropoietin** (*q.v.*).

The bone marrow is composed of differentiated blood cells and their recognizable precursors, undifferentiated progenitor cells, reticular cells, reticular fibers, endothelium-lined sinusoids and adipocytes. Hematopoiesis occurs in the **intrasinusoidal spaces**. All blood cells originate from a population of lymphoid-appearing cells, termed **pluripotent stem cells**, which give rise to committed progenitors of the lymphoid and myeloid series. Pluripotent stem cells (PPSC) are capable of slow self-renewal, whereas the committed progenitor cells differentiate into later stages and their absolute marrow numbers depend upon influx from the PPSC pool.

The amplification and differentiation of hematopoietic progenitors are regulated by polypeptide growth factors called **colony-stimulating factors**. Horse colony-stimulating factors have not been characterized but they are presumed to function similar to those described in humans.

Erythropoietin (Ep) is the most important erythropoietic growth factor. It is produced almost exclusively by the **kidneys** in response to **tissue hypoxia**. Committed erythroid stem cells become progressively more sensitive to Ep stimulation as they mature.

Under homeostatic conditions, marrow production of blood cells approximates the rate of cell destruction. The lifespans of equine erythrocytes and platelets are approximately 155 days and 7 days, respectively, and the circulating half-life of granulocytes is about 10.5 h. Increased use or peripheral loss of marrow-derived blood cells results in production amplification of the necessary component(s). **Complete marrow failure** initially causes enhanced susceptibility to infection due to the loss of granulocytes. Petechial hemorrhages and bleeding secondary to thrombocytopenia follow. Finally pallor and signs of anemia occur.

The **lymphoid stem cell** also arises from the PPSC, but lymphocyte precursor maturation and differentiation are considerably more complex than those of the other hematopoietic cells. Some of the developing lymphocytes are seeded into the thymus, where their maturation into T cells occurs. In mammals, B lymphocyte maturation proceeds in the bone marrow.

Although functionally distinct, T and B lymphocytes (*q.v.*) have a similar morphologic appearance. Circulating lymphocytes, most of which are T cells, are in transit to and from the secondary lymphoid organs where most lymphocyte interactions with antigenic challenge occur. The **spleen** constitutes the largest single mass of lymphocytes in the body. Lymphoid accumulations also occur in great abundance in **lymph nodes** and **near mucosal surfaces**.

The spleen functions only briefly in hematopoiesis during fetal life, but retains this potential into adult life. The unique architecture of the spleen and its fixed phagocytic cells bestow the important function of **filtering** from the blood aged or damaged cells, particulate debris and microorganisms. Hemoglobin from senescent erythrocytes is degraded and iron is stored within phagocytes until it is subsequently released into the plasma for reutilization during erythropoiesis. Splenic macrophages also perform a "pitting function"

by removing inclusions such as **Heinz bodies** (denatured hemoglobin) or intra-erythrocyte parasites from erythrocytes.

In horses, the spleen serves as an important **reservoir** for erythrocytes. Adrenaline-responsive smooth muscle in the equine splenic capsule causes the **packed cell volume** (PCV) to increase during exercise or excitement by as much as 40%. Normalization of red blood cell (RBC) parameters after a period of excitement may require up to 1 h in physically fit horses. The spleen also serves as a **dynamic reservoir of platelets** such that, at any point in time, up to one third of the total blood platelets are retained in the spleen.

HEMOSTASIS

Hemostasis is a complex series of events that functions to arrest bleeding from damaged blood vessels and to maintain blood flow to all body tissues. The processes of coagulation and fibrinolysis, with their respective inhibitors, constitute hemostasis.

Coagulation

The cooperation of platelets and blood procoagulant proteins with the blood vessel wall provides the basis for coagulation, which culminates in the formation of **fibrin**. Immediately after injury, reflex vasoconstriction limits blood loss and the **vessel wall** provides a scaffold for fibrin clot formation. Endothelial cells release substances that activate or inhibit components of coagulation and fibrinolysis.

Platelets interact with a discontinuous vascular surface to form a plug that provides **primary hemostasis**. Platelets adhere to subendothelial collagen and then undergo activation, aggregation and the release reaction. An initial platelet release of adenosine 5′-diphosphate (ADP) into the extracellular environment in response to adhesion promotes **primary aggregation**.

Secondary irreversible aggregation is a consequence of thromboxane (TXA_2) formation and secretion of platelet granule constituents. The phospholipid (PL) necessary at numerous steps during subsequent interaction of coagulant proteins is supplied by platelet factor 3. During and after platelet plug formation the platelet surface protects coagulant proteins from plasma anticoagulants and localizes clot formation. Platelets also prevent spontaneous hemorrhage into the skin and mucous membranes by maintaining "**vascular integrity**".

Coagulation proteins (or coagulation factors) circulate in the peripheral blood as inactive enzymes (**zymogens**). The coagulation "cascade" is a self-amplifying series of proteolytic events in which a zymogen is transformed to a proteinase that effects the subsequent zymogen–proteinase transition. There are two mechanisms by which activated factor X is formed, then coagulation proceeds through thrombin and fibrin production via a single common path.

In the extrinsic pathway, factor Xa is formed via the action of **tissue factor** (TF), which accesses the circulation via inflammation or tissue necrosis. Fibroblasts in the blood vessel adventitia express surface TF constitutively,

while vascular endothelial cells, tissue macrophages and blood monocytes are activated to produce TF by agonists such as **endotoxin** (*q.v.*).

The intrinsic pathway to factor Xa production is initiated when blood is exposed to a **negatively charged surface** such as the platelet plug and/or subendothelial collagen. Through association of the plasma protein factor XII (Hageman factor), prekallikrein and high molecular weight kininogen (HMWK), factor XIIa is formed which perpetuates the intrinsic cascade. Factor VIII generally circulates bound to von Willebrand factor (vWF) in an inactive form, but acquires procoagulant cofactor properties through limited proteolysis by thrombin or factor Xa.

Factor Xa forms a prothrombinase complex with factor Va, PL and Ca^{2+}, which cleaves prothrombin to thrombin. Thrombin dissolves from the PL surface and cleaves fibrinogen to yield fibrin monomers, which spontaneously polymerize. Thrombin activates factor XIII, which crosslinks fibrin and increases the clot's resistance to fibrinolysis.

Plasma **anticoagulant proteins** localize coagulation to the site of injury and thereby protect against **generalized thromboses**. One major anticoagulant mechanism involves antithrombin III (AT III), which accounts for approximately 75% of thrombin-inhibiting activity in plasma. AT III can also neutralize factors Xa, IXa, XIa and XIIa as well as kallikrein and plasmin. **Heparin** produces a conformational change in AT III that results in a 2000-fold acceleration of the latter's inhibitory action.

The second major plasma anticoagulant mechanism is provided by protein C, a liver-derived **vitamin K-dependent** protein that circulates as a zymogen. When thrombin is complexed to endothelial cell thrombomodulin, it activates protein C rather than its other substrates. Activated protein C (APC) cleaves and inactivates factors Va and VIIIa in the presence of Ca^{2+} and PL. This action by APC requires another vitamin K-dependent cofactor, protein S.

Fibrinolysis

Fibrinolysis is activated simultaneously with coagulation and functions to prevent tissue ischemia by the continued presence of fibrin clots. The key **fibrinolytic protein**, plasmin, is formed from circulating plasminogen by the action of several plasminogen activators. The tissue plasminogen activator (tPA) is synthesized primarily by endothelial cells, and both tPA and plasminogen have a high avidity for fibrin. Stasis upstream from an occluded vessel is the primary stimulus for tPA release, and the additional uptake of tPA by the clot tips the balance of hemostasis toward fibrinolysis.

To ensure localization of plasmin activities to the fibrin clot, there is an efficient array of plasma **antifibrinolytic proteins**. Plasminogen activator inhibitor (PAI) rapidly binds and inactivates physiologic concentrations of tPA. Endothelial cells are the primary source of this PAI, although the release of PAI from platelets during coagulation may play an important role in prevention of premature clot lysis.

The inhibition of plasmin activity in the blood is instantaneously carried out by α_2-antiplasmin (AP). During coagulation, AP competes with plasminogen for binding to fibrin, preventing spontaneous lysis of a normal clot.

ANEMIA

Anemia can be functionally defined as **decreased oxygen-carrying capacity of the blood**. Anemia occurs when the PCV is reduced below that which is considered normal for the horse's age, breed and use. However, the PCV must be ≤0.30 L/L before an individual can be classed as anemic.

Anemia develops due to one or more of three pathophysiologic mechanisms:

1. Blood loss
2. Increased RBC destruction (hemolysis)
3. Decreased RBC production.

The bone marrow responds to blood loss and hemolysis by increased **erythropoiesis** (*q.v.*), thus the anemia is regenerative. A **non-regenerative anemia** ensues when the bone marrow does not replace senescent erythrocytes at a normal rate. A bone marrow examination (*q.v.*) is necessary to characterize accurately anemia in horses since peripheral signs of regeneration such as reticulocytosis and polychromasia rarely occur.

Clinical signs of anemia are due to reduced tissue oxygenation and include reduced exercise tolerance, depression, weakness, tachycardia, tachypnea and mucosal pallor. Signs are manifested at a higher RBC mass when anemia develops rapidly since a gradual onset of anemia allows physiologic compensation. A low-grade systolic murmur can sometimes be auscultated when the PCV drops below 0.15–0.18 L/L. Fever, icterus and/or pigmenturia often accompany hemolysis. Epistaxis, hematuria or melena may signal chronic blood loss. Anorexia, lethargy and weight loss suggest an underlying disease process.

LABORATORY EVALUATION

The initial laboratory assessment of anemia includes a **complete blood count (CBC)**, **total plasma protein (TPP)** and **plasma fibrinogen**. There are several unique features of the equine erythron that must be considered during evaluation of the CBC. A horse's PCV cannot be accurately assessed during or after exercise, excitement or endotoxemia since these produce splenic contraction. Splenic contraction in response to **acute hemorrhage** (*q.v.*) also precludes evaluation of the severity of blood loss for the first 12–24 h. Small nuclear remnants called **Howell–Jolly bodies** are occasionally found in erythrocytes of normal horses and do not indicate increased erythropoiesis.

Characterization of anemia as non-regenerative in a horse is most accurately done by **bone marrow examination**. Aspirates to characterize marrow erythropoiesis are most easily obtained from the **sternum** using an 89 mm, 18 G disposable spinal needle. Thin smears should be rapidly air dried, then stained with a modified Romanowsky (Wright) stain. The normal **myeloid–erythroid ratio (M/E)** ranges from 0.5 to 1.5 in horses, thus an M/E ≤0.5 classifies anemia as regenerative.

Equine erythrocytes are small (5–6 μm) and tend to adhere to each other to form a "stack" like coins (**rouleaux**). Marked rouleaux may be confused with autoagglutination, and this tendency for natural aggregation leads to rapid

erythrocyte sedimentation from plasma. Equine plasma is normally quite yellow compared with that of other animals, due to the combined effects of blood carotenoids from green feed and the greater concentration of bilirubin. Fasting causes a marked increase in equine serum bilirubin and can result in **clinical icterus** (*q.v.*). There is no definitive explanation for **fasting-induced hyperbilirubinemia** in horses, but a net decrease in and/or competition for hepatic binding proteins (particularly ligandin) have been proposed. In consideration of hemolytic disease as a cause for icterus in horses, the influence of fasting must be determined.

Red cell morphology should always be evaluated as a routine part of the CBC. Precipitates of oxidized hemoglobin (**Heinz bodies**), parasites, or abnormal cell shape may aid in defining the cause of anemia. The RBC indices are not highly useful in horses since peripheral erythrocytes are nearly always mature. Hemolysis, in vivo or in vitro, causes an increased mean corpuscular hemoglobin (MCH) due to the presence of free plasma hemoglobin.

The **leukogram** and **plasma fibrinogen** are insensitive indicators of chronic inflammatory disease, which may be the cause of anemia. Chronic inflammation may be attended by a normal or only mildly elevated white blood cell (WBC) count in horses, while an intense erythropoietic response to anemia may result in neutrophilia. Both may cause a left shift.

Hyperfibrinogenemia is more indicative of the presence of inflammatory disease than the WBC count in up to 50% of affected horses. The TPP is useful in evaluation of hydration status, and may provide a clue to the cause for anemia. Reduced PCV in the presence of increased TPP, which may be due to hemoconcentration, suggests that the anemia is actually more severe than the PCV indicates. Mild anemia may be masked by dehydration in addition to splenic contraction. An increase in TPP due to **hypergammaglobulinemia** sometimes accompanies chronic infection. Reduction of both the TPP and the PCV is suggestive of **chronic blood loss**.

Generally, history, physical examination and baseline laboratory data allow categorization of the anemia as due to blood loss, hemolysis or inadequate erythropoiesis. Additional laboratory tests can then address the suspected cause for anemia. When more than one mechanism of anemia is suspected, a bone marrow examination (*q.v.*) is necessary to determine the presence or absence of erythroid regeneration.

Treatment

Identification and elimination of the cause, provision of nursing care, ensuring adequate tissue perfusion and minimizing stress are the basis for therapy of anemia in horses. **Blood transfusion** (*q.v.*) should be reserved for those instances in which oxygen delivery to tissues is inadequate to support life.

BLOOD LOSS ANEMIA

The clinical and laboratory findings of blood loss are largely determined by whether this occurs acutely, chronically, externally or internally. Common causes for **acute blood loss** in horses include trauma to the limbs,

post-castration hemorrhage, rupture of a uterine artery at parturition or erosion of the carotid artery by guttural pouch mycosis (*q.v.*). Hypovolemic shock (*q.v.*), characterized by tachycardia, tachypnea, hypothermia, pale and dry mucous membranes, prolonged capillary refill time, cold extremities and muscle weakness, generally develops when blood volume is reduced by more than 30%. Compensatory mechanisms are triggered immediately in an attempt to maintain circulating blood volume.

The spleen masks the extent of blood loss for several hours post hemorrhage by injection of a concentrated mass of stored erythrocytes into the circulation. Catecholamines induce vasoconstriction and increase cardiac output. Plasma volume is expanded by fluid resorption and retention in the vascular system, which continues at a decreasing rate for up to 72 h. A decline in the TPP can be measured within 4–6 h of the insult, but a reduction of the PCV is usually not appreciated until 12–24 h post hemorrhage.

Diagnosis of acute blood loss is based on history of recent hemorrhage, clinical signs and eventual development of anemia accompanied by hypoproteinemia. Hemothorax or hemoperitoneum (*q.v.*) must be documented by ultrasound examination or paracentesis and cytologic evidence of erythrophagocytosis

Treatment aims for acute blood loss are stopping the source of hemorrhage and maintaining circulatory blood volume. Rapid IV administration of **large volumes** (40–80 mL/kg) of sodium-containing isotonic crystalloid solution is necessary to control **hypovolemic shock** (*q.v.*). Preliminary data in horses suggest that smaller volumes of hypertonic saline (4–5 mL/kg 7.5% sodium chloride) may effectively reduce the pathophysiologic sequelae of experimental hemorrhagic shock; however, clinical studies are necessary to evaluate fully this therapy in horses. Hypertonic saline in the face of ongoing hemorrhage may be contraindicated.

Blood transfusion (*q.v.*) is indicated only when the erythrocyte mass is insufficient to maintain adequate tissue oxygenation. This occurs at a higher PCV if anemia develops rapidly. A PCV ⩽0.20 L/L indicates that all erythrocyte reserves have been depleted; however, blood transfusion is unnecessary if the PCV stabilizes at 0.12–0.15 L/L. Relative renal hypoxia causes erythropoietin production that subsequently stimulates the bone marrow to begin replenishing erythrocytes within 4–6 days. The adult equine diet includes an excess of all necessary nutrients for erythropoiesis. Milk may contain insufficient iron. In general, iron-deficient states are extremely uncommon in horses and usually associated with chronic external blood loss. Anemia due to blood loss generally resolves within 4–12 wk.

Slow **chronic blood loss** allows the bone marrow to regenerate erythrocytes as they are lost. Anemia only develops once the rate of erythropoiesis is exceeded by the rate of hemorrhage. Gradual tissue hypoxia allows physiologic adaptation, thus clinical signs of anemia are generally masked until the PCV drops to ⩽0.15 L/L.

Causes of chronic gastrointestinal blood loss include: parasitism (particularly large strongylosis); gastric or duodenal ulcers; non-steroidal anti-inflammatory drug (NSAID) toxicosis; and neoplasia (particularly gastric squamous cell carcinoma) (*q.v.*). Melena is rare. Because chemical tests for fecal occult blood are not highly specific, diagnosis of chronic gastrointestinal blood

loss should be supported by a high index of clinical suspicion and ruling out other sources of hemorrhage.

Blood loss from the **upper respiratory tract** is usually identified by **epistaxis** (*q.v.*). Guttural pouch mycosis, ethmoidal hematoma, fungal rhinitis and neoplasia (*q.v.*) are the most common causes for upper respiratory tract blood loss. Pulmonary bleeding subsequent to severe pneumonia, lung abscess or neoplasia is often occult and only recognized by finding **hemosiderin-laden macrophages** on cytology of a tracheal aspirate or bronchoalveolar lavage specimen (*q.v.*). Exercise-induced pulmonary hemorrhage does not result in anemia. Urogenital neoplasia or vascular anomalies (*q.v.*) may rarely induce chronic blood loss anemia via hematuria, which may be microscopic.

Blood loss anemia can develop due to **hemostatic dysfunction**. Severe coagulation factor deficiencies such as warfarin toxicosis, hemophilia A and other heritable coagulopathies (*q.v.*) generally induce clinically recognizable hemorrhage into joints or other body cavities. **Acute hemorrhage** may follow trauma or surgery. Thrombocytopenia and/or more complex coagulation disorders such as disseminated intravascular coagulation (DIC) (*q.v.*) may be associated with chronic anemia due to mucosal petechial and ecchymotic hemorrhages, epistaxis and occult blood loss from the bowel and urinary tract.

Treatment of chronic blood loss anemia includes identification and treatment of the primary disease process. Chronic external blood loss may lead to iron deficiency (*q.v.*) especially in foals, which have comparatively low body iron stores.

HEMOLYTIC ANEMIA

Hemolytic anemia is associated with **erythrocyte destruction** that exceeds the rate of normal bone marrow erythropoiesis. Intravascular hemolysis occurs in some disease processes, but hemolytic anemia is usually due to extravascular erythrocyte destruction and shortened intravascular lifespan.

Clinical manifestations of hemolysis vary with the rate of development and severity of anemia, as well as the underlying disease process. Clear hematologic evidence of anemia exists when **icterus** is caused by hemolysis. Acute intravascular hemolysis produces hemoglobinemia and hemoglobinuria, manifested as pink plasma and reddish-brown urine, respectively (*q.v.*). Constant or intermittent fever is not uncommon due to underlying infections or active erythrocyte destruction.

There are numerous causes and mechanisms for hemolytic anemia (Table 9.1), which is regenerative anemia without hypoproteinemia. Intensified erythropoiesis is often associated with neutrophilia and regenerative left shift. Total and indirect bilirubin concentrations may be elevated. Other laboratory findings are determined by the cause of the anemia (Table 9.1). In addition to a CBC, TPP and serum bilirubin, the diagnostic evaluation of suspected hemolytic anemia should include thorough blood smear examination, urinalysis, Coombs test and Coggins test (*q.v.*).

Treatment of hemolytic anemia is aimed at the **primary disease process** whenever possible. Massive hemolysis may warrant transfusion with blood, packed red cells or polymerized hemoglobin (*q.v.*).

Table 9.1 Causes of hemolytic anemia

Causes	Diagnosis
Immune-mediated	
Neonatal isoerythrolysis	Hemolytic cross-match
Equine infectious anemia	Coggins test
Autoimmune hemolytic anemia	Coombs test
Secondary immune-mediated anemia (drugs, infection, neoplasia)	History, signs, Coombs test
Incompatible blood transfusion	History, cross-match
Oxidant-induced	
Phenothiazine toxicosis	History, Heinz bodies on blood smear
Onion toxicosis	History, odor, Heinz bodies on blood smear
Red maple leaf toxicosis	History, methemoglobinemia, Heinz bodies on blood smear
Parasitic	
Babesiosis (equine piroplasmosis)	Complement fixation (CF) test
Microangiopathic	
Disseminated intravascular coagulation	Thrombocytopenia and prolonged prothrombin time and/or activated partial thromboplastin time
Acute hepatic failure?	Liver enzymes, biopsy

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IMMUNE-MEDIATED HEMOLYTIC ANEMIA

Antibodies bound to the surface of erythrocytes result in hemolysis. Erythrocytes coated with immunoglobulins or immune complexes are generally removed from the circulation by tissue-fixed macrophages in the spleen, liver and bone marrow (mononuclear phagocyte system, MPS). **Complement-mediated intravascular hemolysis** may occur if sensitizing antibodies are IgM or complement-activating IgG. Immune-mediated hemolysis may be primary (e.g. neonatal isoerythrolysis, transfusion reactions, *q.v.*) or secondary to infections, drugs or neoplasia.

Neonatal isoerythrolysis

Neonatal isoerythrolysis (NI) (*q.v.*) is a hemolytic syndrome in newborn foals mediated by maternal antibodies against foal erythrocytes (alloantibodies) absorbed from the colostrum. The disease most often affects foals of multiparous dams.

Clinical signs and laboratory findings

Foals with NI are born clinically normal but subsequently develop depression, weakness and a reduced suckle response at 12–72 h. The rate and severity of disease are determined by the quantity and activity of absorbed alloantibodies. Affected foals have tachycardia, tachypnea and dyspnea. The oral mucosae are initially pale, then, in foals that survive 24–48 h, become icteric. Hemoglobinuria is rare. Cerebral hypoxia may induce seizures as a preterminal event. Laboratory findings include anemia and hyperbilirubinemia.

Metabolic acidosis and azotemia eventually develop due to tissue hypoxia and the nephrotoxic effects of hemoglobin.

Etiology and pathology

In development of natural NI, the foal inherits from the sire and expresses an **erythrocyte antigen** (alloantigen) (*q.v.*) that is not possessed by the dam. **Blood group incompatibility** between the foal and dam is common but most alloantigens are weak immunogens under the conditions of exposure through parturition or placental leakage. However, factors Aa of the A system and Qa of the Q system are **highly immunogenic**, and antibodies to these induce approximately 90% cases of NI. Mares that are negative for Aa and/or Qa (approximately 19% and 17% of Thoroughbred and Standardbred mares, respectively) are at greatest risk of producing a foal with NI. There are reports of other inducing antigens, including Ab, Qb, Qrs, Qc, Db, Dq, Dc, Da, Ka, Pa and Ua.

Not all mares become sensitized to the incompatible alloantigen of their foals. This generally requires **transplacental hemorrhage** during a previous pregnancy with a foal possessing the same incompatible blood factor. An **anamnestic response** is usually necessary to induce a pathogenic quantity of alloantibodies. Ten per cent of Thoroughbred mares and 20% of Standardbred mares have "natural" antibodies to the Ca blood group antigen. Data suggest that these "natural" antibodies may suppress an immune response to other alloantigens since Aa-negative mares that have anti-Ca antibodies often do not produce antibodies to Aa of their foal's erythrocytes if the latter also contain Ca antigen. Natural alloantibodies have not been associated with NI in horses.

Alloantibodies of sensitized mares are concentrated in the colostrum during the last month of gestation. The foal is normal at birth, since the mare's complex epitheliochorial placentation does not allow in utero antibody transfer. Thus the final criterion for foal development of NI is **ingestion of colostrum** containing alloantibodies specific for foal alloantigens in the first 24 h of life. Ig-coated foal erythrocytes are rapidly removed from circulation by the MPS or lysed intravascularly via complement. Alloantibodies to Aa are potent hemolysins and generally cause a more severe clinical syndrome than other alloantibodies. Primiparous mares may be predisposed to NI by blood transfusion or other exposure to equine blood products.

Diagnosis

Lethargy, anemia and icterus during the first four days of life suggest the diagnosis of NI. Blood loss anemia is attended by pallor, and icterus due to sepsis or liver dysfunction is not associated with anemia. The definitive diagnosis of NI is based upon **demonstration of alloantibodies** in the dam's serum or colostrum that are directed against foal erythrocytes. The hemolytic crossmatch between washed foal erythrocytes and mare serum with an exogenous source of absorbed complement (usually from rabbits) is the most reliable diagnostic test for NI. A number of qualified laboratories routinely perform this diagnostic service. Because some equine alloantibodies act only as hemolysins, agglutination tests may be falsely negative. The jaundiced foal agglutination (JFA) test between colostrum and EDTA-anticoagulated foal blood is a rapid screen for antired blood cell antibodies. False negatives may occur; however, if positive, this test may be used to determine when the colostrum is safe for the foal to nurse.

Treatment

The dam's milk must be withheld during the first 24 h of life and the foal should be fed from an **alternate milk source**. A minimum volume of milk equivalent to 1% of the foal's body weight should be fed every 2 h (e.g. a 50 kg foal should receive 500 mL of mare milk replacer q 2 h). The dam's udder should be **stripped** regularly (<q 4 h) and the milk discarded. In most instances, NI is not apparent until the foal is >24 h of age when colostral antibodies have been depleted and/or the intestinal absorptive capacity for Ig has diminished. Withholding milk at this point is of minimal benefit.

Supportive care is paramount. Affected foals should not be stressed and exercise must be restricted to a box stall. IV fluids may be indicated to minimize the nephrotoxic effects of hemoglobin as well as to correct any fluid deficits and electrolyte/acid-base imbalances. Antimicrobials may be necessary to prevent secondary infections.

When a foal's PCV drops to ≤0.12 L/L, **blood transfusion** (*q.v.*) is warranted to prevent life-threatening cerebral hypoxia. Severe weakness, tachypnea and tachycardia indicate the need for transfusion, even at higher PCVs. Although erythrocytes from the dam are compatible with the foal, they must be **washed free of plasma** in order to prevent administration of additional harmful alloantibodies. Repeated centrifugation with replacement of plasma by saline is necessary to ensure clean packed RBCs. Since most field conditions do not allow safe utilization of dam erythrocytes, **blood-typed individuals** negative for Aa and Qa and free of alloantibodies are optimal donors.

The odds of finding a donor without Aa and/or Qa are higher in Quarter Horses, Morgans and Standardbreds than in Thoroughbreds and Arabians. If an untested donor must be used, **a gelding** with no prior history of blood transfusion is best. Two to four liters of blood **or** 1–2 L of packed erythrocytes should be given over a 2–4 h period. These allogeneic cells have a very short lifespan and represent a burden to the neonatal MPS that may increase susceptibility to infection. In addition, these cells sensitize the foal to future transfusion reactions. Potential harm must be measured against the benefit in each particular situation.

Recently, bovine polymerized hemoglobin (Oxyglobin) has been used to save foals suffering from severe hypoxemia, prior to identification of an appropriate red cell donor. This ultrapurified hemoglobin improves oxygen-carrying capacity of the blood, but the half-life is likely to be <48 h. The recommended dose is 7.5 mL/kg (3 × 125 mL bags for a 50 kg foal).

Prognosis and prevention

The prognosis for NI in foals depends on the quantity and activity of absorbed antibodies and is indirectly proportional to the rate of onset of signs. Like most diseases, NI is much more effectively prevented than treated. Foals from any mare that previously produced a foal with NI should be provided with an alternate colostral source unless the sire has known blood type compatibility with the dam. Mares at risk of producing affected foals (negative for Aa and Qa alloantigens) may be identified by **blood typing** (*q.v.*). Stallions negative for Aa/Qa and suitable on the basis of other criteria may be difficult to identify. It is most reasonable to breed "at-risk" mares as desired then to screen their

serum in **the last month of pregnancy** for the presence of alloantibodies. If alloantibodies (other than those to Ca) are detected, dam colostrum should be withheld and the foal provided with an alternative colostral source. The JFA test has been used to determine when it is safe for the foal to nurse.

Autoimmune hemolytic anemia

Autoimmune hemolytic anemia (AIHA) (*q.v.*) occurs when an individual forms antibodies that bind to its own erythrocytes. **Primary AIHA** is an idiopathic process wherein there is failure to recognize erythrocytes as self. AIHA may arise secondary to infections, drugs or neoplasia and is then referred to as **immune-mediated hemolytic disease**. Both types result in MPS destruction of erythrocytes with or without intravascular hemolysis. AIHA is uncommon in horses but can affect any age, sex or breed.

Clinical signs and laboratory findings

Affected horses have variably severe depression and/or exercise intolerance. Tachypnea and tachycardia are generally present and worsen with exercise. Fever depends on the severity of hemolysis as well as any concomitant disease. Mucous membranes may be moderately icteric. Pigmenturia is uncommon.

Rarely in AIHA, erythrocytes in a blood sample grossly agglutinate. Immune-mediated erythrocyte aggregation persists when the anticoagulated blood is diluted 1:2 in isotonic saline, whereas false autoagglutination due to severe inflammatory disease is easily dispersed. Since equine erythrocytes are small, spherocytosis is rare. Neutrophilic leukocytosis is common subsequent to bone marrow regeneration. **Intravascular hemolysis** causes pink plasma, increased MCH and pigmenturia. **Indirect hyperbilirubinemia** is common.

Etiology and pathogenesis

True autoimmunity results when B lymphocyte cell clones become abnormally reactive and fail to recognize "self". Dysfunction of T suppressor cells or increased activity of helper T cells may have a role. **Secondary AIHA** is often caused by immune complexes that bind to erythrocyte membranes and mediate extravascular hemolysis. In other situations the erythrocyte membrane is altered by the primary disease process and is then no longer recognized as "self". Finally, antigenic stimulation of the immune system may result in antibodies that cross-react with normal erythrocytes. Secondary AIHA has been described in horses with equine infectious anemia (EIA), *Clostridium perfringens* infection, injection site abscesses, lymphosarcoma, other internal neoplasia, protein-losing enteropathy, purpura hemorrhagica, and penicillin therapy (*q.v.*).

Diagnosis

Definitive diagnosis of AIHA is based upon demonstration of patient antibodies that react with their erythrocytes. Autoagglutination is diagnostic of AIHA provided false agglutination is excluded. If true autoagglutination is not evident, diagnosis is most accurately made by agglutination in a **direct antiglobulin (Coombs) test** (*q.v.*), performed by incubating washed patient

erythrocytes with appropriate dilutions of antiserum to equine IgG, IgM and complement components. A false negative Coombs test may occur immediately following a hemolytic crisis, or when corticosteroid therapy has been initiated. The **osmotic fragility test** should not be used for definitive diagnosis of AIHA, since positive results occur during other diseases that compromise erythrocyte membrane function (e.g. oxidative insult).

Horses with AIHA should have a thorough diagnostic work-up in search of neoplasia and a Coggins test for EIA (*q.v.*).

Treatment

Any current medication should be immediately discontinued in an attempt to exclude the possibility of **drug-associated AIHA**. Necessary antimicrobials are replaced by the most chemically dissimilar substitute (e.g. do not replace penicillin with ampicillin). Horses with severe AIHA require **corticosteroid therapy**. All beneficial actions of corticosteroids are unknown, but they will reduce erythrocyte clearance by the MPS and impair autoantibody production. **Dexamethasone** (0.05–0.2 mg/kg, IV or IM once daily) seems to be most effective for initial therapy of equine AIHA. If the PCV does not stabilize within 24–48 h, the dose rate of dexamethasone should be increased to twice daily. The full effect of corticosteroid therapy often requires 4–7 days and blood transfusion may be necessary in the interim. Corticosteroids may worsen a primary infectious process and cause recrudescence of viremia in horses with chronic EIA.

Once the PCV stabilizes at >0.20 L/L, the dose of dexamethasone can be decreased 10% every 24–48 h while carefully monitoring for relapse. When the dose of necessary dexamethasone is ≤0.04 mg/kg daily, therapy can safely be given orally. Corticosteroids should be tapered as soon as possible to the lowest necessary dose and given on alternate days for 1 wk before discontinuation. Dexamethasone can be discontinued when the PCV remains stable during therapy with 0.01 mg/kg q 24–48 h. Prednisolone or prednisone can be used in lieu of dexamethasone (approximately seven times greater dose given q 12 h); however, these are erratically absorbed after oral administration.

Horses that fail to respond to corticosteroids may be treated concomitantly with oral **azathioprine** at a dose of 2 mg/kg/day. Positive results are anecdotal. Blood transfusions are avoided unless absolutely necessary, since the transfused cells are often rapidly lysed by circulating antibodies. When anemia is life threatening, Oxyglobin therapy may be preferable (*q.v.*).

Prognosis and prevention

Some cases of AIHA require treatment for several weeks then recover; horses that require constant corticosteroid therapy are often found to have incurable underlying disease (e.g. lymphosarcoma, *q.v.*).

Equine infectious anemia

Equine infectious anemia (EIA) (*q.v.*) is a multisystemic retroviral disease of Equidae, characterized by **immune-mediated hemolytic anemia**. Horses of all types are affected, but the disease is most prevalent in the southeastern

USA. Because of its importance, EIA will be briefly considered separately from other causes of AIHA.

Clinical signs and laboratory findings

Three forms of clinical disease have been described: acute, subacute to chronic, and chronic inapparent. Clinical signs of acute EIA occur 7–30 days after first exposure to the virus and include fever, depression, anorexia and mucosal petechial hemorrhages. Anemia is not seen at this stage. Horses that have been infected for more than 30 days show the more classic clinical signs of EIA, which include anemia, icterus, edema of the limbs and ventral abdomen, intermittent fever spikes and weight loss. Less common clinical signs are colic, ataxia, abortion and infertility. Deaths usually occur during this subacute to chronic form of the disease.

Most horses recover, but experience **unpredictable periodic flare-ups** of clinical disease. Severe environmental or management stresses and treatment with corticosteroids are known to **induce recrudescence** of EIA. A large number of EIA-infected horses do not show clinical signs. Although only detected by serology, these animals remain **virus carriers** and are a potential source of infection for other horses.

During acute EIA, **thrombocytopenia** is the first and most consistent laboratory finding. **Leukopenia** is often present with mild lymphocytosis and monocytosis. During the subacute to chronic stages of disease, the PCV and RBC count are reduced, with other laboratory indications of hemolysis. The Coombs test is often positive. Hypergammaglobulinemia, increased liver enzymes and proteinuria may develop. Chronic inapparent carriers and chronically infected horses between clinical flare-ups are hematologically normal.

Etiology and pathogenesis

The causative agent of EIA is a high molecular weight, non-oncogenic lentivirus of the retrovirus family. There is wide genetic variation of the antigenic properties of the viral envelope and there is drift, which interferes with development of protective immunity. Viremia is maintained persistently in infected horses, despite a detectable immune response.

The EIA virus is usually transmitted by **blood** from affected horses, although other body secretions could serve as source of infection. **Natural transmission** occurs through the interrupted feeding of horse flies (*Tabanus* spp.) and deer flies (*Chrysops* spp.). Horses showing clinical signs of EIA have a higher viremia and are much more likely to transmit disease than are inapparent carriers. In utero transmission of the EIA virus is possible.

The EIA virus multiplies in macrophages throughout the body and elaborates viral proteins that stimulate humoral and cell-mediated immune responses. Acute disease is associated with **massive virus replication** and destruction of macrophages. The incubation period before clinical signs is usually 1–3 wk, but may be as long as 3 mo. A detectable serologic response is generally attained 2–6 wk after infection and positive serology persists indefinitely.

Signs of subacute-chronic EIA result from virus-induced immunologically mediated tissue damage. Immune complex attachment to erythrocytes via the viral hemagglutinin produces hemolysis. Resultant anemia is worsened by

decreased bone marrow erythropoiesis. Periodic disease flare-ups are due to the immune response to viral antigenic drift.

Diagnosis

The **Coggins test** (*q.v.*), an agar gel immunodiffusion procedure that detects serum antibodies against the EIA virus, is the "gold standard" for confirmation of the disease. Newer ELISA based assays are more sensitive, but have lower specificity. The Coggins test may be falsely negative during acute EIA and false positives occur in foals that have absorbed colostrum from infected dams. Both drawbacks can be overcome by repeated testing.

Treatment

No treatment eliminates EIA virus from the body. **Supportive care** may aid clinical recovery; however, the horse is subject to other clinical episodes of EIA and remains a source of infection.

Prognosis

The prognosis for cure of EIA is poor. Even a horse with inapparent EIA may eventually develop the subacute form. Due to its potential to infect other horses, any horse with a positive Coggins test should be humanely destroyed, unless it can be strictly separated from all other Equidae. Before new horses are introduced to a herd, they should be seronegative for EIA on two tests, separated by 30 days.

OXIDANT-INDUCED HEMOLYTIC ANEMIA

The ingestion of some oxidizing agents causes hemoglobin denaturation by disulfide bond formation between sulfhydryl groups. **Oxidized hemoglobin** subsequently precipitates onto erythrocyte membranes as small aggregates termed **Heinz bodies**. Erythrocytes containing Heinz bodies are more prone to osmotic lysis and are readily removed by the MPS. Certain oxidants transform hemoglobin iron from the ferrous to the ferric state (methemoglobin), which does not transport oxygen. The administration of **phenothiazine** and the ingestion of **onions** or **wilted red maple leaves** have been associated with Heinz body hemolytic anemia (HBHA) in horses. There is generally a history of relevant exposure.

Clinical signs and laboratory findings

Clinical signs of depression, weakness, anorexia, tachycardia and tachypnea are typical. Affected horses are generally icteric. Red maple leaf toxicosis causes brownish discoloration of mucous membranes due to methemoglobinemia. Oliguria and pigmenturia (*q.v.*) are common.

In addition to the reduced PCV and RBC count, hematology often shows increased MCH due to hemoglobinemia. Heinz bodies may appear in blood smears as pale bleb-like projections from erythrocyte membranes; however, they are best visualized with **new methylene blue** stain. Urine is usually positive for blood and protein, plasma creatinine is often elevated and there is

indirect hyperbilirubinemia. Horses with red maple leaf toxicosis may also have brownish discoloration of blood and urine by methemoglobin.

Etiology and pathogenesis

An oxidant metabolite of **phenothiazine** (phenothiazine disulfide) causes HBHA in horses given toxic doses and those with an idiosyncratic sensitivity to the drug. Phenothiazine toxicosis is very uncommon due to its low rate of current usage, however horses with access to ruminant supplements or salt-blocks that contain phenothiazine are at risk. Wild or domestic **onions**, which contain the oxidant allyl propyl disulfide, can cause HBHA but the amount of onions required is rarely voluntarily ingested by horses. Diagnosis is based on the distinct onion odor of breath, urine and feces.

The most common cause of HBHA in horses is **red maple leaf toxicosis**. Horses in the eastern USA grazing areas inhabited by red maple trees (*Acer rubrum*) during the summer and autumn are affected. The syndrome can be reproduced by administration of dried, but not viable, red maple leaves. Affected horses develop marked methemoglobinemia in addition to other signs of acute hemolytic anemia. **Neurologic signs** due to CNS hypoxia and death are common.

Exogenous oxidants produce disease by overwhelming the natural erythrocyte reducing system that protects hemoglobin from the oxygen it carries. Intraerythrocytic reductive capacity is relatively poor in horses. It is not clear why an oxidant will induce HBHA, methemoglobinemia or both. Both oxidative insults are additive in terms of reduced oxygenation of the tissues, and clinical signs of red maple toxicosis are typically more severe than would be suggested by the erythron data. Hemoglobinuria subsequent to IV hemolysis may cause acute renal failure, due to pigment-induced hemodynamic renal ischemia. Associated **renal pathology** may be the limiting factor for recovery in some cases of HBHA.

Diagnosis

The diagnosis of HBHA is based upon history of oxidant exposure, typical clinical signs and the presence of Heinz bodies in the peripheral blood. Heinz bodies are most easily identified on a wet-mount blood film, prepared by mixing one drop of new methylene blue stain with one drop of blood on a glass slide, topped with a cover slip. Heinz bodies appear as bluish-green, refractile granules located near the red cell margin. Chocolate-brown and brownish mucous membranes strongly suggest red maple leaf toxicosis.

Treatment

The horse should be removed from access to the oxidant and housed to minimize stress and exercise. Mineral oil and activated charcoal via nasogastric tube may be helpful if an acute case is identified. The PCV and clinical signs must be monitored closely for development of life-threatening anemia. IV therapy with **isotonic balanced crystalloid solutions** (80–100 mL/kg/24 h) is paramount to ensure hydration and minimize pigment nephrosis. Methylene blue or other reductive therapy is relatively ineffective in horses and may even enhance Heinz body formation. Purified bovine hemoglobin (Oxyglobin) may provide temporary oxygenation of the blood in an acute hemolytic crisis.

Prognosis is determined by the amount of oxidant ingested and its innate activity. Red maple leaf toxicosis carries a poor prognosis, especially when methemoglobinuria is present. Prevention is based on limiting access.

PARASITE-INDUCED HEMOLYTIC ANEMIA

Babesiosis (equine **piroplasmosis** *q.v.*) is the only intra-erythrocytic parasitic disease of horses. It is widely distributed throughout tropical and subtropical areas and to a lesser extent in temperate regions, corresponding to the habitat of natural tick vectors. Affected horses generally have recently traveled to endemic areas, which include parts of Florida, Texas, Mexico, Cuba, Central and South America, and eastern and southern Europe, Asia, Africa, the Middle East and Russia.

Clinical signs and laboratory findings

Clinical disease generally develops 5–28 days after susceptible horses are placed in an endemic area. Signs include fever, depression, anorexia, weakness, ataxia, labored breathing, chemosis, mucosal petechial hemorrhages, icterus and hemoglobinuria. Death may occur within 48 h or intermittent fever and anemia may persist for months. Horses raised in endemic areas often carry *Babesia* without showing signs.

Laboratory data are consistent with hemolytic anemia. Parasitized erythrocytes may be seen on **blood smears** during the **febrile period** but are often absent in the hemolytic crisis. *Babesia* appear as pyriform bodies in groups of two to four with their pointed ends meeting at an acute angle. Intravascular hemolysis and pigment nephropathy may ensue.

Etiology and pathogenesis

Horses are susceptible to infection with the protozoa *Babesia caballi* and *B. equi* (phylum Apicom). Only *B. caballi* is diagnosed in the USA. Natural transmission of *Babesia* spp. occurs via **ticks**, although they may be transmitted mechanically. *Dermacentor nitens*, a tick permanently established in areas where the temperature remains above 16°C (60°F), is the primary vector for *B. caballi*, which can be passed transovarily through tick generations. *B. equi* is only transmitted horizontally (trans-stadially) by species of *Dermacentor, Hyalomma* and *Rhipicephalus*. Intrauterine infection can occur.

Babesia spp. multiply and develop within **host erythrocytes**. Most parasitized erythrocytes are removed via the MPS; however, IV hemolysis can occur. Clinical disease associated with *B. equi* infection is much **more severe** than that caused by *B. caballi* and the mortality rate is higher. Horses that survive clinical babesiosis remain **inapparent carriers** unless treated. Foals born in endemic areas are believed to experience subclinical infection as maternal immunity is waning and develop strong active immunity dependent upon the constant presence of the organism (**premunition**). **Stress**, such as transportation or competition, can induce clinical disease in carrier horses.

Diagnosis

Definitive diagnosis of babesiosis relies upon blood smear demonstration of parasitized erythrocytes or positive serology. However, since brief parasitemia

precedes hemolysis, **diagnosis is best made serologically**. Antibodies to *Babesia* spp. are detectable within 14 days of infection. **The indirect fluorescent antibody test** can differentiate between *B. equi* and *B. caballi*. **Polymerase chain reaction (PCR) tests** are available in some areas, but not totally validated. Appropriate authorities should be contacted prior to collection of samples for diagnosis. Samples must be sent under secure conditions to authorized labs, since *B. equi* has been implicated in human disease.

Treatment

Imidocarb dipropionate depresses parasitemia and usually eradicates *B. caballi* infection (2.2 mg/kg q 24 h × 2). *B. equi* is much more resistant, and imidocarb therapy (4 mg/kg q 72 h × 4) is only 50–60% effective in eliminating infection, particularly of eastern European origin. Imidocarb is a toxic drug and should be used with care. It may cause colic, hypersalivation, diarrhea and/or death. Donkeys often die if given high-dose imidocarb. Supportive care should include rest, IV fluids and NSAIDs. Ketoconazole and clotrimazole have in vitro activity against *Babesia* and may have future therapeutic value.

Prognosis

The prognosis for *B. caballi* infection is fair to good with imidocarb treatment. Prognosis for *B. equi* infection is variable. Disease transmission can be minimized by tick control and sanitary veterinary practices. Identified carrier horses in non-endemic areas should be quarantined until they are effectively treated.

MICROANGIOPATHIC HEMOLYSIS

Thrombosis and/or fibrinoid change within the lumen of small blood vessels can cause damage and lysis of erythrocytes. This microangiopathic hemolytic disease is a characteristic of chronic **disseminated intravascular coagulation** (DIC) and has been reported in horses. Usually hemolysis is mild and any anemia is due to blood loss.

Fulminant intravascular hemolysis has been reported in horses with **terminal liver failure** and DIC. Pathogenic alterations in red cell membrane lipoproteins and metabolism have been suggested in the pathogenesis.

ANEMIA DUE TO INADEQUATE ERYTHROPOIESIS

When the rate of erythropoiesis is inadequate to replenish aged erythrocytes, anemia ensues. This non-regenerative anemia can be caused by:

1. Deficiency of substances essential for erythrocyte production
2. Diseases that interfere with erythropoiesis
3. Conditions that damage normal bone marrow elements.

Anemia solely due to inadequate erythropoiesis develops slowly because equine erythrocytes have a long lifespan. Depressed erythropoiesis associated with blood loss or hemolysis produces a life-threatening anemia. Definitive classification of anemia as non-regenerative requires **bone marrow evaluation** (*q.v.*).

Iron deficiency anemia

Iron deficiency anemia is extremely rare in horses and only develops when the rate of iron loss from the body exceeds the absorption of iron from the diet. Milk is particularly low, while soil and legumes are high in iron. Iron deficiency is usually associated with chronic external blood loss.

Clinical signs and laboratory findings

Clinical signs of iron deficiency do not differ from those of chronic blood loss. Serum iron and percentage saturation of transferrin decrease while the total iron binding capacity increases. Hypoproteinemia is common. Iron deficiency eventually induces **microcytic hypochromic anemia**.

Etiology and pathogenesis

Ulcerative gastrointestinal lesions, such as those induced by NSAID toxicosis and neoplasia (*q.v.*), result in chronic external blood loss. Iron deficiency anemia is particularly prevalent in horses with **gastric squamous cell carcinoma** (*q.v.*). Iron deficiency results in an erythrocyte maturation arrest in the bone marrow. Late rubricytes awaiting hemoglobin synthesis may undergo cell division, but they produce erythrocytes that are smaller than normal and deficient in hemoglobin with a shortened lifespan.

Diagnosis

Serum concentrations of **ferritin**, an intracellular iron storage protein, <45 ng/mL are suggestive of iron deficiency in horses. The presence of bone marrow iron specifically eliminates iron deficiency as the cause for anemia.

Treatment

Therapy should be aimed at identification and correction of the primary disease. Parenteral iron solutions can cause **anaphylactoid reactions** (*q.v.*), thus only oral iron supplementation is safe.

Prognosis

The prognosis depends upon the cause of chronic blood loss. Iron deficiency anemia is reversible.

Anemia of inflammatory disease

Anemia of inflammatory disease (AID) is the **most common anemia** in horses. Clinical signs are usually ascribed to the primary disease process. Hematology reveals a mild non-responsive anemia (PCV 0.23–0.20 L/L) with neutrophilic leukocytosis, hyperfibrinogenemia and/or hypergammaglobulinemia. Serum iron is usually decreased and serum ferritin is increased.

Pneumonia, pleuritis, peritonitis, internal abscesses and neoplasia (*q.v.*) are the most common underlying disorders. The AID develops because the **bone marrow** fails to compensate for a modest decrease in circulating erythrocyte

lifespan. Impaired erythropoiesis is due to altered iron metabolism and sequestration by cells of the MPS. Interleukin 1, tumor necrosis factor and other cytokines released in the "acute phase" response to infection may have a role in inhibition of erythropoiesis.

The presence of **non-responsive anemia** in the face of clinical and laboratory evidence of chronic disease is generally suggestive of AID. Therapeutic efforts should be aimed at the **underlying disease**, which determines prognosis.

Anemia associated with renal disease

A defective marrow response to erythropoietin in combination with reduced erythrocyte longevity accounts for the anemia of renal disease. Therapy must be aimed at the renal disease (*q.v.*); prognosis is poor.

Myelophthisic anemia

Myelophthisic anemia is due to destruction of the normal marrow habitat by neoplastic or inflammatory tissue. The net result is **pancytopenia**. Because of the shorter half-life of granulocytes and platelets, bleeding and infections generally precede anemia, which is exemplified by lethargy, anorexia and mucosal pallor. Hematology reveals severe neutropenia and thrombocytopenia in addition to non-responsive anemia.

Myelophthisic anemia has been described in horses with several types of **myeloid neoplasia** (*q.v.*), wherein a marrow-derived blood cell proliferates at the expense of all others. Myelophthisic disease could also result from metastasis of neoplasia to the bone marrow, although this is exceedingly rare in horses. Diagnosis is confirmed by documenting the proliferation of atypical cells by **bone marrow examination**. Occasionally, abnormal cells are found in the peripheral blood. Blood transfusions are only palliative and hematopoietic neoplasia is considered fatal in horses.

Bone marrow aplasia

Bone marrow aplasia (**aplastic anemia**) is caused by failure of stem cells to differentiate because of intrinsic damage or due to interruption of their interactions with supporting cells that constitute the microenvironment. The net result is marrow hypoplasia associated with pancytopenia. Aplastic anemia is very uncommon in horses and generally is an acquired disorder. Rare cases have been associated with phenylbutazone.

Clinical signs and laboratory findings

The clinical features of aplastic anemia are similar to those accompanying myelophthisic disease. **Hemorrhagic diathesis** secondary to thrombocytopenia (e.g. epistaxis, mucosal petechial hemorrhages, or prolonged hemorrhage following injections) is often the first indication of disease. Neutropenia causes increased susceptibility to infections and intermittent fever, weight loss and exercise intolerance ensue. Neutropenia, monocytopenia and

thrombocytopenia occur first, followed by severe anemia. Blood loss often hastens the development of anemia and some cases may have a positive Coombs test. **Absolute lymphopenia** is not uncommon.

Etiology and pathogenesis

The cause for marrow aplasia cannot be proven in most instances. A diverse array of chemicals, drugs, ionizing radiation, viral infections, bacterial toxins and immune-mediated diseases have been implicated. Regardless of the exact cause, pluripotent stem cells (*q.v.*) fail to differentiate in aplastic anemia. Immunologic rejection of stem cells probably plays a role.

Diagnosis

The diagnosis of aplastic anemia is based upon **peripheral pancytopenia** and **fatty bone marrow** with essentially empty stroma. Because sternal bone marrow aspirates are frequently contaminated by peripheral blood, a **core marrow biopsy** (*q.v.*) from the rib or ileal wing should be examined histologically. Benign lymphoid nodules may create confusion with lymphosarcoma (*q.v.*). Biopsies from at least two sites are necessary to substantiate definitively marrow failure.

Treatment

Treatment includes removing the horse from any possible causative drugs, chemicals or environmental toxins and providing supportive care until spontaneous remission occurs. Early, **intense broad-spectrum antimicrobial therapy** should be instituted.

Immunosuppressive drugs or myelostimulatory androgens have produced discouraging results in humans with marrow aplasia and are largely unproven in horses. The treatment of choice for human aplastic anemia is bone marrow transplantation, which is an unlikely treatment option in horses. Blood or platelet transfusions only provide temporary relief. Use of human erythropoietin may ultimately cause red cell aplasia in horses, since it causes the production of antibodies that cross-react with the equine erythropoietin.

Prognosis

Too few horses with aplastic anemia have been studied to give a clear indication of prognosis.

ERYTHROCYTOSIS (POLYCYTHEMIA)

Erythrocytosis is defined as an elevation of PCV and RBC count above those considered normal. Relative erythrocytosis is common in horses, whereas absolute erythrocytosis is exceptionally rare.

Relative erythrocytosis describes a relative increase in the PCV and RBC count, and is usually due to a reduction in plasma volume (**dehydration**). Relative erythrocytosis also accompanies splenic contraction, which induces a

red cell mass at the upper end of normal, combined with a low normal plasma volume. Clinical evidence of dehydration such as **tacky mucous membranes** and **reduced skin pliability** suggests dehydration (*q.v.*). Endotoxemia or other forms of shock (*q.v.*) may be manifested by tachycardia, cool extremities and mucosal congestion or pallor.

Relative erythrocytosis is definitely diagnosed by resolution of the condition following **IV fluid replacement**. Therapy is aimed at fluid administration necessary to maintain hydration and treatment of the primary disease process.

Absolute erythrocytosis refers to an increased circulating RBC mass without change in plasma volume. Irrespective of etiology, absolute erythrocytosis causes a number of clinical manifestations due to expanded blood volume and increased blood viscosity. These include **"muddy" hyperemia of mucous membranes**, lethargy and weight loss subsequent to decreased cardiac output, hemorrhagic diathesis and/or an increase in thrombotic complications.

PRIMARY ERYTHROCYTOSIS

Autonomous proliferation of erythroid progenitors rarely occurs. This may be a single cell disorder or a component of **polycythemia vera** (*q.v.*), in which there is also abnormal proliferation of myeloid cells and megakaryocytes. The diagnosis of primary erythrocytosis is based on demonstration of increased erythrocyte mass without excessive erythropoietin (Ep) production. Affected patients have erythrocytosis that is not responsive to IV fluid therapy.

Therapy of primary erythrocytosis includes **phlebotomy** to keep the PCV $\leqslant$0.50 L/L. **Hydroxyurea** causes reversible bone marrow suppression and has been used successfully in people and dogs with primary erythrocytosis but there is no experience with its use in horses. Prognosis for cure is poor.

SECONDARY ERYTHROCYTOSIS

Increased concentrations of Ep or erythropoietin-like compounds result in secondary erythrocytosis.

Physiologically appropriate erythrocytosis, the most common form of absolute erythrocytosis, is due to **chronic tissue hypoxia**. Residence at **high altitude** (above 2200 m) and some **congenital heart defects** cause a compensatory increase in plasma Ep in horses. Diminished atmospheric oxygen tension produces an inadequate driving force for tissue oxygenation and horses may develop an increased erythrocyte mass. Congenital cardiac disorders, such as **tetralogy of Fallot** (*q.v.*), that produce right to left shunting of blood away from the lungs cause absolute erythrocytosis.

Physiologically appropriate erythrocytosis can be diagnosed by documenting low arterial pO_2. Oxygen delivery is impaired when the PCV >0.60 L/L and at this point phlebotomy (*q.v.*) is indicated. The optimal PCV for patients residing at high altitudes or those with right to left cardiac shunts can only be determined by trial and error.

Physiologically inappropriate erythrocytosis is due to the autonomous elaboration of Ep. Neoplasia of the liver or kidney and non-malignant renal disorders (*q.v.*) may induce Ep production. Erythrocytosis may rarely accompany chronic hepatic disease in horses.

ALTERATIONS IN WHITE BLOOD CELL NUMBERS

Leukocytosis or leukopenia in horses is almost always subsequent to changes in the total neutrophil count. Leukocytosis may be attributed to pathologic or physiologic causes, but **leukopenia is always considered pathologic**.

NEUTROPHILIA

Neutrophilia often occurs with a normal WBC count. **Physiologic neutrophilia** accompanies exercise, excitation, transport or other stress that induces catecholamine or corticosteroid release, which causes temporary mobilization of the marginal neutrophil pool. Catecholamines also induce lymphocytosis while corticosteroids cause lymphopenia. The circulating cells are mature, with normal morphology, and there is no other hematologic evidence of inflammation.

Pathologic neutrophilia results from inflammatory disease, and bacterial infection is the most common cause. Acutely after infection, there may be an increased number of immature neutrophils (usually bands) in the blood, which is termed a "**left shift**". Neutrophilia is most common as a bacterial infection is being localized, especially in concert with abscess formation (*q.v.*). **Rebound neutrophilia** often follows endotoxin-induced neutropenia (*q.v.*) and is generally a good prognostic sign. Once an infection is localized or chronic, left shift is rare, and horses often show only mild, mature neutrophilia with normal total WBC count. Less common causes for pathologic neutrophilia include tissue destruction by neoplasia, severe injury or surgery, parasitic or mycotic infections and autoimmune diseases (*q.v.*). An increased number of circulating abnormal neutrophils is a feature of granulocytic leukemia (Box 9.1).

Neutrophil morphology can help determine the cause for neutrophilia (or neutropenia) or indicate disease in a horse with a normal leukocyte count. Bacterial infections, particularly those caused by Gram-negative organisms, result in cytoplasmic and nuclear alterations in developing neutrophils. These "toxic changes" are reflected in the peripheral blood by neutrophil cytoplasmic basophilia, foaminess, vacuolation, purple "toxic" granules and bluish **Dohle bodies**. Rarely, bizarre giant forms occur. Inflammation subsequent to other

Box 9.1 Differential diagnosis for neutrophilia

- Excitement/exercise
- Stress/corticosteroid therapy
- Strangles (*Streptococcus equi* infection)
- Chronic pneumonia/pleuritis
- Chronic peritonitis/abdominal abscess
- Other internal abscessation
- Chronic salmonellosis or other colitis
- Cellulitis
- Thrombophlebitis
- Purpura hemorrhagica or other vasculitis
- Bacterial endocarditis
- Cholelithiasis
- Pyelonephritis
- Severe parasitism
- Lymphosarcoma or other internal neoplasia
- Pituitary adenoma (Cushing's disease)
- Systemic fungal infection
- Autoimmune hemolytic anemia
- Granulocytic leukemia

insults is not associated with neutrophil "toxic" changes. The neutrophils in granulocytic leukemia show cytologic criteria for neoplasia.

NEUTROPENIA

As opposed to neutrophilia, **neutropenia is always pathologic** and reflects underlying disease. The most common cause for neutropenia in horses is endotoxemia (*q.v.*). This may accompany Gram-negative bacterial infections, which are particularly prominent in neonates, or gastrointestinal disorders, especially colitis (*q.v.*).

Endotoxin acutely causes neutrophils to marginate along the walls of small capillaries, particularly in the lung. For neutrophil numbers to return to normal, at least partial resolution of endotoxemia and release of new neutrophils from the bone marrow are required. Left shift is very common during acute sepsis/endotoxemia. If the numbers of immature neutrophils in the blood exceed the number of mature neutrophils, the left shift is said to be **degenerative**. This is a poor prognostic sign that indicates the presence of overwhelming endotoxemia and/or depletion of bone marrow neutrophil reserves. Endotoxemia results in neutrophil toxic changes, the degree of which reflects the severity of endotoxemia.

Viral diseases and **anaphylaxis** (*q.v.*) may also cause neutropenia (Box 9.2). Rarely, neutropenia is due to a reduction in bone marrow precursors, subsequent to myelophthisic disease or aplastic anemia (*q.v.*).

LYMPHOCYTOSIS

Physiologic leukocytosis due to catecholamine release during excitement or exercise causes lymphocytosis as well as neutrophilia in young horses. Lymphocytosis is uncommon in horses >2 yr old, but may rarely accompany chronic viral infections or autoimmune disease. Lymphocytic leukemia is very rare in horses.

LYMPHOPENIA

Lymphopenia accompanies any pathologic state that induces endogenous glucocorticoid release and the **exogenous administration of corticosteroids**.

Box 9.2 Differential diagnosis for neutropenia

- Acute salmonellosis
- Acute toxic colitis
- Acute peritonitis
- Gram-negative septicemia
- Neonatal septicemia
- Duodenitis/proximal jejunitis
- Acute pleuropneumonia
- Acute metritis
- Equine ehrlichial colitis (Potomac horse fever)
- Equine ehrlichiosis (*Ehrlichia equi*)
- Anaphylaxis
- Equine influenza
- Rhinopneumonitis
- Myelophthisic disease (myeloid neoplasia)
- Aplastic anemia

Causes of lymphopenia include acute viral infection, endotoxemia, severe bacterial infection, septicemia, immunodeficiency and malnutrition (*q.v.*). Persistent lymphopenia indicates a poor prognosis.

EOSINOPHILIA

Eosinophilia is uncommon in horses. Although it is usually caused by tissue **parasite migration** (*q.v.*) or **allergy** (*q.v.*), the latter cannot be excluded by absence of eosinophilia. Systemic neoplasia and chronic granulomatous disease processes have rarely been associated with eosinophilia. A multisystemic eosinophilic syndrome has been described in horses, characterized by weight loss, diarrhea and rare respiratory signs. The cause is unknown and long-term prognosis is poor.

HEMATOPOIETIC NEOPLASIA

The most common internal malignant neoplasia of horses is lymphosarcoma (*q.v.*). Although the disease arises from the hematopoietic system, peripheral blood evidence of equine lymphosarcoma is exceedingly rare. Other forms of hematopoietic neoplasia are uncommon in horses.

LYMPHOSARCOMA

Four anatomic forms of lymphosarcoma have been described in horses (generalized, intestinal, mediastinal, cutaneous), however the forms substantially overlap clinically and pathologically. Lymphosarcoma has been documented in horses of both sexes ranging from birth to 25 yr old, but most affected are 5–10 yr old. Lymphosarcoma is reported in 2–5% of horses that are necropsied.

Clinical signs and laboratory findings

Clinical manifestations are highly variable depending upon organ involvement and duration of disease. The most common clinical signs of lymphosarcoma are chronic weight loss, ventral edema and regional lymphadenopathy. Peripheral lymphadenopathy is not consistently present. Thoracic cavity involvement may cause tachypnea, dyspnea, coughing and pleural effusion. In addition to weight loss, intestinal lymphosarcoma may cause colic or diarrhea. Subcutaneous lymphosarcoma nodules have been reported in horses, with or without internal organ involvement. Localized tumors may result in dysphagia, nasal discharge, chemosis, ataxia and jugular venous distension. Splenic enlargement, internal lymphadenopathy or abdominal masses may be rectally palpated. Signs may occur acutely and intermittent fever is not uncommon.

Laboratory findings are highly variable. **Non-regenerative anemia** (*q.v.*) and **hyperfibrinogenemia** are common. Lymphocytic leukemia with peripheral lymphocytosis is rare, but **atypical neoplastic lymphocytes** may be found in the peripheral blood in approximately 30% of cases. The total plasma protein varies, but the albumin–globulin ratio is often reduced. Polyclonal gammopathy is common, and monoclonal gammopathy associated with serum hyperviscosity and a hemorrhagic diathesis has been described.

Coombs positive immune-mediated hemolytic anemia and/or thrombocytopenia may occur. Hypercalcemia is rare in association with pseudohyperparathyroidism.

Etiology and pathogenesis

Clinical signs and laboratory changes are generally due to infiltration and loss of normal organ function, physical obstruction by tumor masses, and/or excessive generation of tumor cell products. Some neoplastic lymphocytes are of T cell lineage and may have immunosuppressive effects. Other neoplastic lymphocytes arise from auto-reactive B cell clones and produce antibodies responsible for gammopathies and/or immune-mediated cytopenias. Neoplastic proliferation of natural killer cells was described in one case. Extensive intestinal infiltration produces malabsorption, which contributes to hypoalbuminemia and weight loss.

Diagnosis

Lymphosarcoma is diagnosed by demonstration of **neoplastic lymphocytes** in affected tissue. Histologic examination of a tumor mass or affected lymph node is the most reliable method, and **excisional biopsies** (*q.v.*) are optimal. Unless tissues are accessible for biopsy, ante mortem diagnosis is difficult. Definitive diagnosis is only rarely possible on a peripheral blood smear, but may be made by cytologic evaluation of bone marrow, pleural effusion or peritoneal fluid. Radiography and/or ultrasonography may be useful to locate, and perhaps enable biopsies of, masses in the thorax or abdomen. Often, lymphosarcoma must be diagnosed by laparotomy or post mortem examination.

Neoplastic lymphocytes usually appear as large lymphoid cells with a variable nuclear–cytoplasmic ratio, multiple nucleoli, nuclear chromatin clumping, cytoplasmic basophilia and vacuolation. Mitotic figures and/or binucleate cells may be seen. The cytologic diagnosis of lymphosarcoma requires experience, since normal "reactive" lymphocytes and mesothelial cells resemble well-differentiated neoplastic cells. **Histologic destruction** of normal tissue architecture by lymphoid cells aids the diagnosis.

Treatment

Transient improvement in **systemic lymphosarcoma** has occurred following use of cytotoxic drugs (*q.v.*), immunostimulants (*q.v.*) and/or corticosteroids; however, long-term response is poor and debilitation ultimately occurs. The localized cutaneous form of lymphosarcoma may respond to corticosteroids but often recurs in a more pathogenic form when treatment is stopped.

Prognosis

The prognosis for lymphosarcoma is grave. Most horses die or are destroyed for humane reasons within 6 mo of the onset of signs (except for the cutaneous form where the horse can survive for years).

PLASMA CELL MYELOMA

Plasma cell myeloma (**multiple myeloma**), a systemic proliferation of neoplastic plasma cells, is very rare in horses. Reported clinical signs include

weight loss, weakness, recurrent fever, ventral edema, hemorrhages, lameness and ataxia. Renal failure and infections are not uncommon, but osteolysis as seen in humans and dogs does not consistently occur.

Laboratory findings include anemia and hyperproteinemia with monoclonal gammopathy. Hypercalcemia, azotemia and/or light-chain proteinuria (**Bence Jones proteins**) are variable. Criteria for diagnosis include **bone marrow or soft tissue plasmacytosis**, evidence of invasiveness, and the presence of monoclonal gammopathy or light-chain proteinuria. Definitive differentiation from lymphosarcoma (*q.v.*) may be difficult in some cases.

MYELOID NEOPLASIA

Myeloid neoplasia is characterized by the unregulated proliferation of a bone marrow-derived blood cell line. Forms of myeloid neoplasia described in horses include:

1. Granulocytic leukemia
2. Myelomonocytic leukemia
3. Monocytic leukemia
4. Eosinophilic myeloproliferative disorder.

There appears to be no age predilection. Predominant clinical signs include depression, weight loss, and those described for myelophthisic and aplastic anemias (*q.v.*). Affected horses are anemic and have thrombocytopenia. The total WBC count may be elevated, normal or reduced, but abnormal leukocytes have been invariably found in the peripheral blood. Abnormal leukocytes predominate in **bone marrow aspirates**. Treatment with cytotoxic agents has been unsuccessful.

HEMOSTATIC DYSFUNCTION

Disorders of hemostasis (**coagulopathies**) are characterized by hemorrhagic diathesis of variable severity and/or thrombosis. The latter is manifested as organ failure or edema of tissue proximal to the obstruction.

THROMBOCYTOPENIA

A **reduced number of circulating platelets** may be due to reduced platelet lifespan, platelet sequestration, or failure of megakaryocyte maturation within the bone marrow. The spleen normally stores platelets, but hypersplenism does not appear to cause thrombocytopenia in horses. Platelet production failure is usually caused by **myelophthisic disease** or **aplastic anemia** (*q.v.*), both of which are rare. The most common cause of thrombocytopenia is reduced lifespan of circulating platelets. Over-utilization is generally a component of a more extensive coagulopathy such as **disseminated intravascular coagulation** (*q.v.*). Idiopathic thrombocytopenia is probably due to **immune-mediated platelet destruction**.

Profound thrombocytopenia in a horse with minimal evidence of hemorrhage should be re-evaluated. Improper blood collection, inadequate volume of anticoagulant or platelet clumping in EDTA can cause **spuriously low** platelet counts. **EDTA-induced platelet clumping** is more common in patients with

prolonged severe illness. If **pseudothrombocytopenia** (*q.v.*) is suspected, the platelet count should be determined on a blood sample anticoagulated with 3.8% **sodium citrate**. If the citrated sample has a significantly higher platelet count than blood collected in EDTA, true thrombocytopenia is unlikely.

Idiopathic thrombocytopenia

Thrombocytopenia without other recognizable evidence of hemostatic dysfunction characterizes idiopathic thrombocytopenia (ITP). Any horse may be affected, although ITP seems to be more prevalent in young adult Thoroughbreds.

Clinical signs and laboratory findings

Petechial hemorrhages on mucous membranes, the nictitans and/or sclerae are characteristic. Epistaxis, hyphema, occult melena, hematuria, bleeding from injections or wounds and hematomas following minor trauma may occur. Other signs are referable to the presence of any underlying disease.

Laboratory findings include severe thrombocytopenia ($\leqslant 40\,000/\mu L$), prolonged bleeding time and abnormal clot retraction. The prothrombin time (PT), activated partial thromboplastin time (APTT) and thrombin time (TT) are normal. Serum concentrations of fibrin or fibrinogen degradation products (FDP) may be mildly increased. If the condition is chronic, anemia and hypoproteinemia may occur.

Etiology and pathogenesis

The clinical course and therapeutic response of ITP in horses suggests a similarity to immune-mediated thrombocytopenia in humans and dogs, where **surface antibodies cause phagocytic destruction of platelets** by the MPS. The platelet-associated immunoglobulin (Ig) in **primary ITP** is usually complement-fixing IgG. The mean half-life of circulating platelets and the platelet count are inversely proportional to the quantity of platelet-associated IgG and/or complement components. The spleen seems to be the major site of platelet phagocytosis. The bleeding diathesis posed by thrombocytopenia is caused by insufficiency of numerous hemostatic functions (*q.v.*).

Megakaryocyte numbers generally increase as a compensatory response to ITP, but autoantibodies may cause decreased platelet production by megakaryocyte destruction and/or prevention of newly formed platelets from entering the circulation. The potential mechanisms for autoantibody production in ITP are similar to those described for AIHA (*q.v.*). **Secondary ITP** results from non-specific binding of immune complexes to the platelet surface. Thrombocytopenia has been reported in horses secondary to EIA, lymphosarcoma and AIHA (*q.v.*).

Drugs implicated in the pathogenesis include phenylbutazone, aspirin, heparin, quinidine, penicillin, erythromycin, sulfonamides, tetracycline and gold salts. **Drug-induced ITP**, except that due to gold therapy, generally abates within days after the offending agent is discontinued.

Diagnosis

Clinical evidence of **small blood vessel hemorrhage** and **severe thrombocytopenia** in a horse with normal coagulation times (PT, APTT) and neutrophil

count are presumptive evidence of ITP. **Response to corticosteroids** (see below) adds support to the diagnosis. Definitive diagnosis of immune-mediated thrombocytopenia requires demonstration of increased platelet-associated Ig, currently not commercially available. Any suspicion of myelophthisis (*q.v.*) can be ruled out by bone marrow examination.

Treatment

The rationale of initial treatment for ITP is very similar to that described for AIHA. Any medication should be stopped or replaced by the chemically most dissimilar substitute. In the unlikely event of life-threatening hemorrhage, a **transfusion** (*q.v.*) of fresh whole blood (8–16 mL/kg BW), platelet-rich plasma or platelet concentrate should be administered.

Horses with suspected ITP generally respond favorably to corticosteroids. In addition to their effects on the immune response and MPS clearance, corticosteroids improve capillary integrity and increase thrombocytopoiesis. **Dexamethasone** (0.05–0.2 mg/kg IM or IV s.i.d.) usually causes an increased platelet count within five days, although full benefit may not be evident for 1–3 wk. Once the platelet count is $> 100\,000/\mu L$, the dosage of dexamethasone can be decreased by 0.01 mg/kg daily while monitoring for a relapse. Prednisolone (initial dose 1 mg/kg IM q 12 h) may be used in lieu of dexamethasone, however it often is not as effective. Corticosteroids should be continued until the platelet count has been normal for at least five days. If glucocorticoid administration proves necessary beyond 2 wk, then alternate morning low dose therapy (0.01 mg/kg dexamethasone) should be continued for 10 more days.

Alternate methods for treating ITP in horses are largely unproven. **Splenectomy** to remove the major site of platelet destruction is successful in some humans and dogs with ITP. Post-splenectomy sepsis is a major risk of this procedure. The cytotoxic drug, **vincristine** (0.01–0.025 mg/kg IV q 7 days), combined with glucocorticoids, has been successfully used to treat horses with ITP refractory to corticosteroids alone. There are no data regarding the effect of azathioprine and cyclophosphamide in equine ITP. Due to their potential to induce severe bone marrow suppression, cytotoxic drugs should be used with extreme caution, and only in horses that are non-responsive to corticosteroids for at least 10 days.

Prognosis

Most horses with ITP recover within 3–4 wk if treated appropriately. This suggests that many cases are secondary, although the initiating cause is rarely found. Chronic, recurrent ITP, requiring prolonged corticosteroid therapy, has been reported in horses. Horses with EIA or underlying neoplasia obviously have a poor prognosis.

CLOTTING FACTOR DEFICIENCY

Disseminated intravascular coagulation

Disseminated intravascular coagulation (DIC) is a form of hemostatic dysfunction that occurs in horses with **severe underlying disease processes**.

DIC is a pathologic activation of coagulation that causes microvasculature clotting and may lead to hemorrhage subsequent to procoagulant consumption and/or the action of fibrinolytic by-products. Disease processes that cause DIC in horses include gastrointestinal disorders that induce colic (particularly enteritis/colitis), localized and/or systemic sepsis, systemic neoplasia and hemolytic anemia (*q.v.*).

Clinical signs and laboratory findings

Due to its heterogeneous and dynamic nature, the clinical manifestations of DIC vary from diffuse thrombosis and ischemic organ failure to severe hemorrhagic diathesis. In horses, DIC is more a thrombotic disorder than one causing massive hemorrhage. **Thrombosis of peripheral veins** tends to be a prominent manifestation of equine DIC. Sometimes a **jugular vein** will undergo **complete thrombosis** within hours of a routine blood sampling procedure.

Other clinical manifestations of thrombosis depend upon the organ involved. **Renal hypoperfusion** (*q.v.*) and subsequent failure produces signs of anorexia, depression, gastrointestinal ileus and oliguria/polyuria. **Gastrointestinal microthrombosis** may induce colic, complicating the clinical picture in horses with primary gastrointestinal disease. **Digital ischemia** frequently accompanies DIC in horses and may play a key role in development of acute laminitis (*q.v.*). Pulmonary microthrombosis may rarely cause tachypnea and hypoxemia. Microangiopathic hemolysis, hemoglobinemia and hemoglobinuria are rare in horses with DIC.

Depending upon the rate of DIC, horses develop a tendency for hemorrhage characterized by petechial or ecchymotic hemorrhages on mucous membranes/sclerae and bleeding following venepuncture or minor trauma. Spontaneous epistaxis, hyphema and melena occur less commonly. Life-threatening hemorrhage is rare in horses with DIC, unless there is initiating trauma (e.g. nasogastric intubation).

Numerous tests of hemostasis may be abnormal during DIC. Increased consumption causes reduced plasma concentrations of platelets, some coagulation factors, fibrinolytic proteins, anticoagulants and antifibrinolytic proteins with a secondary increase in FDP. Laboratory changes of DIC may include thrombocytopenia; prolonged PT, APTT and TT; reduced plasma concentrations of fibrinogen, factor V, factor VIII, AT-III, plasminogen and α_2-antiplasmin (AP); and increased serum concentrations of FDP and soluble fibrin monomer. None of these tests is always sensitive, or specific for DIC, but one consistent feature of DIC is the presence of **multiple hemostatic abnormalities**. Serial analyses of hemostatic data should reveal reduced platelet numbers and a trend toward prolongation of the PT, APTT and/or TT.

Etiology and pathogenesis

Disease processes that trigger DIC generate excessive procoagulant activity and/or cause abnormal surfaces to contact blood. The nature and intensity of the procoagulant force, the concentration of natural coagulation inhibitors, and the functional capacity of the MPS play vital roles in determining whether an individual develops DIC. Gastrointestinal diseases that cause **colic** and **bacterial sepsis** are the most common disorders associated with

DIC in horses. In both, endotoxins, the lipopolysaccharide (LPS) portion of Gram-negative bacterial cell walls, gain access to the blood and initiate severe morbidity and mortality.

The equine gastrointestinal tract normally contains a large quantity of luminal endotoxins, only a small amount of which are absorbed into the portal blood and then removed by the liver. **Intestinal ischemia** or edema induced by strangulating obstruction, thromboembolic infarction and severe colitis (*q.v.*) allows luminal endotoxins to be absorbed at a rate which overcomes Kupffer cell clearance capacity, with resultant endotoxemia. Gram-negative sepsis, which is particularly common in equine neonates, causes endotoxemia and is a frequent initiator of DIC.

Endotoxins have numerous procoagulant effects. Endotoxins directly activate factor XII, can cause endothelial cell damage and TF release, stimulate platelets to release TXA_2 and induce granulocytes and macrophages to release platelet-activating factor (PAF). Most importantly, endotoxins stimulate macrophages to produce a procoagulant activity (PCA) that functions identical to TF. Other LPS-induced macrophage products, particularly interleukin (IL-1) and tumor necrosis factor (TNF), amplify these procoagulant actions. Endothelial cells, perturbed by LPS, IL-1 and/or TNF, do not express sufficient thrombomodulin, causing the anticoagulant actions of AT-III and activated protein C (APC) to be reduced. Finally, endotoxemia inhibits fibrinolysis by increased plasma concentrations of plasminogen activator inhibitors (PAI), and downregulation of protein C.

Other mechanisms may also trigger DIC during sepsis. **Circulating antigen–antibody** complexes can disrupt endothelium as well as directly activate factor XII. Inflammatory destruction of tissue may result in TF release and/or PCA production by activated leukocytes. The final common path of any triggering mechanism for DIC involves generation of **excess thrombin and plasmin**. Anticoagulants (AT-III and protein C) may become depleted during DIC. **Fibrinopeptides A and B**, liberated during fibrin formation, induce vasoconstriction that compounds hypoperfusion. Polymerized fibrin entraps platelets and damages red cells. Microangiopathic hemolysis provides ADP and phospholipid (PL) to continue the process of DIC.

Thrombin formation is linked to the systemic generation of plasmin, primarily via tPA release from underperfused tissues. The resultant FDP predispose to hemorrhage by interfering with thrombin activity, fibrin monomer polymerization and platelet function. Paradoxically, combined clotting factor consumption and fibrinolysis potentiate bleeding at the same time that disseminated thromboses occur. Tissue-fixed macrophages of the spleen and liver normally remove activated clotting factors and FDP from the circulation, and plasma concentrations are increased only when the formation rate exceeds the clearance ability of the MPS. **Shock** or diseases associated with excessive tissue debris (e.g. sepsis, metastatic neoplasia) will reduce the function of the MPS and predispose to DIC.

Diagnosis

Numerous tests of hemostatic function may be abnormal, but no one test consistently or specifically indicates the presence of DIC. Laboratory criteria for

the diagnosis of DIC must always be interpreted in the light of the patient's **underlying disease**. The diagnosis of DIC is made by clinical signs in specific disease settings and laboratory data only provide support.

The combination of **thrombocytopenia** with **prolongation of the PT** and/or **APTT** (*q.v.*) strongly suggests the presence of DIC in horses. Thrombocytopenia may also occur with ITP, bone marrow aplasia or myelophthisic disease (*q.v.*); however, these latter conditions are not associated with other abnormalities of hemostatic function (e.g. PT, APTT). The PT is a crude measure of the extrinsic and common coagulation pathways and the APTT assesses function of the intrinsic and common pathways. Clotting times are not sensitive and only become prolonged when the tested factors are ⩽30–50% normal, i.e. late in the genesis of coagulopathy. Thus, thrombocytopenia alone may occur early in DIC.

Adult horses with DIC uncommonly develop hypofibrinogenemia. Because infection, endotoxemia and/or inflammation generally initiate coagulopathy in horses, the **acute-phase hepatic response** to increase fibrinogen synthesis probably compensates for consumptive loss. Serum FDP concentration ⩾40 μg/mL usually indicates DIC, but the absence of FDP does not rule it out. Early in DIC, there often is MPS compensation and/or degradation of FDP to undetectable forms. Severe inflammation, localized intravascular coagulation or other hemorrhagic disorders, like ITP, can increase serum FDP, but the concentrations rarely exceed 40 μg/mL.

Treatment

Treatment of DIC is controversial and the only widely accepted modalities are treatment of the primary disorder with general supportive measures to combat shock and maintain tissue perfusion. **IV fluids** help to reduce organ dysfunction caused by microvascular thrombosis. Septic conditions require appropriate antimicrobial therapy. Necrotic tissue, purulent exudate and non-viable bowel should be removed whenever possible. **Flunixin meglumine** (0.25 mg/kg IV q 8 h) reduces eicosanoid generation and may be useful for endotoxemia. **Corticosteroids are not indicated** since they reduce the phagocytic action of the MPS and potentiate the vasoconstrictor effects of catecholamines.

Life-threatening hemorrhage is an indication for fresh plasma administration (15–30 mL/kg) to replace utilized coagulant, anticoagulant and/or fibrinolytic proteins. Concomitant **heparin administration** (*q.v.*) may help to prevent further thromboses, although the appropriate dose and rate in horses are unknown.

Controlled studies have not been performed in horses, but experience suggests that **aggressive therapy of the primary disease** is the most effective treatment for DIC.

Prognosis

The prognosis for DIC depends upon the severity of the primary disease process and how effectively the latter is treated. Mild DIC associated with gastrointestinal-induced endotoxemia generally resolves; however, debilitating sequelae such as laminitis or renal failure (*q.v.*) may ensue. Once blood incoagulability predominates, the prognosis for DIC is grave.

Warfarin toxicosis

Warfarin, a coumarin derivative anticoagulant, has been used therapeutically in some horses to treat navicular disease (*q.v.*) but is still used widely in some countries as a rodenticide in grain stores and yards to which horses may have access.

Clinical signs and laboratory findings

Coagulopathy is usually manifested by **mucosal ecchymotic hemorrhages**, hematomas, epistaxis and/or prolonged bleeding from minor trauma. Petechial hemorrhages do not occur. The earliest laboratory indication of warfarin toxicosis is **prolongation of the PT**. As the disease progresses, **APTT becomes prolonged**. Horses may develop **blood loss anemia** and **hypoproteinemia**.

Etiology and pathogenesis

Therapeutic amounts of warfarin may become toxic by a **cumulative effect** if there is **concurrent use of highly protein-bound drugs** such as phenylbutazone, etc., and/or there is a dietary alteration with **reduced vitamin K intake**. Warfarin antagonizes the enzyme responsible for regeneration of active vitamin K, which is necessary for liver production of the clotting factors II, VII, IX and X. Factors VII, IX, X and II have increasingly greater half-lives and depletion of factor VII causes prolongation of the PT within 36 h of toxicosis. Over the next 2–3 days, factors II, IX and X become deficient. Warfarin is **rapidly absorbed** from the gastrointestinal tract, then highly bound to plasma proteins. This protein-bound portion of warfarin acts as a reservoir for the free active drug.

Hypoalbuminemia, or the use of other protein-bound compounds such as **phenylbutazone** and chloral hydrate, can **enhance the toxicity of warfarin** by allowing a greater proportion of circulating unbound form. Rapid withdrawal of drugs that induce hepatic microsomal enzyme metabolism (e.g. **rifampicin**, **chloramphenicol**) may **potentiate warfarin toxicosis** since its metabolism is enhanced by these drugs. Finally, hepatic dysfunction or reduced content of dietary vitamin K (e.g. by feeding good to poor quality roughage) can precipitate warfarin toxicosis.

Diagnosis

Warfarin toxicosis is diagnosed by history of exposure, hemorrhagic diathesis without petechiae and prolonged PT/APTT with no other hemostatic abnormalities. Occasionally, hemorrhage precedes abnormal laboratory data by up to 24 h.

Treatment

Warfarin access must be discontinued. **Vitamin K_1** (1 mg/kg SC) should be administered every 6 h until clinical signs have abated and the PT is normal for at least two days. Treatment may be necessary for several days due to continued gastrointestinal absorption of warfarin and time required for clotting

factor production. Vitamin K_3 has poor therapeutic benefit and may induce nephrotoxicosis. Life-threatening hemorrhage can be controlled by **transfusion of plasma** (4–20 mL/kg), which must be fresh to ensure active coagulation factors. Life-threatening anemia can be treated with whole blood transfusion (*q.v.*).

Prognosis

Prevention is based on limiting access of horses to rodenticides and carefully monitoring the therapeutic use of warfarin. Other drugs (particularly **phenylbutazone** and other highly plasma protein bound COX-2 inhibitors) should be limited during warfarin therapy. Initially, the PT is monitored daily and the dose of warfarin adjusted as needed to achieve <2-fold increase.

During **warfarin therapy**, e.g. for navicular syndrome (*q.v.*), the PT should be checked at least twice weekly and more often if there is a change in diet, concurrent disease or other medication.

Congenital coagulation disorders

Selected deficiencies of factor VIII (hemophilia A), factors IX and XI, prekallikrein and the contact phase of intrinsic coagulation have been reported in horses. By far the most common congenital coagulopathy is **hemophilia A**. This sex-linked recessive **heritable** condition has been reported in Thoroughbreds, Standardbreds and Quarter Horses. Only **homozygous males** are clinically affected.

Clinical signs and laboratory findings

Clinical signs of excessive hemorrhage are usually manifested within the first few weeks of life. SC and/or IM hematomas and joint swellings due to **hemarthroses** are the most common complaints. Affected joints are not hot or painful to palpation but foals may have a **stiff gait**. Hemorrhage into body cavities may cause colic, depression and/or dyspnea. There is increased tendency to bleed following minor trauma and surgical procedures. Petechial hemorrhages are noticeably absent and epistaxis is rare. The only abnormal hemostatic test is **prolonged APTT**.

Etiology and pathogenesis

Hemophilia A is inherited as a sex-linked recessive trait and affected horses are unable to form functional factor VIII. Procoagulant factor VIII (factor VIII:C) generally circulates in a complex with a high molecular weight protein called **von Willebrand factor (vWF)**, part of which is immunologically active and termed factor VIII-related antigen (VIII:RA). The synthesis and secretion of factor VIII:C is decreased in patients with hemophilia A. Plasma and endothelial concentration of vWF are normal and plasma VIII:RA may even be increased. Deficiency of factor VIII:C compromises intrinsic coagulation. The severity of the resultant hemorrhagic diathesis is inversely correlated with the plasma concentration of factor VIII:C. Severe, moderate and mild hemophilic bleeding is associated with factor VIII:C activities of <1% of normal, between 1% and 5%, and between 5% and 20%, respectively.

Diagnosis

Horses with hemophilia A have APTT prolonged at least twice normal while other hemostatic tests are normal. The APTT can be corrected by **mixing patient plasma 1:1 with normal horse plasma**. Definitive diagnosis of hemophilia A is based on a specific assay for factor VIII activity that is <20% of normal. Carrier mares generally have factor VIII:C between 30% and 60% of normal. Since factor VIII:C >50% of normal is necessary to prevent hemorrhage after surgery or major trauma, some carrier mares may be at risk of bleeding.

Treatment

The most effective treatment for hemophilia is **transfusion** with fresh plasma. The half-life of transfused factor VIII:C is only 8–13 h, necessitating daily transfusions in severely affected patients. The use of **desmopressin** (1-deamino-8-D-arginine-vasopressin), or **DDAVP**, has not been explored in horses. Affected horses should be rested in a safe enclosure such that the chances of trauma are minimized.

Prognosis

The long-term prognosis for hemophilia A is poor. There is no cure, and therapy is only palliative. Most affected foals die or are destroyed because of **progressive debilitation** by 6 mo of age, although a mildly affected Thoroughbred was described at 3 yr of age.

Removal of **carrier mares** from the breeding population is the basis for prevention of affected foals. Definitive diagnosis of hemophilia A in a colt documents the mare as a carrier. Factor VIII:C may be elevated from the last trimester through 60 days post partum, thus carrier mares may have normal concentration at this time.

THROMBOPHLEBITIS

Inflammation of a vein associated with its thrombosis is termed thrombophlebitis. The mere presence of a thrombus initiates phlebitis. **Septic thrombophlebitis** occurs when there is bacterial or fungal infection of the thrombus and adjacent vessel wall. Although there are many factors that predispose to thrombophlebitis, alteration of normal hemostasis is necessary in the pathogenesis.

Clinical signs and laboratory findings

Often the initial sign is congestion and edema of tissues normally drained by the thrombosed vessel. Because **jugular thrombophlebitis** is most common in horses, head edema and hyperemia of the oral and nasal mucosae are prominent (*q.v.*). The thrombosed vessel feels like a firm, **cord-like structure**. Heat, pain, perivascular swelling, neck stiffness, fever and draining exudates strongly suggest sepsis. The development of collateral circulation from the affected tissue (usually face) is manifested as **numerous superficial small arborizing vessels**. Neutrophilia and hyperfibrinogenemia may accompany septic thrombophlebitis.

Etiology and pathogenesis

Causative factors of thrombophlebitis include stasis of normal blood flow, injury to the vessel wall and a hypercoagulable state. **Vessel wall injury** probably has a major role in the pathogenesis, since severe or septic thrombophlebitis most frequently involves vessels that have been catheterized, have undergone multiple venepunctures and/or been infused with irritant solutions. Most cases of thrombophlebitis result from a combination of vessel wall trauma and a hypercoagulable state. This increased tendency for the formation and maintenance of fibrin is inherent in the pathogenesis of thrombophlebitis, as well as DIC.

As discussed for DIC, thrombophlebitis most commonly accompanies endotoxin-mediated disease processes in horses, especially gastrointestinal diseases that cause colic (*q.v.*). **Endotoxin** is thrombogenic in numerous ways, as discussed under DIC. Insufficient anticoagulant mechanisms can also predispose to thrombosis, and severe protein-losing disease processes may be attended by thrombophlebitis. In horses, **hypoproteinemia** often attends NSAID toxicosis, salmonellosis and other causes of acute toxic colitis, infiltrative bowel diseases such as granulomatous enteritis and lymphosarcoma, and chronic glomerulonephritis (*q.v.*).

Diagnosis

Thrombophlebitis of the jugular or other peripheral veins can usually be diagnosed by clinical signs alone. Ultrasonography may allow detection of an occult thrombosis that is altering venous flow. Cavitation (hypoechoic area) suggests **sepsis**. Clinical diagnosis of deep vein thrombosis is usually not possible and there are no definitive laboratory tests. Definitive diagnosis of septic thrombophlebitis relies on isolation of a **pathogen** from the thrombus or peripheral blood. Positive culture of an appropriately removed catheter tip (to prevent skin contamination) may be confirmatory.

Treatment

Non-septic thrombophlebitis generally resolves with time and supportive care to reduce inflammation and improve blood supply to the area. At the first sign of thrombophlebitis, any catheter should be **aseptically removed and cultured**. Needle puncture of the involved vein is contraindicated. **Hydrotherapy** of the affected area and **topical dimethyl sulfoxide** (50%) may be useful.

Septic thrombophlebitis necessitates systemic antimicrobial therapy. The choice of drugs may be directed by the results of culture from a catheter tip, exudate or blood. Since the latter is usually not possible, **broad-spectrum antimicrobial** therapy should be continued for at least 10 days or until there is clinical and laboratory evidence of sepsis resolution. Persistent perivascular pain, intermittent fever and leukocytosis may be indications for surgery to drain an abscess or remove a section of the involved vein.

Client education and prevention

The prognosis for thrombophlebitis is determined by the location and extent of involvement of the vein, presence of sepsis and the underlying disease

process. Non-septic thrombophlebitis generally resolves quickly with appropriate supportive care. Mild, localized cases of septic thrombophlebitis generally respond to conservative therapy with antimicrobials, although there is a minor risk of **thromboembolism** to the heart and lungs. Other life-threatening sequelae include bacterial septicemia and external hemorrhage due to vessel wall necrosis. Persistent morbidity associated with thrombophlebitis warrants surgical intervention, which carries a fair prognosis. Horses with severe endotoxemia generally have a poor prognosis.

Effective treatment of the underlying disorder is the most effective way to minimize the contribution of hypercoagulability to thrombophlebitis. Proper catheter care is paramount in reducing the incidence of thrombophlebitis (Box 9.3). **Repeated needle puncture** of large veins should be avoided in patients with hypercoagulability. Small samples may be taken by 25 G needle from a facial vein; large samples should be aseptically removed from a catheter.

VASCULITIS

Vasculitis is a general term referring to inflammation of blood vessels; it may be primary or secondary to some underlying disease. Vasculitis in horses generally develops as a **hypersensitivity reaction** to an infectious, toxic or neoplastic process. Hypersensitivity vasculitis is characterized by predominant involvement of small blood vessels in the skin. The most common inflammatory pattern is **leukocytoclasis**, defined by the presence of neutrophilic nuclear debris in and around the involved vessels, with necrosis and fibrinoid changes.

Clinical signs and laboratory findings

Vasculitis is characterized by well-demarcated areas of **cutaneous edema** involving any portion of the body. The distal extremities and ventral body wall are most commonly affected. The edema is often hot and painful and affected horses are depressed and reluctant to move. Hyperemia, petechiae with or without ecchymotic hemorrhages and ulcerations, are commonly present on mucous membranes of the mouth, nose, vulva, etc. Other signs are variable and may reflect edema, hemorrhage and infarction in other systems. Lameness, colic, diarrhea, dyspnea and/or ataxia rarely occur. Secondary complications such as laminitis, thrombophlebitis and localized infections are common.

Laboratory findings may reflect chronic inflammation (e.g. neutrophilia, mild anemia, hyperglobulinemia and hyperfibrinogenemia). The platelet count is generally normal. With renal involvement, creatinine may be elevated and urinalysis may reveal hematuria and/or proteinuria.

Etiology and pathogenesis

The antigenic stimulus of **hypersensitivity vasculitis** is usually a microbe, drug, toxin or foreign protein. The deposition of circulating immune complexes is widely accepted as the major event in the pathogenesis of vasculitis. Deposited immune complexes activate complement with resultant formation of potent chemotactic factors. Infiltrating neutrophils release lysosomal and other cytoplasmic enzymes that directly damage vessel walls. Vessel wall leakage and luminal compromise result in edema, hemorrhage, thrombosis

Box 9.3 Proper intravenous catheter use

Insertion
- Aseptic technique (surgical scrub and sterile gloves)
- Subcutaneous tunnel prior to vein entry optimal
- Smallest bore catheter that is practical
- Least thrombogenic catheter material
- Secure to skin (sutures)
- Cover with aseptic bandage, if possible

Use
- Aseptic technique for all injections
- Sterile solutions only
- Change injection lines every 24 h
- Flush with heparinized (10 IU/mL) saline solution every 6 h

Maintenance
- Change every 72 h if not tunneled
- Catheterize another vein
- Remove at first evidence of swelling, heat, pain or exudate at site
- Culture tip of suspect catheters

and ischemia in supplied tissues. Vascular dysfunction characterized by vasoconstriction and platelet aggregation further contributes to **tissue ischemia**.

Factors that determine which individuals develop hypersensitivity vasculitis remain undefined. Genetic and acquired alterations of immunoregulatory mechanisms that result in reduced immune complex clearance by the MPS are likely to be important. Physical factors such as blood flow turbulence, hydrostatic pressure and previous endothelial damage are likely to determine the size, type and location of blood vessels involved. Increased hydrostatic pressure in affected postcapillary venules results in a propensity for lesion formation in the skin of dependent body portions.

Diagnosis

Definitive diagnosis of vasculitis is based on typical histologic changes in involved vessels. Full thickness **punch skin biopsies** (>6 mm in diameter) from an affected area should be preserved in 10% formalin. **Michel's transport medium** is used for samples to detect immune complexes by immunofluorescence. Multiple biopsies from various sites are optimal since histologic lesions and/or immune complexes are patchily distributed; however, there is increased risk of cellulitis and/or exuberant granulation tissue (*q.v.*) on the distal limbs. Often the diagnosis of vasculitis must be made on clinical grounds and response to therapy.

Specific equine vasculitic syndromes

Equine purpura hemorrhagica (EPH) is believed to be an allergic response to streptococci or equine influenza virus (*q.v.*). This vascular syndrome typically

occurs 2–4 wk after infection by *Streptococcus equi* (strangles) (*q.v.*). Exposure of a **previously sensitized horse** to infected horses may also precipitate EPH. Rarely EPH may follow infections with *Strep. zooepidemicus* or influenza. Immune complexes containing IgA and a protein of *Strep. equi* have been demonstrated in the blood vessels of horses with EPH. Serum IgA titers to *Strep. equi* are higher in horses with EPH, but titers of IgG are curiously decreased. The significance of these findings remains unclear because EPH is difficult to reproduce experimentally.

Classical signs of EPH include **mucosal petechial hemorrhages** and **demarcated areas of edema** on the limbs, ventral abdomen, head and trunk. Edema of other tissues may cause dysphagia, dyspnea, colic, lameness or renal disease. Hematology generally reflects **chronic inflammation**. Moderate anemia (PCV 0.20–0.25 L/L) may develop due to fluid shifts or shortened erythrocyte lifespan. Tentative diagnosis of EPH is based on history and clinical signs. **Leukocytoclastic venulitis** in the dermis and subcutaneous tissue of a skin biopsy supports the diagnosis. Although most horses with EPH respond to therapy (see below), some cases are refractory. Deaths are usually secondary to laminitis (*q.v.*) or septic complications.

Equine viral arteritis (EVA) is caused by an RNA virus of the genus *Arterivirus*. There are numerous strains of EVA virus (*q.v.*) with variable pathogenicity. Infection classically occurs via inhalation of aerosol secretions from an affected horse, but **venereal transmission** may play a significant role in EVA dissemination.

Clinical disease of variable severity or an inapparent infection may follow EVA exposure. Clinical signs, after an incubation period of 2–13 (mean 7) days, may include fever, depression, anorexia, periorbital and palpebral edema, conjunctivitis, ocular and nasal discharge, edema of the legs and ventral abdomen and/or respiratory distress. Pregnant mares infected during the last trimester generally abort 5–30 days after the febrile response and they may not show other clinical signs. The fetus is usually autolyzed.

Definitive diagnosis of EVA (*q.v.*) requires **viral isolation** or **seroconversion**. The EVA virus may be isolated from nasopharyngeal and conjunctival swabs, citrated blood early in the course of the disease, and semen or placental and fetal fluids. Immunochemistry and PCR may replace virus isolation. A 4-fold increase in serum antibody titer to EVA virus in two samples collected 10–14 days apart is considered evidence of infection. Affected horses usually recover with supportive care within 3 wk. Infected stallions can remain **persistent carriers/shedders** of the EVA virus in semen. Infection by EVA can be prevented by use of a modified live vaccine at least 3 wk prior to exposure.

Infection with the **equine infectious anemia (EIA)** virus (*q.v.*) may cause **necrotizing vasculitis** of the skin or other organs. Classical signs include fever, icterus, mucosal petechiae, ventral edema, anemia and weight loss. Diagnosis of EIA is confirmed by an agar gel immunodiffusion (Coggins) test for serum antibodies to the EIA virus. Horses remain viremic.

Infection by the rickettsial agent ***Anaplasma phagocytophila*** (*q.v.*) may cause a vasculitic syndrome. Although the disease originally termed **equine ehrlichiosis** usually occurs in northern California, individual cases have been reported in other states and countries. Its distribution overlaps that of the tick reservoir, *Ixodes pacificus*. Horses over 3 yr of age are more severely affected

and signs include fever, depression, anorexia, mucosal petechial hemorrhages, icterus, ventral limb edema, weakness, ataxia and/or reluctance to move. Hematology often reveals mild to moderate leukopenia, thrombocytopenia and anemia. *A. phagocytophila,* which infects granulocytes, is antigenically distinct from *Neorickettsia risticii,* the etiologic agent for **Potomac horse fever** (*q.v.*). Infection confers immunity for up to 2 yr that is not associated with a carrier state. Diagnosis is based on serology and active cases have a 4-fold rise in titer over 4 wk. Affected horses generally recover within 2 wk with supportive care alone, but **oxytetracycline** (7 mg/kg IV s.i.d. for 5 days) usually causes a prompt remission of clinical signs within 1–2 days.

Horses may develop **idiopathic vasculitic syndromes** with uncharacterized pathogenesis and unpredictable clinical course. Clinical signs often resemble EPH (*q.v.*) but may include intermittent fever, weight loss, alopecia, hyperkeratosis and hypopigmentation of the skin.

Treatment

Therapy of vasculitis is aimed at **reducing any known antigenic stimulus**, reducing vessel wall inflammation, normalizing the immune response and providing supportive care. **Hydrotherapy** and **pressure wraps** help to reduce limb edema. Horses that become unwilling or unable to drink require **fluids** IV or via nasogastric tube. Horses with dyspnea secondary to upper respiratory tract edema require tracheostomy. Phenylbutazone, flunixin meglumine or other NSAIDs **reduce vascular inflammation** and provide analgesia. The incidence or severity of cellulitis (*q.v.*) and other septic sequelae may be minimized by **antimicrobials**.

No treatment effectively eliminates the viruses of EVA or EIA from the body. Oxytetracycline therapy is indicated to considerably shorten the clinical course of ehrlichiosis (*q.v.*). Horses thought to have **EPH** should receive **penicillin** (22 000 IU/kg procaine benzylpenicillin G IM q 12 h or potassium benzylpenicillin G IV q 6 h) for at least 2 wk although the sensitizing infection has usually resolved by the time there are signs of EPH. **Idiopathic vasculitis** can be difficult to treat because the antigenic stimulus remains undefined and may not be easily eliminated. Any drug used at the time when signs occur should be discontinued. Underlying infection or neoplasia should be sought.

The use of **corticosteroid therapy** for the treatment of hypersensitivity vasculitis is controversial, however horses with EPH or idiopathic vasculitis usually respond favorably to corticosteroids. Whether the main effect of the latter is anti-inflammatory or immunosuppressive is unknown. The dose and rate of dexamethasone (0.05–0.2 mg/kg IV or IM q 12–24 h) necessary to effect reduction in edema should be given. Prednisolone (0.5–1 mg/kg IM q 12 h) is often not as effective as dexamethasone. Once edema starts to resolve, the corticosteroid dose can be gradually reduced (by 10–15%, q 24–48 h) while the horse is monitored carefully for any signs of relapse. Horses with EPH may require corticosteroid therapy for up to 6 wk before edema permanently resolves. Intermittent disease flare-ups, which require increasing the corticosteroid dose above a previously efficacious level, may occur. Oral prednisolone and prednisone are not recommended since they are erratically absorbed. **Antimicrobials are indicated** throughout the period of systemic corticosteroid administration.

Prognosis

The prognosis of vasculitis depends upon the cause. With early aggressive therapy most horses recover from EPH within 4 wk although numerous sequelae may prolong the convalescence. **Dermal infarction** often leads to skin sloughing followed by exuberant granulation tissue in the distal limbs.

BLOOD AND PLASMA THERAPY

Whole blood administration should be used only as a temporary life-saving procedure to improve oxygen delivery to the tissues during anemia. Crossmatch compatible equine erythrocytes are lost from circulation within 4 days of administration and the increased cellular debris that must be processed by the MPS may immunocompromise the patient. **Blood transfusion** blunts renal production of erythropoietin, thus impeding a bone marrow response that is highly important for ultimate recovery from anemia. If compatible whole blood is not available, bovine polymerized hemoglobin (Oxyglobin) may be used (*q.v.*) but the beneficial effects likely wane after 24–48 h.

Plasma may be administered to provide immunoglobulins, hemostatic factors, enzymes and transport proteins, as well as to maintain vascular oncotic pressure. Diseases that may benefit from plasma therapy include failure of passive transfer in foals, protein-losing enteropathy or nephropathy, DIC or other coagulopathies (*q.v.*). Horses with total plasma protein ≤4 g/dL and hemoconcentration and/or associated peripheral edema, and all those with a total plasma protein ≤3 g/dL, warrant a plasma transfusion.

DONOR SELECTION AND MANAGEMENT

Blood donor selection by **compatibility testing** is recommended to prevent fatal transfusion reactions as well as to maximize in vivo survival of transfused erythrocytes. Compatibility testing to identify the presence of antibodies to allogeneic erythrocytes (alloantibodies) in the donor or recipient is complicated by the high degree of **equine blood group polymorphism** (*q.v.*). Although a completely compatible donor is a near impossibility, testing can help to avert severe transfusion reactions by identification of existing alloantibodies.

The most immunogenic of equine alloantigens, Aa of the A system and Qa of the Q system, are highly prevalent among light horse breeds. Transfusion of blood containing these alloantigens to horses that lack them results in a high titer of alloantibodies that mediate severe hemolysis upon subsequent exposure. Horses can also become sensitized by previous pregnancy or therapy with erythrocyte-contaminated blood components (e.g. plasma).

The **saline agglutination crossmatch** is performed by incubating washed erythrocytes from donor (major) and recipient (minor) with serum from the other, followed by gross and microscopic examination for clumping. Hemolysins, which comprise many equine alloantibodies, are not detected by the routine crossmatch and are reliably diagnosed by adding absorbed rabbit serum to provide complement to the reaction mixture. Special handling and storage of rabbit serum limits hemolysin testing to specialized hematology laboratories.

In an emergency, the **agglutination crossmatch** is recommended but test results may not always predict a serious transfusion reaction. The first transfusion is generally well tolerated because natural equine alloantibodies are rare and weakly reactive. In a life-threatening situation, a horse <3 yr old with no history of blood or plasma therapy is the best potential donor. Alloantibodies to incompatible alloantigens may develop within days, making subsequent transfusions from the same or a different donor hazardous.

Horses that lack alloantigens Aa and Qa as well as serum alloantibodies are the best blood or plasma donors. Such horses can be identified by sending serum and blood, anticoagulated with acid citrate dextrose (ACD) solution, from a number of potential donors to a laboratory experienced in equine blood typing. Suitable donors are most easily found among Quarter Horses and Standardbreds. Multiparous mares should not be considered. Identified donors should be **retested annually** or after any major illness to ensure lack of serum alloantibodies.

For **plasma donor selection**, only alloantibodies to recipient erythrocytes (minor crossmatch) must be considered. Although the best donor would lack all erythrocyte alloantibodies, donors lacking antibodies for Aa and Qa are usually adequate. Plasma harvested without centrifugation is usually contaminated with erythrocytes in a quantity sufficient for recipient sensitization. Thus, plasma donors would optimally lack alloantigens Aa and Qa.

BLOOD COLLECTION

Blood (9 parts) should be aseptically collected into sterile bottles or bags containing ACD solution (1 part). The ACD solution can be made by mixing 11 g dextrose, 9.9 g sodium citrate and 3.3 g citric acid, qs ad 300 mL with distilled water, then autoclaved. Adult horses can donate 8–10 L of blood (20–25% of blood volume) every 30 days. This amount is more than needed for a foal and is usually therapeutic for severe anemia in the adult. Blood for transfusion should be used immediately or stored upright in a refrigerator (4°C) for less than 24 h.

PLASMA PREPARATION

Plasma can be produced by collecting the liquid portion of whole blood that has been centrifuged or allowed to sit at room temperature for 1–2 h. This manual technique is simple but carries the risks of bacterial contamination and recipient sensitization. Cell-free sterile plasma is optimally produced by **plasmapheresis** wherein whole blood is withdrawn and separated into its component parts (plasma, erythrocytes, granulocytes, platelets), plasma is collected, and the remaining blood components are returned to the donor. There are many sources of commercially available frozen plasma from donors that lack Aa and Qa alloantigens and serum alloantibodies. Immunoglobulins are preserved for at least a year in frozen plasma, but hemostatic proteins deteriorate.

BLOOD COMPONENTS

Concentrates of specific equine plasma components could provide more focused therapy in certain situations, but as yet are unavailable. Plasma components

that are useful in the human include concentrated immunoglobulins, cryoprecipitate, purified fibronectin, and the anticoagulant proteins AT III and protein C.

Centrifugation apheresis allows collection of granulocyte, platelet and/or erythrocyte concentrates. Granulocyte transfusion may improve survival in neonatal foal septicemia. Platelets and erythrocytes would be useful in treatment of life-threatening thrombocytopenia or anemia (*q.v.*).

TRANSFUSION TECHNIQUE

Blood products should be **warmed to 37°C in a water bath**, then administered IV through a **blood filter**. Vital signs of the recipient are recorded prior to transfusion, then 0.1 mL blood or plasma per kg body weight should be administered over 10 min. If attitude and vital signs do not change, the transfusion is continued at a rate of 5–20 mL/kg/h. In the absence of hypovolemia, slower flow rates are optimal to prevent volume overload and to allow detection of delayed adverse reactions prior to excessive blood delivery. **The transfusion should be stopped immediately if the recipient shows any change in demeanor** (see below).

The necessary dose of whole blood for a severely anemic horse can only be estimated. In most instances, replacing 20–40% of the calculated loss is sufficient to maintain life until the bone marrow responds. A drop in the PCV from 36% to 12% in a 500 kg horse (total blood volume is 8% BW or 40 L blood) would represent loss of about 27 L of blood, thus 6–8 L of blood should be therapeutic. A rule of thumb for plasma therapy is that IV infusion of 7 L of plasma containing protein at 7 g/dL in a 500 kg horse raises the TPP by approximately 1 g/dL.

POTENTIAL COMPLICATIONS

Signs of a "**transfusion reaction**" include restlessness, tachypnea, dyspnea, tachycardia, piloerection, sweating, defecation and muscle fasciculations. Hemolysis or anaphylaxis is mediated by recipient antibodies to donor blood components.

Improperly obtained, handled or administered blood components may cause endotoxemia and/or complement activation. Rarely, citrate in the ACD solution may result in **hypocalcemia**.

At the first sign of a problem, the transfusion should be stopped immediately and replaced by **isotonic crystalloid solution**. **Flunixin meglumine** (1.1 mg/kg IV) may be indicated and **calcium gluconate** should be given if hypocalcemia is identified. Collapse or profound dyspnea should be treated with **epinephrine** (adrenaline) (0.01–0.02 mL/kg of 1:1000 solution IM). Another blood or plasma donor should be identified unless the adverse reaction is known not to be immunologically mediated.

Chapter 10

The gastrointestinal and digestive system

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Chapter contents

INTRODUCTION

Diseases of the gastrointestinal and digestive system are among the most common problems affecting horses. Mortality and treatment costs exceed those associated with other systems. Gastrointestinal and digestive system diseases cause dysphagia, colic, endotoxic shock, weight loss, diarrhea and liver failure (icterus, hepatoencephalopathy, photosensitization).

DISEASES OF THE ESOPHAGUS

ESOPHAGEAL IMPACTION

Etiology and pathogenesis

Obstruction or "**choke**" is the most common of the esophageal disorders in the horse. Common predisposing factors include feed changes, poor dentition, trauma, inadequate water intake, foreign bodies, and ingestion of dry, coarse feed items (dry grains, ears of corn and pelleted feeds). **Gluttonous horses** that rapidly eat feed without proper mastication or ingest bedding also are at risk of developing esophageal impaction. The lodging of dry material in the esophagus may initiate impaction formation.

Irritation of the esophageal mucosa and esophageal distension may cause **esophageal spasm**, thereby worsening esophageal impaction. Long-standing impaction can result in ulceration and necrosis of the esophageal wall. **Ulceration** of the esophageal wall can lead to esophageal spasm leading to recurrence of impaction. Severe necrosis can result in **perforation**.

Clinical findings and diagnosis

The horse with a physical obstruction of the esophagus may exhibit dysphagia, coughing and nasal regurgitation of food material, water and saliva from the mouth and nostrils. The horse may make repeated attempts at ingestion followed by extension of the head and neck to facilitate swallowing. This is often accompanied by **odynophagia** (painful swallowing), head-tossing and other signs of agitation and frustration.

The time from ingestion to the onset of clinical signs is dependent on the location of the obstruction within the esophagus and can vary from

immediately after ingestion to 10–12 s following ingestion. After an initial excitatory period, forced attempts at swallowing become less frequent, and distress and frustration are replaced by depression, anorexia, electrolyte imbalances and dehydration. Intermittent signs of obstruction may indicate a more complex underlying disease and justify further diagnostic evaluation. **Aspiration pneumonia** (*q.v.*) is a frequent complication of esophageal obstruction.

Diagnosis of esophageal obstruction often is based on clinical signs. Esophageal obstruction can be confirmed by attempting to pass a **nasogastric tube**, which cannot be passed beyond the site of obstruction. Palpation of the neck may reveal enlargement of the cervical esophagus. Crepitation and diffuse cervical enlargement may denote **cellulitis** (*q.v.*) resulting from perforation of the esophageal wall. Thoracic auscultation and ultrasound should be performed to ascertain and monitor the development of aspiration pneumonia.

Transtracheal aspiration (*q.v.*) provides a sample for cytology and bacterial culture as an aid in determining the identity and antimicrobial sensitivity of the bacterial organisms causing pneumonia. Gram-positive cocci (especially *Streptococcus* spp.), Gram-negative enteric bacteria (*Escherichia coli, Proteus* spp., *Klebsiella* spp. and *Pseudomonas* spp.) and anaerobic bacteria are all common. **Aspiration pneumonia** (*q.v.*) sometimes results in severe consolidation, abscessation or pleuritis, which can best be evaluated with thoracic radiography and ultrasonography.

Horses with esophageal obstruction that recurs or does not resolve after conservative therapy should be evaluated for esophageal foreign body, ulceration, stricture, diverticulum and megaesophagus (*q.v.*).

Endoscopy and radiography are helpful for definitive diagnosis. The endoscope length must be 200 cm to examine the entire esophagus. A flexible endoscope with insufflation and irrigation capabilities is necessary for a thorough and complete examination. Endoscopic examination is best performed by fully inserting the endoscope into the insufflated esophagus and then slowly withdrawing it. Ulceration, stricture, diverticulum or dilatation may be seen. With the esophagus relaxed, normal longitudinal mucosal folds should be seen. The mucosa should be white to pale pink in color. Insufflation causes flattening of these folds and permits evaluation of luminal diameter. **Transverse folds** can be iatrogenically produced by moving the endoscope aborally and should not be mistaken for mural lesions.

Survey radiographs may reveal the presence of a feed impaction or foreign body. Radiography performed within 24–48 h after relieving the obstruction may reveal **dilatation of the esophagus** in the area of the obstruction, visible as air contrast. **Barium**, given orally as a paste (85% with 120 mL water), or as a liquid (72% with 420 mL water) under pressure via a nasogastric tube, will delineate the longitudinal mucosal folds and localize the obstruction. Escape of barium into the surrounding tissues indicates **rupture** of the esophagus.

Liquid barium (480 mL) followed by air (480 mL) provides a double contrast study and is best for evaluation of the mucosal lesions, such as circumferential mucosal ulcers secondary to feed impactions. Swallowing during contrast studies may produce radiographic artifacts that mimic an esophageal stricture. **Xylazine** (0.25–1.1 mg/kg IV) and **butorphanol** (0.02–0.08 mg/kg IV)

or **detomidine** (0.01–0.02 mg/kg IV) given 5 min before the study helps to eliminate this artifact by suppressing the swallow reflex.

Manometric techniques to evaluate esophageal dysfunction are routinely used in human medicine and have been developed for use in horses. The availability and technical difficulty of this procedure, however, has limited its use in equine practice.

Treatment and prognosis

Prompt therapy is vital to successful management of esophageal impactions. Feed impactions become **more inspissated** over time, thereby making removal more difficult and complications more likely. Impactions present for only a few hours can sometimes be relieved by sedating the animal with **xylazine** (0.25–1.1 mg/kg IV) and **butorphanol** (0.02–0.08 mg/kg IV) or **detomidine** (0.01–0.02 mg/kg IV) to reduce swallowing, thereby decreasing the frequency of contractions of the esophagus. Access to food and water should be prevented.

Nasal intubation with **gentle warm water lavage** under xylazine sedation is successful in relieving most simple impactions. If gentle lavage fails, a cuffed nasogastric tube may be placed in the sedated animal thereby allowing the lavage to be performed under moderate pressure without reflux of fluid back into the pharynx. External massage may increase the efficacy of lavage. If this is unsuccessful, the animal should be muzzled to prevent food or water intake and administered **balanced, isotonic IV fluids**. After softening the impaction by rehydration of the patient, sedation and lavage should be repeated. Excessively aggressive lavage can result in severe aspiration or esophageal damage and/or perforation. Attempting to remove the impaction by applying pressure with a nasogastric tube often lodges the impaction in the narrower, more distal esophagus or causes perforation of the esophagus.

Relaxation of the esophagus would facilitate removal of the obstruction by preventing **esophageal spasm**. Detomidine, xylazine, butorphanol and guaifenesin only slightly reduce the strength of contractions of the esophagus but these sedatives do reduce the **frequency of contractions** of the esophagus by reducing the attempts to swallow. **Oxytocin** (0.11–0.22 IU/kg IM) and **acepromazine** (0.04–0.06 mg/kg IV) have a slight effect on the strength of contraction of the esophagus, thereby minimally reducing the impact of spasm.

Because these medications lack a pronounced effect on esophageal contraction, general anesthesia and intubation with a **cuffed endotracheal tube** may be necessary in cases that are refractory to standing warm water lavage. This technique reduces the likelihood of aspiration, provides more esophageal muscular relaxation, and reduces the chance of perforation.

Following relief, **feed should be withheld** for at least 24 h to allow esophageal function to return to normal. After 24–48 h, frequent interval, small volume, soft, moist mashes (alfalfa pellets or complete feed) and/or grass should be fed for 1–7 days. Feeding of hay and other dry feeds **should not be resumed** until it is felt that the esophagus has healed and returned to normal function. In some cases, endoscopic examination is needed to assess resolution of **secondary esophageal damage**. Horses should not be allowed to ingest bedding or other foreign material. Fresh water should be available at all times and electrolyte abnormalities corrected with oral or IV solutions.

Broad-spectrum antimicrobial therapy should be instituted for at least 7 days for **aspiration pneumonia** (*q.v.*). Long-term antimicrobial therapy is necessary in cases in which significant lung damage due to aspiration has occurred. Any underlying problems (e.g. management and dentition) should be corrected.

Impactions that do not respond to conservative therapy should be definitively identified, localized and relieved by **surgical intervention**. Either extraluminal massage or longitudinal esophagotomy may be performed. The goals of surgery are to relieve the obstruction and to return the esophagus to near normal size and function with minimal contamination and stricture formation at the surgical site. This requires strict asepsis and meticulous surgical technique. **Longitudinal esophagotomy** with primary closure of the incision results in minimal complications when performed in a region of normal esophagus. This procedure has a favorable prognosis for first intention healing and is preferred over manipulations that may induce further esophageal trauma. Postoperative therapy includes **withholding of feed and water** for 48–72 h with IV fluid therapy to correct electrolyte and acid–base abnormalities. Broad-spectrum antimicrobial drugs should be administered perioperatively if esophagotomy is performed or if there is a risk of **aspiration pneumonia** (*q.v.*). Beginning 48 h after surgery, frequent interval, small volume, soft, moist mashes should be fed for 7–10 days.

Impactions of short duration that are properly managed have a **good prognosis**. Reimpaction with premature ingestion of coarse feed and aspiration pneumonia (*q.v.*) are the most common complications. Impactions of long duration (⩾24 h) are accompanied by damage to the esophageal wall and more severe aspiration and have a more guarded prognosis. Esophageal impactions requiring surgery have a **guarded prognosis**. Stricture formation, fistula formation, incisional dehiscence and descending cellulitis with resulting pleuritis are all possible complications, which occur with a higher incidence when the esophageal wall is compromised. Esophageal impactions leading to perforation have a grave prognosis.

ESOPHAGEAL FOREIGN BODY

Etiology and pathogenesis

Ears of corn, pieces of wood, wire, and medication boluses can all become lodged within the esophagus. These result in trauma to the mucosa and distension of the esophageal wall. Prolonged distension of the esophagus can lead to **mucosal necrosis and tearing of the muscular layer**, which may progress to perforation. The presence of the foreign body, swelling of the wall, and accumulation of feed material lead to obstruction of the esophageal lumen (*q.v.*).

Clinical findings and diagnosis

Clinical findings are similar to those found with impactions (*q.v.*). If the foreign body is located within the cervical esophagus it may be externally palpable, however **extreme caution** should be used during palpation to prevent further trauma to the wall. When there is **perforation** of the esophagus,

diffuse cervical cellulitis and abscessation are readily apparent (*q.v.*). Diagnosis usually is made by radiography and/or endoscopy.

Treatment and prognosis

If a secondary impaction is present, it must be relieved before attempting to remove a foreign body. Non-surgical methods for removal include **endoscopically guided retrieval** or pushing the object into the stomach by use of a **nasogastric tube**. Because the risk of esophageal trauma and perforation with these techniques is great, surgery is preferred.

Longitudinal esophagotomy with primary closure results in minimal complications when performed in a region of normal esophagus. Postoperative therapy includes withholding of feed and water for 48–72 h with IV fluid therapy to correct electrolyte and acid-base abnormalities. Broad-spectrum antimicrobial drugs should be administered. Following the initial postoperative period, frequent interval, small volume, soft, moist mashes should be fed for 7–10 days.

ESOPHAGEAL STRICTURE

Etiology and pathogenesis

Narrowing of the esophageal lumen due to stricture formation is usually present as an annular lesion and may be classified into three types:

1. **Mural lesions** that involve the adventitia and muscularis
2. **Esophageal rings** or webs that only involve the mucosa
3. **Annular stenosis** that involves all the layers of the esophageal wall.

Strictures usually result from **circumferential damage** to the esophagus, which heals with fibrous tissue. Impactions of **extended duration** with resultant circumferential mucosal irritation and ulceration, esophageal trauma resulting from attempts at relieving an obstruction, and surgical correction of previous annular lesions (*q.v.*) are common forms of trauma leading to stricture. Gastrointestinal disease resulting in **secondary reflux esophagitis** (*q.v.*) may result in stricture formation. Severe external cervical trauma occasionally will cause esophageal damage that heals with a stricture.

Clinical findings and diagnosis

The clinical signs associated with esophageal stricture are caused by **secondary feed impaction** at the proximal aspect of the constricted segment. Thus the clinical presentation of stricture is similar to that of esophageal obstruction. Endoscopic examination after removal of the secondary feed impaction will generally reveal the stricture. Maximal reduction in esophageal lumen size occurs up to 30 days after esophageal trauma or surgery; therefore, follow-up examination may be necessary. If the impaction is corrected without detection of the stricture, recurrent obstruction is likely.

Stricture formation usually impedes the passage of a **nasogastric tube** into the stomach and may be identified endoscopically or by positive pressure contrast radiography. Swallowing during contrast studies may produce **radiographic artifacts** that mimic an esophageal stricture. IV xylazine, given 5 min

prior to examination, suppresses the swallow reflex and reduces this swallowing artifact.

Treatment and prognosis

Conservative management of stricture formation is directed at **dilating the stenotic segment** of esophagus and is most successful in early cases. Post-surgical strictures and those following circumferential mucosal ulceration may be dilated by feeding **small quantities of a low bulk** diet over a period of several months. Grass and mashes made of complete feed or alfalfa pellets are satisfactory diets. Concurrent non-steroidal anti-inflammatory drug (NSAID) therapy, phenylbutazone (2.2–4.4 mg/kg b.i.d. PO or IV), may be helpful. Following circumferential esophageal ulceration, maximal reduction in luminal diameter occurs at approximately 30 days post obstruction but this returns to normal by 60 days from the original insult. Therefore, if possible, it is important to **postpone surgical intervention** for at least 60 days, to assess maximal luminal diameter and corresponding clinical response to conservative therapy. **Bougienage** (passing a cylinder into a passage) has also been used in the management of equine esophageal stricture.

Chronic strictures (⩾60 days in duration) have a mature cicatrix that is usually unresponsive to conservative attempts at dilatation. These may be corrected by esophagomyotomy, partial or complete resection and anastomosis, or a patch graft (*q.v.*) using the sternocephalicus or brachiocephalicus muscle.

Mural strictures respond well to **esophagomyotomy** and have the best prognosis for recovery without re-stricture. In this procedure the esophagus is incised longitudinally through the stricture to the level of the mucosa. The myotomy is not closed but the surrounding tissues are apposed.

Longitudinal esophagomyotomy and mucosal resection are used to relieve strictures caused by mucosal rings or webs and annular cicatricial lesions involving all layers of the wall. In cases of extensive stricture formation where the mucosa cannot be closed, regeneration of the mucosa will occur within the muscularis and adventitia. This procedure is indicated when myotomy fails to correct the stricture, since it carries a greater risk of re-stricture than myotomy alone.

The diameter of the esophageal lumen may also be increased in cases of extensive stricture and annular stenosis through use of a **patch graft** utilizing the **sternocephalicus or brachiocephalicus muscle**. Under general anesthesia, the surgical procedure begins by approaching the esophagus via the ventral midline or laterally. After nasogastric intubation, a longitudinal incision is initially made through the muscularis from a point 3 cm distal to and extending 3 cm proximal to the stricture. The incision is then extended through the submucosa and mucosa. The caudal portion of the muscle belly of the brachiocephalicus or sternocephalicus is mobilized by blunt dissection. The muscle should maintain its proximal and distal attachments and should be freely movable as to not exert tension on the closure with movement of the neck. Routine closure with suction drains is performed, and extraoral alimentation is preferred for 10 days. Indwelling nasogastric tubes will only stimulate salivation and increase the incidence of fistula formation.

Complete resection and anastomosis of the esophagus should be reserved for cases of rupture in which the muscularis is severely compromised.

Placement of an **esophagostomy tube** distal to the lesion for extraoral alimentation greatly facilitates healing and minimizes incisional complications. An indwelling nasogastric tube is not recommended due to stimulation of saliva formation, thus increasing the incidence of fistula formation.

The prognosis for correction of esophageal strictures is guarded. Conservative management of early strictures is sometimes successful. However, surgical management of chronic strictures often is complicated by re-stricture, fistula formation, incisional dehiscence and descending cellulitis with resulting pleuritis (*q.v.*). Surgical procedures and diseases of the esophagus in the cervical area may also result in **laryngeal hemiplegia** (*q.v.*) because of the close proximity of the recurrent laryngeal nerves.

ESOPHAGEAL DIVERTICULUM

Etiology and pathogenesis

Diverticula of the esophagus are a rare cause of dysfunction. They are usually acquired lesions and may be classified into two types. A **traction or true diverticulum** results from **periesophageal fibrosis**, causing an outward tenting of all the layers of the esophageal wall. These commonly develop at a site of an esophagotomy or traumatic wound of the esophagus that is allowed to heal by second intention. They may also occur at a surgical or traumatic site where leakage of saliva has induced inflammation or abscess formation.

A **pulsion or false diverticulum** results from protrusion of mucosa and submucosa through a defect in the muscular layers of the esophageal wall. Pulsion diverticula may result from fluctuations in intraluminal pressure and damage of esophageal musculature by impacted feed material. In the horse **external trauma** is the most common cause of diverticula.

Clinical findings and diagnosis

Diverticula of the esophagus should be suspected when enlargement of the cervical area and dysphagia are present, yet **a nasogastric tube can be passed** into the stomach without difficulty. **Positive contrast radiography** confirms the diagnosis. During barium swallow esophograms, **traction diverticula** are spherical and have a wide area of communication with the esophagus. **Pulsion diverticula** are flask shaped and have a narrow area of communication with the esophagus. Positive pressure contrast studies that distend the esophageal lumen and outline the opening of the diverticula may assist in differentiation between the two types. Endoscopy is also useful in localizing the lesion and determining the size of the opening of the evagination.

Traction diverticula, even when large, produce minimal clinical signs and rarely require treatment. Pulsion diverticula, however, tend to enlarge progressively, thereby increasing the possibility of esophageal obstruction and rupture.

Treatment and prognosis

Diverticulectomy should be performed when the mucosal sac is very large and the communication with the esophagus is narrow. Pulsion diverticula may be repaired surgically by either diverticulectomy with resection of the

mucosal–submucosal sac followed by reconstruction of the mucosa, submucosa and muscularis, or inversion of the mucosal–submucosal sac with reconstruction of the muscularis.

Mucosal inversion is the preferred procedure for most cases because it minimizes the risk of postoperative complications such as dehiscence or leakage, infection, fistula formation and postoperative re-obstruction. Soft, moist feed mashes should be fed for 4–6 days following surgery and treatment with antimicrobial drugs is indicated when contamination is encountered during surgery. Prognosis is dependent on the type, size and duration of the diverticulum. If the esophageal lumen is not invaded and the integrity of the esophageal wall is intact, the overall prognosis for recovery is good.

INTRAMURAL CYST

Etiology and pathogenesis

Esophageal mural cysts are a rare cause of dysphagia and are usually located between the mucosa–submucosa and muscularis of the esophageal wall. They are often lined with stratified squamous epithelium and filled with keratinaceous material (epithelial inclusion cysts). These cysts are most commonly seen in young horses and are believed to be a **developmental anomaly**.

Clinical findings and diagnosis

Dysphagia, regurgitation and a palpable soft tissue mass in the cervical area are clinical signs usually associated with mural cysts. Failure of or resistance to complete passage of a nasogastric tube is also a common finding. Contrast radiography demonstrating a mural filling defect, ultrasonography and endoscopy often provide a definitive diagnosis.

Treatment and prognosis

Surgical repair is accomplished through enucleation of the cyst with inversion or resection of redundant mucosa. A longitudinal esophagomyotomy is performed with meticulous dissection of the intact cyst away from the esophageal wall without perforation of the mucosa. The redundant mucosa is then treated by inversion, preferably, or by diverticulectomy if the mucosal sac is too large to invert. Prognosis for recovery is good if the cyst can be resected en bloc and the mucosa is not invaded.

ESOPHAGITIS

Etiology and pathogenesis

Esophagitis may be caused by ingested irritants (e.g. topical irritant medications or blisters, blister beetles or cantharidin toxicity), prolonged use of a nasogastric tube, or reflux of gastric or gastroduodenal contents (*q.v.*). NSAID therapy can lead to esophageal ulceration. The result can be **inflammation, erosion and ulceration** of the esophageal mucosa. Chronic inflammation produces pain and may decrease esophageal motility. In severe cases, megaesophagus can result.

Lower esophageal and gastric inflammation may reduce the tone of the lower esophageal sphincter, thereby causing or perpetuating inflammation of

the lower esophagus. **Reflux esophagitis** most often occurs in foals with gastric paresis or gastric outlet obstruction caused by gastric ulceration. Duodenogastric reflux may occur in horses with duodenitis/proximal jejunitis or small intestinal obstruction.

Clinical findings and diagnosis

Esophageal inflammation causes **pain**, which is usually manifest as anorexia, stretching the neck, odynophagia (*q.v.*) and ptyalism (excessive salivation). These signs may be most obvious when the animal is attempting to eat. Dysphagia may result if esophageal motility is affected. The diagnosis can be made via **endoscopic examination** by revealing a hyperemic, edematous, eroded or ulcerated esophageal mucosa.

Treatment and prognosis

Exposure to the caustic agent should be removed and the esophagus allowed to rest. Slurries made of pelleted feed and grass should be fed frequently in small amounts. The animal should not be allowed to eat coarse roughage. Reflux esophagitis should be treated with the proton pump antagonist, **omeprazole** (4.4 mg/kg PO), or H_2-receptor antagonists such as **cimetidine** (20 mg/kg PO t.i.d. or 4.4 mg/kg IV q.i.d.) and **ranitidine** (6 mg/kg PO or IV b.i.d.) to decrease gastric acid production.

Metoclopramide (0.02–0.1 mg/kg SC q 4–12 h) and **bethanechol** (0.03 mg/kg SC or 0.4 mg/kg PO q 6–8 h) increase the tone of the lower esophageal sphincter and distal esophageal and gastric motility and, therefore, may be useful in foals with gastric paresis and reflux esophagitis. Metoclopramide and bethanechol should not be used in animals with **gastric outflow obstruction**. Metoclopramide sometimes causes neurologic side effects. The prognosis with esophagitis is usually good. In the case of some **ingested toxins** (e.g. cantharidin), the resulting systemic disease is of greater consequence than the esophagitis. The prognosis is poor if severe megaesophagus (*q.v.*) develops.

MEGAESOPHAGUS

Etiology and pathogenesis

Megaesophagus is **esophageal dilatation** resulting in accumulation of food material and fluid within the esophageal lumen. Megaesophagus can be idiopathic or secondary to numerous primary disease processes. **Congenital idiopathic megaesophagus** has been reported in a few weanling foals. **Secondary megaesophagus** most often results from reflux esophagitis and chronic esophageal obstruction, such as that caused by vascular ring anomalies, lymphosarcoma involving cervical or mediastinal lymph nodes, or abscessation (*q.v.*).

Neuromuscular diseases may disrupt esophageal motility and cause chronic dilatation and ineffectual esophageal contraction. Dysphagia associated with esophageal disease has been reported in horses with botulism, equine protozoal myeloencephalitis, equine herpesvirus, and damage to the vagus nerve from trauma, neoplasia and lymphadenopathy (*q.v.*).

Clinical findings and diagnosis

Clinical signs of megaesophagus include **nasal reflux** of food and water. **Aspiration pneumonia** (*q.v.*) is a common sequel and, therefore, fever, coughing and dyspnea are often present. In cases of secondary megaesophagus, signs of the primary disease process (e.g. weakness, ataxia, etc.) are common.

Esophageal dilatation can be demonstrated by **contrast radiography** and **endoscopy**. Dilatation and accumulation of contrast material on sequential radiographs confirm the presence of impaired esophageal clearance. On esophagoscopy, dilatation, absence of peristaltic waves, and pooling of feed or fluid are observed. In cases of esophageal obstruction or esophagitis, the primary lesion may be observed via contrast radiography and esophagoscopy. A thorough neurologic examination and CSF analysis are indicated if megaesophagus is suspected to be a complication of a **primary neurologic disease** (*q.v.*).

Treatment and prognosis

In **secondary megaesophagus**, therapy for the obstruction, esophagitis, neurologic disease or neuromuscular disease should be instituted. There is no specific therapy for idiopathic megaesophagus; however, **metoclopramide** (0.02–0.1 mg/kg SC q 4–12 h) and **bethanechol** (0.03 mg/kg SC or 0.4 mg/kg PO q 6–8 h) may be used to improve distal esophageal peristalsis. Because aspiration causes mixed bacterial contamination of the lung, broad-spectrum antimicrobial coverage is necessary. **Dietary management** is necessary to prevent further pulmonary soilage and to maintain nutrition and hydration. If the resulting dysphagia is severe and prolonged, parenteral or enteral feeding will be necessary. If the dysphagia is incomplete, a **slurry** of pelleted feed or grass may be fed.

The prognosis depends upon the severity and cause of the dilatation. The prognosis for return of esophageal function is poor if the dilatation is severe and long-standing. Cases in which nasal reflux of food material and **pulmonary soilage** can be avoided by proper dietary management have a better prognosis. The prognosis in secondary megaesophagus depends upon the prognosis associated with the primary disease process. In foals with congenital megaesophagus, function may return to normal as the foal matures.

ESOPHAGEAL NEOPLASIA

Etiology and pathogenesis

Neoplastic diseases of the esophagus are rare. **Squamous cell carcinoma** (*q.v.*) is the most common and may extend from its origin in the squamous epithelium of the stomach. Other reported neoplasms of the equine esophagus include fibromas and melanomas. Clinical signs result from **esophageal obstruction** (*q.v.*).

Clinical findings and diagnosis

Clinical signs reflect esophageal **pain** and/or obstruction and include anorexia, stretching the neck, odynophagia, ptyalism and dysphagia. Diagnosis is based on endoscopy, radiography and biopsy. Endoscopy will reveal a **nodular mass**, which may be ulcerated. Double contrast radiography

may reveal an ulcerated mass. Ultrasound examination from the left cranial abdomen may reveal a mass in the wall of the stomach. **Multiple biopsies** should be obtained via endoscopy. Small biopsies of the mass surface obtained via endoscopy most often reveal surface necrosis and bacterial contamination. Attempts should be made to obtain samples of tissue deep to the surface. The stomach should also be examined. Double contrast radiography may reveal an ulcerated mass.

Treatment and prognosis

There is no treatment for horses with esophageal neoplasia.

DISEASES OF THE STOMACH

GASTRIC ULCERATION

Etiology and pathogenesis

The specific etiology of gastric ulceration in horses is unknown. Gastric acid hypersecretion, disturbances of gastric mucosal blood flow, impaired production of prostaglandin (PG) E or the gastric mucus/bicarbonate layer, and gastric emptying disorders are potentially involved in the initiation of gastric ulceration. Furthermore, after ulceration occurs, gastric acid **prevents healing** of the gastric mucosa. Other disease processes (e.g. foal diarrhea and neonatal sepsis), **stressful conditions** (e.g. horses in show and race training) and medication (e.g. NSAIDs [*q.v.*]) are factors commonly associated with a higher incidence of ulceration.

Modern management practices in which horses are stall confined and eating high energy feeds intermittently (e.g. twice daily) rather than grazing continuously on roughage are major factors in development of gastroduodenal ulceration.

Clinical signs and diagnosis

Clinical signs in **foals** with gastric ulcers depend upon the region of the stomach involved. In most foals with gastric ulcers, lesions are distributed throughout the squamous mucosa. These foals may be **asymptomatic** or exhibit poor growth, rough haircoat, a "pot belly" appearance, bruxism, salivation, colic, dorsal recumbency and, sometimes, diarrhea. Lesions can occasionally result in hemorrhage that rarely is associated with anemia or hypoproteinemia. Healing of antral or pyloric lesions can lead to pyloric stricture and obstruction (*q.v.*).

Gastric ulcer syndrome (GUS) also occurs in yearlings and mature horses with an overall prevalence of approximately 10%. Studies have found **squamous ulceration** in 70–100% of racehorses and around 60% of other performance horses. Ulceration of the **glandular mucosa** of the stomach occurs in 60% of horses in a hospital setting. Clinical signs in mature horses classically include **anorexia** and **chronic intermittent colic** of varying severity. Vague clinical signs include **poor performance** or failure to perform to expectations, decreased body condition, poor-quality haircoat and decreased concentrate

consumption. Colic signs in some horses with gastric ulceration are post prandial. Many horses with endoscopic evidence of disease may appear to be clinically normal.

Gastroduodenal ulceration is diagnosed by observation of typical clinical signs, endoscopic findings and response to therapy. A presumptive diagnosis of gastric ulceration can be made when typical clinical signs are observed, other causes of these signs are ruled out, and a response to administration of agents used to treat gastroduodenal ulceration is observed.

Confirmation of the presence of gastroduodenal ulceration is only made by **endoscopic examination**. Lesions occur predominantly in the squamous mucosa adjacent to the margo plicatus. Lesions at the cardia are common and require retroflexion of the endoscope to be observed. In foals >1 mo of age and horses, fasting and sedation will facilitate this procedure. In some neonatal foals, the stomach can be examined with a 100 cm endoscope; however, in older foals a 200 cm endoscope is needed. A 200 cm endoscope is required for examination of the duodenum in foals up to 6 mo of age. Examination of the duodenum in older animals requires a 300 cm endoscope.

Treatment and prognosis

The therapeutic strategy for gastric ulceration is reduction of gastric acid secretion, thereby allowing healing of the damaged mucosa, by use of proton pump antagonists (**omeprazole** 4 mg/kg daily) or H_2-receptor antagonists (**cimetidine** 20 mg/kg PO t.i.d. or 4.4 mg/kg IV q.i.d.; **ranitidine** 6.6 mg/kg PO or IV b.i.d.). Appetite, signs of colic and diarrhea should begin to improve within 48 h of therapy, which should be continued for approximately 28 days.

Because many cases require therapy of longer duration, assessment of ulcer healing via endoscopic examination is useful for determining the duration of therapy. Recurrence has been documented after endoscopic confirmation of healing in some horses. **Maintenance therapy** (omeprazole 2–4 mg/kg daily) has been used in some cases to prevent recurrence of gastric ulceration. A recent study of performance horses revealed that the occurrence and recurrence of gastric ulceration was the same with a lower dose of omeprazole (1 mg/kg/day) as that in horses treated with omeprazole at 2 mg/kg/day. Studies to document the overall impact of preventative therapy on the incidence of gastric ulceration have not been performed.

Other drugs may be useful in combination with H_2-receptor antagonists. **Sucralfate** (2–4 g PO q.i.d.) has been used in combination with H_2-receptor antagonists for treatment of gastric ulcers in horses. Sucralfate promotes synthesis of PGE, stimulates mucus secretion and protects ulcerated mucosa during healing. PGE inhibits gastric acid secretion and promotes mucosal blood flow, mucus production and mucosal cell division. **PGE analogues** have been effective therapy for gastric ulcers in humans but have not been used clinically in horses due to expense. **Antacids** have limited efficacy in treatment of gastric ulcers in horses due to the large doses (200 mL/500 kg BW) required.

The prognosis with gastric ulceration is good if appropriate therapy is continued for an adequate period of time and if complications do not develop. On the other hand, animals with **duodenal ulceration** are less responsive to therapy and more likely to develop complications. Complications that may result from gastroduodenal ulceration include gastroesophageal reflux,

megaesophagus with aspiration pneumonia, gastric paresis, pyloric or duodenal stricture, gastric or duodenal perforation, and ascending cholangitis and hepatitis (*q.v.*).

GASTRITIS

Etiology and pathogenesis

Gastritis occurs secondary to the reflux of duodenal contents from the pylorus to the stomach. The gastric inflammation probably results from exposure to bile acids and gastric acid. **Intestinal reflux** results from either small intestinal obstruction or ileus (*q.v.*).

Clinical findings and diagnosis

Clinical findings result from small intestinal obstruction or ileus and, therefore, include signs of abdominal pain, nasogastric reflux, and rectal palpation of distended small intestine. If an endoscopic examination is performed, the inflamed, eroded and/or ulcerated gastric mucosa will be seen.

Treatment and prognosis

The gastritis will resolve after the cause of the small intestinal obstruction and ileus is removed. It is necessary to frequently **remove fluid** accumulating in the stomach via nasogastric intubation to prevent excessive gastric distension and rupture. The prognosis depends upon the disease causing the small intestinal obstruction.

GASTRIC IMPACTION

Etiology and pathogenesis

Although gastric impaction is not a common disease in horses it is occasionally diagnosed as a cause of colic (*q.v.*). The cause is unknown but may be associated with ingestion of **coarse roughage** and **inadequate water** intake.

Clinical findings and diagnosis

Gastric impaction causes anorexia and varying degrees of abdominal pain. Rectal examination is normal. Diagnosis can be made when endoscopic examination or laparotomy reveals a large volume of desiccated ingesta in the stomach. Mild cases probably respond to therapy without definitive diagnosis.

Treatment and prognosis

Nasogastric lavage with small amounts of water (1–2 L; as described to reflux a horse) and **IV balanced polyionic fluids** (such as acetated Ringer's; 50–100 mL/kg/day) are recommended to hydrate the impacted ingesta, thereby facilitating passage. However, if surgery is attempted due to the severity of the clinical signs, the impaction may be removed by injecting 4 L sterile saline solution into the stomach and massaging the impaction. Postoperative care includes lavaging the stomach to remove remnants of the impaction. Severe gastric impaction can result in **gastric rupture** (*q.v.*) with

medical or surgical therapy, although the prognosis improves if treated early, before severe desiccation and distension occur.

GASTRIC NEOPLASIA

Etiology and pathogenesis

Neoplastic diseases of the equine stomach, including squamous cell carcinoma, lymphosarcoma, mesothelioma and gastric adenocarcinoma (*q.v.*), occur infrequently. **Squamous cell carcinoma**, originating in the gastric squamous epithelium, is by far the most common. These tumors may metastasize, cause gastrointestinal bleeding or obstruct the cardia.

Clinical findings and diagnosis

Gastric squamous cell carcinoma occurs most frequently in older horses. Presenting signs often include **weight loss**. Horses may develop **intermittent colic** due to obstruction of the cardia or metastasis to other abdominal organs. Colic occurring immediately after eating is especially common. Obstruction of the cardia can result in megaesophagus (*q.v.*) and/or nasal regurgitation of food. Horses with thoracic metastasis often develop thoracic effusion, which may cause tachypnea (*q.v.*). Melena, anemia and hypoproteinemia may occur in horses with gastrointestinal bleeding. Occasionally squamous cell carcinoma causes gastric rupture (*q.v.*) and peritonitis (*q.v.*). Diagnosis can be made by cytologic examination of peritoneal fluid in horses with abdominal metastasis.

Treatment and prognosis

There is no treatment for horses with gastric neoplasia.

PYLORIC HYPERTROPHY

Etiology and pathogenesis

The cause of muscular hypertrophy of the pylorus is unknown. Although this is a rare cause of colic, it has been diagnosed in a few young horses.

Clinical findings and diagnosis

Horses with pyloric hypertrophy present with signs of abdominal pain and nasogastric reflux. Rectal examination does not reveal intestinal distension. Hypochloridemic metabolic alkalosis may result from reflux of gastric fluid. Both chronic intermittent and acute abdominal pain occur in horses with pyloric hypertrophy.

Treatment and prognosis

Pyloric hypertrophy has been successfully treated via **pyloromyotomy, Weinberg modified Heineke—Mikulicz pyloroplasty** and a **side-to-side gastroduodenostomy**. These surgical techniques are not routine, and the small number of cases makes determination of the long-term prognosis difficult. IV therapy with 0.9% saline solution should precede surgery in animals with hypochloridemic metabolic alkalosis.

DISEASES OF THE SMALL INTESTINE CAUSING COLIC

INTRODUCTION

Approximately 34% of all colic cases at referral institutions involve small intestine diseases.

Abnormalities of the equine small intestine may be broadly classified as either **physical** or **functional** obstructions. **Non-strangulating physical obstructions** may be caused by either intraluminal masses or reduction of the lumen by intramural thickening or extramural compression. **Strangulating obstructions** can follow incarceration of intestine through internal or external hernias, intussusception, or a greater than 180° twist of a segment of intestine on its own mesentery.

Functional obstruction, referred to as adynamic or **paralytic ileus**, may be either idiopathic in origin, result from **inflammatory disease** (e.g. duodenitis and proximal jejunitis [*q.v.*]), or result from **serosal irritation** due to surgical manipulation. The majority of cases of small intestinal colic (58–80%) are caused by **strangulating lesions** and the remainder by simple and functional obstructions. The ileum is involved in 41–46% of all small intestinal obstructions.

Intestinal obstruction prevents the aboral movement of gastrointestinal contents, thereby resulting in **distension** of the intestine. As the distension increases, venous drainage from the intestinal wall is impaired and the mucosa becomes congested and edematous. If the obstruction persists for a prolonged period of time, significant compromise of intestinal vascular integrity may result in mucosal ischemia. **Shock** (*q.v.*) will develop with prolonged ileus due to decreased oral intake and accumulation of fluid in the intestinal lumen. With progressive distension, **gastric rupture** (*q.v.*) may occur.

In strangulating obstructions, the above events are combined with rapid tissue hypoxia and ischemia of the affected segment leading to necrosis and transmural leakage of endotoxin. **Cardiovascular deterioration** rapidly follows transperitoneal absorption of endotoxin resulting in hypovolemia and endotoxic shock (*q.v.*). For these reasons it is important that small intestinal lesions are identified early in the disease process, based on a thorough history and physical examination.

Abdominal pain, small intestinal **distension** (identified by transrectal palpation and abdominal ultrasound examination), **nasogastric reflux** and decreased or **absent borborygmi** are common clinical signs in patients with small intestinal disease. The expression of abdominal pain can depend on the temperament of the horse, the degree of restraint, administration of sedatives or analgesics, and mental attitude. Reduced or absent borborygmi may be encountered with obstruction developing at any site in the gastrointestinal tract. Ultrasonographic examination can also be used to assess the presence or absence of intestinal motility in individual segments of bowel. **Strangulating obstructions** usually cause severely distended, turgid small intestine.

With both non-strangulating and functional obstructions, mild to moderate **distension of small intestine** commonly is present. The severity of small intestinal distension can be assessed via rectal examination and ultrasonographic examination of the abdomen. In cases of ileal impaction, ileocecal and jejunojejunal intussusception, and inguinal hernias, transrectal palpation may

Table 10.1 Analgesics for control of acute abdominal pain

Analgesic	Dosage	Efficacy
Flunixin meglumine	0.25–1.1 mg/kg IV or IM	Excellent
Detomidine hydrochloride	0.01–0.04 mg/kg IV or IM	Excellent
Xylazine hydrochloride	0.2–1.1 mg/kg IV or IM[1]	Good
Butorphanol tartrate	0.02–0.08 mg/kg IV or IM[2]	Good
Ketoprofen	1.1–2.2 mg/kg IV	Good
Dipyrone	10 mg/kg IV or IM	Poor
Phenylbutazone	2.2–4.4 mg/kg IV	Poor

[1] *Repeated administration may compromise colonic motility.*
[2] *IV administration may cause excitement if used alone. Often combined with xylazine or detomidine.*

reveal the specific etiology of the obstruction. Small intestinal distension may also occur with large intestinal obstruction or displacement, causing secondary extraluminal compression of the small intestine.

Therapy for small intestinal lesions includes controlling pain, maintenance of cardiovascular and metabolic status, and establishing a patent and functional intestine. Pain control is accomplished by **gastric decompression** via a nasogastric tube and administration of visceral and centrally acting analgesics (Table 10.1). Maintenance and support of cardiovascular and metabolic status is achieved by IV administration of balanced, isotonic fluids. In most cases of physical obstruction, **ventral midline exploratory celiotomy** is necessary for identification and correction of the inciting lesion.

NON-STRANGULATING OBSTRUCTIONS

Non-strangulating obstructions cause partial or complete luminal obstruction without significant compromise of the vascular integrity of the intestine. These may be classified as intraluminal or extraluminal obstructions. **Intraluminal obstructions** include ascarid impactions, feed impactions, ileal hypertrophy and neoplasia (*q.v.*). **Extraluminal** causes of intestinal obstruction include intra-abdominal masses, adhesions and abscesses (*q.v.*).

Ascarid impaction

Etiology and pathogenesis

Heavy ascarid (*Parascaris equorum*) infestation (*q.v.*) can lead to intraluminal obstruction in foals, weanlings and yearlings (median age of 5 mo, range of 4–24 mo). The affected animals usually have a poor parasite control program leading to heavy infestation with ascarids. **Ascarid impactions** commonly follow use of **high efficacy anthelmintics** such as ivermectin, which inhibit neuromuscular transmission, thereby paralyzing the ascarid. Intussusception, peritonitis and intestinal rupture (*q.v.*) are possible sequels to ascarid impaction. Foals usually develop immunity to the parasite by 6 mo to 1 yr of age and, therefore, ascarid impactions are uncommon in adult horses.

Clinical findings and diagnosis

Clinical signs are dependent on the duration and degree of small intestinal obstruction and may include unthriftiness, poor haircoat and mild to severe

abdominal pain. **Nasogastric reflux** is usually present and may contain ascarids. Transrectal examination reveals multiple loops of distended small bowel. The diagnosis is based on signalment, history conducive of heavy ascarid infestation and clinical signs consistent with small intestinal obstruction.

Treatment and prognosis

Partial obstruction of the intestine with ascarids may be treated medically with **intestinal lubricants** (e.g. mineral oil), **analgesics** (e.g. flunixin meglumine and/or xylazine ± butorphanol tartrate; see Table 10.1), **balanced polyionic IV fluids** (acetated Ringer's; 50–60 mL/kg/day) and **low efficacy anthelmintics** (e.g. fenbendazole 5 mg/kg PO) to prevent further impaction. If obstruction is complete or if medical therapy is unsuccessful, **surgical intervention** is necessary to relieve the obstruction. **Multiple enterotomies** may be necessary to remove the obstruction. Mortality rates can be as high as 92%, with peritonitis and adhesions accounting for most deaths.

Ileal impaction

Etiology and pathogenesis

The most common site for intraluminal **feed impactions** of the small intestine is the ileum; however, impactions of the jejunum and duodenum have been reported. The incidence of the disease appears to vary with geographic location, being most common in Europe and the southeastern USA. Mares and Arabians are over-represented in ileal impactions.

The etiology of **ileal impactions** is unknown. An association with feeding fine, high roughage forage, such as coastal Bermuda hay, during the fall/autumn season has been suggested. It is possible that feed material accumulates in the ileum producing an obstruction. **Spasmodic contractions** of the ileum and absorption of water from the lumen worsen the impaction over time. Ileal hypertrophy, mesenteric vascular thrombotic disease, tapeworm infestation (*Anoplocephala perfoliata*) and ascarid impaction (*Parascaris equorum*) (*q.v.*) are less common causes of ileal impaction.

Clinical findings and diagnosis

Clinical signs associated with ileal impaction are variable and depend on the duration of the impaction. Most often the condition occurs in adult horses. Immediately following the impaction, the horse demonstrates signs of moderate to severe **abdominal pain** due to focal intestinal distension and spasmodic contraction around the impaction. Animals usually respond transiently to analgesic therapy.

Early in the disease course, transrectal palpation may reveal a 5–8 cm diameter, firm and smooth-surfaced viscus originating at the cecal base and coursing from right of midline obliquely downward and to the left of midline. Normal borborygmal sounds are usually auscultated. Nasogastric reflux may be absent in these early stages.

During the 8–10 h following the initial episode of colic, small intestinal and gastric distension develops due to the prevention of aboral flow of intestinal contents, thereby resulting in recurrence of signs of pain. **Dehydration and**

depression develop. Nasogastric reflux eventually develops and gastric decompression often provides temporary analgesia. **Borborygmal sounds** become diminished or absent. Transrectal examination reveals multiple loops of moderate to severely distended small intestine. The impaction is often **not palpable** at this time because of displacement and concealment by other loops of distended small intestine.

Hemogram, electrolytes, blood gases and abdominocentesis are usually within normal limits. However, hemoconcentration and elevated peritoneal fluid protein followed by elevated peritoneal nucleated cell count may be observed in long-standing disease.

Treatment and prognosis

Initial therapy of horses with ileal impaction is supportive and should include **gastric decompression**, **balanced polyionic IV fluids** (e.g. acetated Ringer's; 50–100 mL/kg/day), **analgesics** (e.g. flunixin meglumine; see Table 10.1) and intensive monitoring.

Occasionally, the impaction may resolve with medical therapy, however **surgical therapy** usually is necessary. If colic signs persist, ventral midline exploratory celiotomy with reduction of the obstruction by manual extraluminal massage provides the best prognosis for complete recovery. Mixing of the impaction with distal jejunal fluid or direct infusion of the impaction with sterile saline solution or carboxymethylcellulose will facilitate reduction of the impaction. When marked mural edema and congestion are present, evacuation of the ileal contents through a jejunal enterotomy will facilitate reduction of the impaction without excessive manipulation of the bowel.

If resection and anastomosis or bypass (ileocecostomy or jejunocecostomy) is required to relieve the obstruction, the prognosis for survival is reduced.

Ileal hypertrophy

Etiology and pathogenesis

Muscular hypertrophy of the distal ileum may produce narrowing of and partial obstruction of the intestinal lumen. Primary or idiopathic hypertrophy of the muscularis externa and muscularis mucosae is thought to be the result of either **autonomic imbalances** that produce **uncontrollable peristalsis** or a response to neurogenic stenosis of the ileocecal valve. Secondary muscular hypertrophy may result from mucosal damage or strongyle larval migration (*q.v.*). The transition from normal to abnormal bowel is gradual and the hypertrophy occurs in both the circular and longitudinal layers of the muscularis.

Clinical findings and diagnosis

Partial obstruction of the small intestine may produce **chronic weight loss**, lethargy and intermittent signs of mild to moderate abdominal pain. The horse may experience intermittent signs of colic for weeks to months, and in some cases years. Sequential colic episodes often increase in severity. **Transrectal palpation** during these episodes reveals multiple loops of distended small intestine. Complete obstruction produces persistent, moderate to severe abdominal pain that is only temporarily responsive to analgesics.

Definitive diagnosis of partial or complete obstruction is made at surgery or post mortem examination.

Treatment and prognosis

Partial obstruction may respond to medical therapy (see ileal impaction, *q.v.*) but recur at a later time. Surgical correction is performed via ventral midline exploratory celiotomy. Longitudinal ileal myotomy, ileocecostomy or jejunocecostomy may be performed to relieve or bypass the obstruction created by ileal hypertrophy. If no chronic distension of the small bowel has occurred, the prognosis for survival is good.

Intra-abdominal adhesions

Etiology and pathogenesis

Peritoneal adhesions form in response to either peritoneal inflammation or the presence of foreign material in the abdominal cavity. Adhesions may be initiated by peritonitis, ischemic necrosis, bacterial infection, parasite larval migration or surgical manipulation (*q.v.*). Traumatic tissue handling, peritoneal contamination, tissue dehydration, hemorrhage, improper surgical technique and postoperative ileus **all predispose** to adhesion formation.

Intra-abdominal adhesions may be present without altering intestinal function or may cause intestinal obstruction by distortion, stricture or direct compression of the intestinal lumen. **Fibrous adhesions** also form a potential internal hernial orifice or predispose to volvulus. Postoperative adhesions may be formed in 5–7 days and cause clinical signs within 14 days. Most clinical signs associated with intra-abdominal adhesion formation become apparent within 4–8 wk postoperatively.

Clinical findings and diagnosis

Small intestinal adhesions may be present without causing clinical signs. However, following abdominal surgery or peritonitis, a small percentage (22%) of horses later develop recurrent episodes of moderate to severe **abdominal pain** due to adhesions. Clinical and laboratory findings are similar to those described above for horses with ileal impaction (*q.v.*). If adhesions are associated with an active peritonitis, depression, pyrexia, leukocytosis, and elevated peritoneal protein fluid concentration and nucleated cell count may be present. Transrectal palpation reveals **small intestinal distension** and in rare cases adhesions may be palpable. Diagnosis is usually made by history and surgical or post mortem examination findings.

Treatment and prognosis

Every effort should be made to minimize adhesion formation at the time of original insult or surgery. NSAIDs, heparin, carboxymethylcellulose and other pharmacologic agents have been used to minimize adhesion formation, however no drug has been shown unequivocally to prevent their formation without causing other deleterious effects.

In cases that are at a high risk of developing postoperative intra-abdominal adhesions, **sterile carboxymethylcellulose** (1–2 L) may be placed into the

abdomen before closing. In cases where a resection and anastomosis is performed, a bioresorbable hyaluronate–carboxymethylcellulose membrane may be applied over the surgical site to prevent adhesion formation. **Sodium heparin** (intra-abdominal instillation of 40–80 IU/kg in 1 L of 0.9% NaCl) may be added to this regimen, if postoperative hemorrhage is not anticipated to be a problem. Non-traumatic, aseptic, proper surgical technique, constant tissue irrigation and **fastidious hemostasis** should be employed to minimize postoperative complications secondary to adhesion formation.

Surgical intervention includes adhesiolysis and resection and anastomosis of the affected segment of bowel to re-establish luminal patency. Adhesiolysis can also be performed via laparoscopy within 10 days following initial surgery. The prognosis is guarded at best, due to a high incidence of recurrence. Less than 20% of repeat celiotomy cases survive long term.

Neoplasia

Etiology and pathogenesis

With the exception of **lipomas** (*q.v.*), obstruction of the small intestine caused by intra-abdominal neoplasia is rare. Other neoplasms that have been reported to cause small intestinal obstruction by infiltration and stenosis include squamous cell carcinoma, lymphosarcoma, adenocarcinoma, leiomyoma, leiomyosarcoma, ganglioneuroma and fibroma (*q.v.*).

Clinical findings and diagnosis

Clinical signs associated with intra-abdominal neoplasia may include weight loss, fever, anorexia, mild abdominal pain, diarrhea and dependent edema. An intra-abdominal mass may be palpable on transrectal examination. Abdominocentesis may yield neoplastic cells, however multiple attempts and cytospin of samples are often necessary.

Treatment and prognosis

Surgical exploratory or post mortem examination is often necessary to obtain a definitive diagnosis. Prognosis for intra-abdominal neoplasia is **poor** due to local infiltration and metastasis. Focal benign neoplasms may respond favorably to surgical resection, but these are not a common occurrence in the horse abdomen.

STRANGULATING OBSTRUCTIONS

Strangulating obstructions cause **complete luminal obstruction** combined with significant compromise of the vascular integrity of the intestine. **Vascular occlusion** can be either exclusively **venous**, resulting in hemorrhagic strangulation, or **arterial and venous**, resulting in ischemic strangulation.

The hypoxia and ischemia that develop rapidly lead to **necrosis** of the involved segment of intestine. As a result, physical deterioration from hypovolemic and endotoxic shock occurs rapidly in horses with strangulating lesions. Equine small intestinal strangulating obstructions include small intestinal volvulus, lipomas, intussusception and herniation (*q.v.*).

In patients with **small intestinal strangulating obstruction**, therapy is aimed at controlling pain, maintaining cardiovascular and metabolic status, and establishing a patent and functional intestine. Pain control is accomplished by gastric decompression via a nasogastric tube and administration of visceral and centrally acting analgesics (see Table 10.1). Maintenance and support of cardiovascular and metabolic status is achieved by IV administration of **balanced, isotonic fluids**.

Surgical exploration via ventral midline celiotomy is necessary for identification and correction of the lesion. The prognosis is dependent on the duration of illness and amount of intestine affected. With early detection and rapid treatment the prognosis is good. In cases of prolonged duration or cases requiring resection of greater than 60–70% of the small intestine, the prognosis is poor.

Volvulus

Etiology and pathogenesis

A volvulus is the **rotation** of a segment of intestine around the long axis of its mesentery. Although most cases are not accompanied by predisposing lesions, adhesions, infarctions, intestinal incarcerations, pedunculated lipomas and mesodiverticular bands (*q.v.*) can predispose to volvulus. Abrupt dietary changes and verminous arteritis have also been incriminated. The length and segment of the intestine involved is variable, but the ileum is frequently involved due to its fixed attachment at the ileocecal junction.

Clinical findings and diagnosis

Horses presenting with a strangulating obstruction of the small intestine usually exhibit an **acute onset** of progressive, moderate to severe, continuous pain that may initially be responsive to analgesics. However, the effectiveness of analgesics rapidly declines as the disease progresses. There is **rapid, progressive cardiovascular deterioration** indicated by poor peripheral perfusion (hyperemic or cyanotic mucous membranes with a prolonged capillary refill time, and a rapid, weak pulse). Hypovolemia and hemoconcentration develop much more rapidly than in cases of simple obstruction. Hypoproteinemia may develop due to losses of protein via damaged vasculature and mucosa in the ischemic segments.

Nasogastric reflux is often present but, in contrast to simple obstructions, decompression may not provide analgesia. Transrectal examination usually reveals moderate to severe small intestinal distension, and mild tension on the mesentery may elicit a painful response. However, the lack of palpable small intestinal distension does not rule out the possibility of a strangulating lesion, as the distended intestine may be beyond the reach of the examiner.

Abdominocentesis may yield normal or serosanguineous fluid with elevated peritoneal protein concentration ($\geq$3.0 g/dL) and nucleated cell count ($\geq$10 000 cells/μL). The devitalized section of intestine may be isolated from the peritoneal cavity (e.g. within the omental bursa) and the peritoneal fluid analysis may not accurately reflect the degree of intestinal change.

Treatment and prognosis

The strangulated intestine is identified and exteriorized via **ventral midline celiotomy**. The direction of rotation of the segment involved may be determined by palpation of the mesentery at surgery. After correction of the volvulus, intestinal viability should be evaluated and resection and anastomosis performed if deemed necessary by the surgeon. At least 20–30 cm of normal bowel should be included at each end of the resected segment to ensure adequate vascularity at the site of anastomosis.

Surgical management of small intestinal volvulus must be accompanied by **aggressive supportive medical therapy**. Pre- and postoperative management of horses that retain sufficient viability of the small intestine, or those in which resection and anastomosis are successfully performed, includes **nasogastric decompression** as needed, antimicrobial drugs (e.g. **potassium benzylpenicillin** 22 000 IU/kg IV q.i.d. and **gentamicin sulfate** 6.6 mg/kg IV s.i.d.; and **metronidazole** 15–25 mg/kg t.i.d. per rectum), and treatments for endotoxemia (*q.v.*). **Balanced polyionic IV fluid therapy** is needed in volumes (75–100 mL/kg/day) to correct dehydration, to replace fluids lost in nasogastric reflux, and to support venous return during cardiovascular shock. Administration of IV hypertonic saline (1–2 L of 7% NaCl/450 kg BW) will improve cardiovascular function for several hours.

In horses with severe (<4 g/dL) hypoproteinemia, administration of **colloidal solutions** is necessary to maintain oncotic pressure for adequate circulation volume. Fresh or thawed frozen **plasma** (6–10 L/450 kg BW) is ideal to restore oncotic pressure and provide functional proteins beneficial for clotting, immunity and modulation of the systemic inflammatory process. Alternatively, administration of **synthetic solutions** (hetastarch 6%, 5–10 mL/kg) may result in adequate transient volume expansion.

Horses with ischemic damage to intestinal segments generally absorb large amounts of endotoxin, thereby causing further cardiovascular deterioration. Treatment to dampen the systemic inflammatory response associated with endotoxemia is frequently beneficial. Choice of treatment options is based on severity of disease, renal function and hydration status.

The most important strategy in management of endotoxemia is aggressive management of the primary disease process (e.g. **rapid removal of devitalized segments**). Available are **immune sera and plasma** collected from donors inoculated with portions of endotoxin molecules derived from Gram-negative bacteria. The resulting antibodies may bind circulating endotoxin and render it inactive; however, results of experimental studies are not definitive. **Polymyxin B** is an aminoglycoside antibiotic that binds and neutralizes endotoxin and decreases the systemic effects of endotoxemia when administered at 2000 IU/kg slow IV t.i.d. Side effects include nephrotoxicity and neurotoxicity; patients therefore should be monitored closely, especially during use of other nephrotoxic medications, azotemia and dehydration. Treatment of endotoxemia also involves inhibition of mediator synthesis.

Non-steroidal anti-inflammatory drugs (especially **flunixin** meglumine 0.25 mg/kg t.i.d. or 1 mg/kg b.i.d. IV or IM) are most often employed for this purpose. **Pentoxifylline** (8 mg/kg PO t.i.d.) **combined with flunixin** meglumine may be slightly more beneficial than flunixin meglumine alone.

Inactivation of oxygen-derived radicals is sometimes attempted with **dimethyl sulfoxide** (DMSO 0.1–1 g/kg/day IV as a 10% solution).

Because **laminitis** (*q.v.*) is a common complication associated with all inflammatory and ischemic disease in horses, frog supports are recommended preventatively in these patients. Digital pulses and signs of lameness should be monitored closely.

Antimicrobial therapy is needed for treatment of the **peritonitis** (*q.v.*) that commonly accompanies ischemic intestinal disease and celiotomy with intestinal resection. **Broad-spectrum therapy** is essential: those drugs commonly employed include penicillin (procaine benzylpenicillin 22 000–44 000 IU/kg IM b.i.d. or potassium benzylpenicillin 22 000–44 000 IU/kg IV q.i.d.), gentamicin (6.6 mg/kg IV s.i.d.) and metronidazole (15–25 mg/kg PO or per rectum t.i.d.).

Postoperative ileus is a common complication of intestinal ischemia and resection in horses. Consequences include prolongation of hospitalization and fatalities. This is best minimized by adherence to good surgical techniques and supportive therapy. Motility-enhancing drugs have been advocated but information regarding dosages and efficacy of these medications in horses is variable. For postoperative ileus associated with small intestinal lesions, **2% lidocaine** (loading dose of 1.3 mg/kg IV followed by continuous infusion of 0.05 mg/kg/min) is commonly selected. Other prokinetics include **erythromycin lactobionate** (2.2 mg/kg in 1 L of saline IV q.i.d. or b.i.d.), **metoclopramide** (0.04 mg/kg/h continuous IV infusion), and **cisapride** (0.1 mg/kg IV or IM t.i.d.). For large intestinal lesions, **neostigmine** is often used at 0.0044 mg/kg SC or IV repeated q 2–4 h. If there is no response and abdominal pain is not noted, the amount can be increased by 2 mg increments to a total of 10 mg per treatment. Postoperative ileus involving the cecum is most frequently treated with **erythromycin lactobionate** (*q.v.*).

The effect of **lidocaine** on intestinal function is thought to result from blockade of inhibitory sympathetic and parasympathetic reflexes, anti-inflammatory properties, inhibition of free radical formation, reduced circulating catecholamine concentrations and direct stimulation of smooth muscle. Systemic administration of lidocaine is also thought to significantly attenuate the perception of pain by depressing the spiking activity amplitude and conduction time of both myelinated A and unmyelinated C fibers.

Erythromycin is thought to promote intestinal motility by initiating the migrating motor complex via motilin receptors. **Metoclopramide** promotes the release of acetylcholine from post-synaptic cholinergic neurons via activation of 5-hydroxytryptomine receptors, antagonizes the inhibitory influence of dopamine on intestinal smooth muscle, and blocks the α_2-adrenergic receptors. **Cisapride** selectively enhances the release of acetylcholine from post-ganglionic neurons in the myenteric plexus via stimulation of serotonergic receptors and antagonism of dopaminergic receptors. **Neostigmine** enhances large colon motility by inhibiting cholinesterase activity, thereby prolonging the presence of acetylcholine in the neuromuscular junction.

The proposed causes of ileus are complex and involve a combination of factors such as neural dysfunction, electrolyte disturbances, intestinal edema and local and regional ischemia with reperfusion injury. Thus the most effective therapy is likely a **combination of agents** that act by different or

complementary mechanisms. Most clinicians change medications if no response is obtained within 72 h.

The prognosis is dependent on the duration of illness and amount of intestine involved in the volvulus. With early detection and rapid treatment the prognosis is good. In patients with **long-standing strangulation**, postoperative peritonitis, ileus and adhesion formation are common. There is a high incidence of postoperative malabsorption and weight loss when resection of >60–70% of the small intestine is required, and euthanasia should be considered in these cases.

Pedunculated lipoma

Etiology and pathogenesis

Pedunculated lipomas are a common cause of **small intestinal strangulation** or obstruction in horses >15 yr of age. In a recent study, the mean age of horses with strangulating lipoma was 19.2 yr. Ponies, Arabians and Quarter Horses appear to be predisposed to lipoma formation. **Multiple lipomas** usually attach to the mesentery by a fibrovascular stalk of variable length. They are often incidental findings during exploratory surgery or necropsy, but these suspended masses have the potential to incarcerate a segment of small intestine and produce obstruction or, more commonly, strangulation (*q.v.*).

Clinical findings and diagnosis

Pedunculated lipomas should be suspected in horses >15 yr of age that demonstrate signs consistent with **small intestinal obstruction**. Strangulation obstruction by lipomas is characterized by acute, persistent abdominal **pain**, hemoconcentration and decreased borborygmal sounds. Nasogastric reflux usually is present, but may be absent early in the disease. Multiple loops of small intestine are evident on transrectal examination and elevations in peritoneal fluid protein concentration and nucleated cell count reflect the degree of **intestinal necrosis**.

Treatment and prognosis

Surgical correction involves abdominal exploration via ventral midline celiotomy, ligation and transection of the pedicle and lipoma, and resection and anastomosis of the affected segment of bowel. The ileum and jejunum are the most commonly affected segments of the small intestine. To minimize recurrence, **multiple lipomas**, even if not involved with the lesion, should be removed. The prognosis is favorable with early diagnosis and prompt treatment. Pre- and postoperative supportive therapies (see volvulus, *q.v.*) are necessary. If devitalized bowel cannot be safely resected or if peritonitis has progressed the prognosis is poor.

Herniation

Herniation of the small intestine may be classified as internal or external hernias. **Internal hernias** occur within the abdominal cavity and do not contain a hernial sac. Displacement of the small intestine through the epiploic foramen,

cecocolic fold, mesenteric defects, and rents in the gastrosplenic and broad ligaments are examples of such lesions. Mesodiverticular bands and Meckel's diverticulum are two congenital abnormalities that are also included in this category.

External hernias extend beyond the limits of the abdominal cavity and include inguinal, umbilical (including strangulating parietal hernias), ventral abdominal and diaphragmatic hernias.

Epiploic foramen herniation

Etiology and pathogenesis

The epiploic foramen is a **potential opening** approximately 4–6 cm in length that separates the omental bursa from the peritoneal cavity.

At one time, aged horses were thought to be predisposed to epiploic foramen entrapment due to enlargement of this space by atrophy of the right caudate lobe of the liver. In a recent study, no correlation was found between occurrence and age of affected horses. The average age for horses with epiploic foramen was 9.6 yr in that study. Herniation through the foramen may occur as a left to right or, less commonly, a right to left displacement when the horse is in dorsal recumbency.

Clinical findings and diagnosis

Clinical signs of **epiploic foramen herniation** are usually similar to those of horses with volvulus (*q.v.*). However, many horses may exhibit only mild signs of pain, and have no nasogastric reflux or palpable intestinal distension. In these horses, **peritoneal fluid analysis** (*q.v.*), which usually yields serosanguineous fluid with elevated protein concentration and nucleated cell count, is the most useful diagnostic test in determining the severity of the lesion and the need for surgical intervention. **Sequestration of the abnormal bowel in the omental bursa** may limit the impact of the incarcerated bowel on the peritoneal fluid and rectal examination findings.

Treatment and prognosis

Surgical exploration is often needed to confirm the diagnosis, at which time **decompression of the bowel** and careful manual dilatation of the foramen and reduction of the hernia can be performed. Decompression can be achieved with a **jejunotomy** and removal of luminal contents prior to reduction to minimize the amount of dilatation necessary to correct the hernia. Excessive trauma during dilatation of the foramen can result in fatal rupture of the caudal vena cava or portal vein.

After reduction of the herniation, **intestinal viability** should be evaluated and resection and anastomosis performed if necessary. Pre- and postoperative supportive therapies (see volvulus, *q.v.*) are necessary. Prognosis for surgical correction is dependent on the duration of illness and amount of intestine requiring resection, but is considered poor due to the difficulty encountered in reduction of the hernia.

Cecocolic fold herniation

Etiology and pathogenesis

The proximal aspect of the cecocolic fold can be a site for herniation and entrapment of the small intestine, most commonly the ileum and distal jejunum. The cecocolic fold attaches the lateral teniae of the cecum and the lateral free teniae of the right ventral colon. The exact etiology of this condition is unknown, but one hypothesis is that pressure from the small intestine on the cecocolic fold may cause hernia formation leading to intestinal strangulation.

Clinical findings and diagnosis

Clinical signs of cecocolic fold herniation are usually similar to those of strangulating obstruction (*q.v.*). Rectal examination commonly reveals small intestinal distension. Nasogastric intubation usually results in moderate reflux depending on the duration of the obstruction. In these horses, peritoneal fluid analysis (*q.v.*), which usually yields serosanguineous fluid with elevated protein concentration and nucleated cell count, is a useful diagnostic test in determining the severity of the lesion and the need for surgical intervention.

Treatment and prognosis

Surgical exploration is often needed to confirm the diagnosis, at which time decompression of the bowel and careful manual dilatation of the cecocolic fold defect and reduction of the hernia can be performed. After reduction of the herniation, **intestinal viability** should be evaluated and resection and anastomosis (jejunocecostomy) performed if necessary. Pre- and postoperative supportive therapies (see volvulus, *q.v.*) are necessary. The cecocolic fold defect is not closed primarily, and the defect is not reported to predispose affected horses to reoccurrence of this or other strangulating lesions. Prognosis for surgical correction is dependent on the duration of illness and amount of intestine requiring resection, similar to other strangulating small intestinal lesions.

Mesenteric defects

Etiology and pathogenesis

Defects or rents in the mesentery, gastrosplenic or broad ligaments, mesodeferens and greater omentum provide a potential site for intestinal incarceration or strangulation (*q.v.*). Mesenteric defects most often occur in the small intestinal mesentery, and less commonly in the large and small colon mesentery. Defects most commonly are acquired as a result of either severe **blunt abdominal trauma** or surgical manipulation of the bowel and mesentery. A segment of intestine passes through the defect and becomes incarcerated or strangulated.

Mesodiverticular bands, congenital remnants of a vitelline artery and its associated mesentery, extend from one side of the mesentery to the antimesenteric border of the jejunum. These normally atrophy during the first trimester of pregnancy. Failure of the band to atrophy results in formation of a **triangulated mesenteric sac**. A loop of intestine may become incarcerated in the sac, thereby leading to mesenteric rupture with resulting herniation and strangulation. **Meckel's diverticulum** is a remnant of the vitelline duct that

forms a blind extension from the antimesenteric surface of the distal jejunum or ileum. Occasionally, a fibrous band will persist from the apex of Meckel's diverticulum to the umbilicus, forming the vitelloumbilical band. Small intestine can become entangled and strangulate around this band.

Clinical findings and diagnosis

Clinical signs are similar to those described for horses with other strangulating obstructions (*q.v.*). Acute onset of severe abdominal pain, positive nasogastric reflux, evidence of small intestinal distension on transrectal examination and rapid systemic deterioration are often present. **Abdominocentesis** may yield normal or serosanguineous fluid with elevated protein concentration and nucleated cell count. Severity of the signs is dependent on the location, duration and extent of the lesion. Exploratory celiotomy is necessary for definitive diagnosis.

Treatment and prognosis

Surgical correction includes reduction of the hernia with resection and anastomosis of devitalized bowel. Pre- and postoperative supportive therapies (see volvulus, *q.v.*) are necessary. The **hernial ring** often requires **manual dilatation** to reduce the hernia. The mesenteric rent or tear should always be closed. A defect near the root of the mesentery is extremely difficult to close because of limited exposure. Care should be taken not to suture the mesenteric vasculature during repair.

Gastrosplenic ligament incarceration

Etiology and pathogenesis

Incarceration of the small intestine through the **gastrosplenic ligament** is relatively uncommon. The ligament attaches the left aspect of the greater curvature of the stomach to the hilus of the spleen and continues ventrally with the greater omentum. Defects in the ligament are usually acquired as a result of **trauma.** The distal jejunum and ileum are most often involved in the incarceration with herniation occurring in a caudal to cranial direction. The intestine becomes situated craniolateral to the spleen and lateral to the stomach.

Clinical findings and diagnosis

Clinical signs are similar to those described for horses with strangulating obstruction (*q.v.*). Acute onset of severe abdominal pain, positive nasogastric reflux, evidence of small intestinal distension on transrectal examination and rapid systemic deterioration are often present. Distended small intestine may not be palpable early in the disease process due to the cranial location in the abdomen. **Abdominocentesis** may yield normal or serosanguineous fluid with elevated protein concentration and nucleated cell count. Severity of the signs is dependent on the location, duration and extent of the lesion. Ventral midline celiotomy is often necessary for definitive diagnosis.

Treatment and prognosis

Surgical correction utilizes ventral midline exploratory celiotomy and gentle traction on the involved segment of bowel to reduce the hernia. Pre- and

postoperative supportive therapies (see volvulus, *q.v.*) are necessary. Since the ligament is relatively avascular, digital enlargement of the rent facilitates reduction with minimal risk of serious hemorrhage. No attempt is made to close the defect in the ligament due to inadequate surgical exposure and friability of the tissue.

Inguinal hernia

Etiology and pathogenesis

Acquired inguinal hernias in **stallions** are often associated with breeding or other strenuous exercise and almost always cause acute onset of severe abdominal pain. Sudden increases in intra-abdominal pressure or an enlarged internal inguinal ring may be predisposing factors. Inguinal hernias usually occur unilaterally and occur more frequently in Standardbreds, Saddlebreds and Tennessee Walking Horses than in other breeds. Inguinal herniation and evisceration may also be a complication to castration.

Congenital inguinal hernias in **foals** usually close spontaneously as the foal matures and rarely cause intestinal problems. However, **scrotal herniation** may require surgical correction when the bowel ruptures through the parietal tunic and **migrates subcutaneously**.

Clinical findings and diagnosis

Acquired inguinal and scrotal herniations in the stallion almost invariably produce acute intestinal obstruction (*q.v.*) that requires **immediate surgical intervention**. Incarcerated bowel becomes strangulated in several hours and hypovolemic and endotoxic shock (*q.v.*) rapidly cause **systemic deterioration**.

The hernia is usually indirect and unilateral with the incarcerated intestinal segment descending through the vaginal ring and contained within the tunica vaginalis. Affected horses demonstrate a rapid onset of moderate to severe abdominal **pain**. Palpation of the scrotum usually reveals a **firm, swollen, cool testicle** on the affected side. Early in the disease process, scrotal swelling may not be obvious. The loop of herniated small bowel may be palpable per rectum descending into the inguinal canal. With increasing duration of herniation the signs of typical strangulating obstruction, such as tachycardia, dehydration, endotoxemia and rapidly **progressive cardiovascular deterioration**, develop.

Abdominocentesis usually yields fluid with elevated protein concentration and nucleated cell count. Direct hernias with rupture of the vaginal tunic in newborn foals may cause mild pain and depression, local edema and subsequent abscessation. These are usually not reducible and are treated as surgical emergencies.

Treatment and prognosis

Correction requires ventral midline and inguinal incisions to achieve adequate surgical exposure and reduction. Reduction with resection and anastomosis of the affected bowel, unilateral castration and inguinal herniorrhaphy are usually required.

Inguinal herniation in colts may be contained in the vaginal tunic or may rupture through the tunic and lie subcutaneously. Those within the vaginal tunic may be manually reduced and usually spontaneously correct, but those that

rupture through the tunic require surgical repair via inguinal and scrotal incisions. Pre- and **postoperative supportive therapies** (see volvulus, *q.v.*) are necessary.

Prognosis for recovery is good if reduction and repair are performed within a few hours of herniation, before strangulation. The prognosis worsens with increasing duration before correction. The prognosis for breeding soundness is good if only one testicle is involved.

Diaphragmatic hernia

Etiology and pathogenesis

Diaphragmatic hernia may be **congenital** or **acquired** and is a rare cause of abdominal pain in horses. These hernias most often result from strenuous exercise, a hard fall, striking a stationary object while running, being struck by a large object, or parturition/dystocia (*q.v.*).

Clinical findings and diagnosis

Clinical signs associated with **diaphragmatic hernia** include abdominal pain, tachypnea and dyspnea. The severity of signs is dependent on the size of the hernial opening and degree of visceral herniation. Although the presence of viscera within the thoracic cavity may decrease the audibility of breath sounds and cause dullness during percussion, auscultation and percussion of the thorax does not always reveal abnormalities. Radiography and ultrasound may be diagnostic, demonstrating fluid- or ingesta-filled loops of intestine in the thorax. Because increases in pleural fluid protein and cell count may reflect the presence of devitalized intestine in the thoracic cavity, thoracocentesis may be a useful diagnostic aid. An exploratory celiotomy is often necessary for a definitive diagnosis.

Treatment and prognosis

Closure of the defect is accomplished by direct suturing or placement of a synthetic mesh over the defect. Diaphragmatic hernias located ventrally are accessible via a ventral midline celiotomy. With a dorsal hernia, the incision is extended 15 cm laterally in a paracostal fashion for adequate exposure. Prognosis for surgical repair is poor due to inadequate surgical exposure and a high incidence of postoperative complications such as septic pleuritis, implant failure and hernia recurrence.

Intussusception

Etiology and pathogenesis

Small intestinal intussusception usually occurs in younger horses and involves invagination of a segment of bowel (intussusceptum) and its mesentery into the lumen of an adjacent distal segment of bowel (intussuscipiens). Continued peristalsis progressively draws more bowel and its mesentery into the intussusception, thereby causing **venous congestion, edema and, eventually, infarction and necrosis** of the involved segment. **Complete small intestinal obstruction** and **strangulation** usually results.

Intussusception results from alterations in intestinal motility. Enteritis, abrupt dietary changes, heavy ascarid (*Parascaris equorum*) or tapeworm (*Anoplocephala*

perfoliata) infestation (*q.v.*), anthelmintic treatment and intestinal anastomosis (*q.v.*) have all been implicated as inciting factors. In most cases, however, **no inciting factor** is identified. Jejunojejunal and jejunoileal intussusceptions are most common in foals. Ileocecal intussusceptions are most common in adults.

Clinical findings and diagnosis

Jejunal and ileocecal intussusceptions usually cause acute, moderate to severe abdominal pain. Clinical signs vary with the degree and duration of the condition. Most commonly, intussusception leads to **complete intestinal obstruction** and strangulation of the intussusceptum, causing an **acute onset** of **persistent abdominal pain**. Nasogastric reflux develops and progressive dehydration and hypovolemia rapidly ensue. Transrectal examination reveals loops of distended small intestine and occasionally the intussusception may be palpated. With an ileocecal intussusception, a turgid segment of bowel may be palpable within the cecum. Ultrasonographic findings of the involved bowel are usually described as a "**bulls-eye**" appearance with a segment of bowel within another segment.

Elevated peritoneal protein concentration and nucleated cell count reflect devitalization of the affected bowel. Peritoneal fluid analysis, however, may not accurately reflect the degree of intestinal compromise due to isolation of the devitalized intussusceptum within the intussuscipiens.

Cases of **chronic ileocecal intussusception** have been described in which long-term, partial obstruction causes intermittent or continual abdominal pain, weight loss, poor general physical condition and varying degrees of anorexia and depression. This may continue for weeks to months but eventually leads to an acute episode of severe abdominal pain corresponding to complete obstruction of the intestine.

Treatment and prognosis

Surgical correction includes manual reduction of the intussusception and resection and anastomosis of the affected intestine (end-to-end jejunal anastomosis, ileocecostomy or jejunocecostomy). Some intussusceptions cannot be reduced due to the length of bowel involved, venous congestion and edema, and thus require total resection and anastomosis. Even if the intestinal segment appears viable, resection and anastomosis should be strongly considered due to the possibility of mucosal necrosis, serosal inflammation and postoperative adhesion formation. Pre- and postoperative supportive therapies (see volvulus, *q.v.*) are necessary.

The prognosis after early diagnosis and surgical repair of jejunal, ileal or ileocecal intussusception is good. If the intussusception is advanced and irreducible, the prognosis is fair to poor due to the likelihood of ileus, peritonitis and postoperative complications.

INFLAMMATORY AND/OR ISCHEMIC DISEASES

Duodenitis/proximal jejunitis

Etiology and pathogenesis

Duodenitis/proximal jejunitis is a distinct syndrome characterized by transmural inflammation, edema and hemorrhage in the duodenum and proximal

jejunum. The small intestinal mucosa and sometimes the small intestinal contents are a **red or red-brown color**. The stomach and proximal small intestine are moderately distended with fluid, whereas the distal jejunum and ileum are usually flaccid. Histologic lesions include hyperemia and edema of the mucosa and submucosa, villus epithelial degeneration and sloughing, neutrophil infiltration, hemorrhages in the muscular layer and fibrinopurulent exudation on the serosa. The cause of this extensive intestinal damage is unknown. *Clostridium perfringens* (*q.v.*) is one suspected etiologic agent.

The clinically relevant events that result from the intestinal damage are proximal small intestinal distension and nasogastric reflux, dehydration, and hypovolemic and endotoxic shock. The primary cause of the intestinal distension and reflux is probably accelerated transmucosal movement of fluid. The resulting inflammation and distension may alter intestinal motility resulting in **adynamic ileus**.

Clinical findings and diagnosis

Clinical signs include acute abdominal pain, **copious amounts of nasogastric reflux** (10–20 L; often red-brown colored fluid), rectal examination finding of moderate to severe small intestinal distension, absent borborygmal sounds, tachycardia, dehydration, slight increase in body temperature (38.6–39.1°C), hyperemic mucous membranes and prolonged capillary refill time. Although the abdominal pain usually abates after gastric decompression, the animal remains severely depressed.

Clinical laboratory findings include an increased packed cell volume (PCV) and total plasma protein (hemoconcentration), elevated creatinine concentration (pre-renal or renal azotemia), elevated peritoneal fluid protein concentration, mild to moderate elevation of peritoneal white blood cell (WBC) count (5000–15 000 cells/μL), hyponatremia, hypokalemia, hypochloremia and sometimes metabolic acidosis (poor perfusion). Complete blood count may reveal a normal, increased (neutrophilia due to inflammation) or decreased (neutropenia and left shift due to endotoxemia and consumption) WBC count. Definitive diagnosis can only be made via gross examination of the duodenum and proximal jejunum at surgery or post mortem. **Laminitis** (*q.v.*) is a common complication.

The clinical findings overlap with strangulating obstruction and nonstrangulating obstruction (*q.v.*). Therefore, cases with colic, small intestinal distension and nasogastric reflux present a diagnostic challenge to the clinician. After initiation of nasogastric decompression, the abdominal pain usually abates and is replaced by depression in patients with duodenitis/proximal jejunitis. On the other hand, severe or progressive abdominal pain and serosanguineous abdominal fluid should be considered signs of strangulating or nonstrangulating obstruction.

Treatment and prognosis

There is no specific treatment other than aggressive supportive therapy. Because voluminous gastrointestinal reflux is produced consistently for 3–7 days, periodic **gastric decompression** (**approximately every 2 h**) is necessary to prevent distension potentially leading to pain and rupture. Food and oral

medication should be withheld until small intestinal function returns. Because **clostridial infection** is one suspected etiology, treatment with **penicillin** (potassium benzylpenicillin 22 000–44 000 IU/kg IV q 6 h) is recommended. Surgery should be avoided.

Management of horses with duodenitis and jejunitis includes nasogastric decompression as needed, IV fluids, antimicrobial drugs and treatments for endotoxemia (*q.v.*). IV crystalloid therapy (e.g. acetated Ringer's solution 50–100 mL/kg/day) is needed in volumes to correct dehydration, to replace fluids lost in nasogastric reflux, and to support venous return during cardiovascular shock. Blood gases and serum electrolyte concentrations should be monitored and IV solutions altered as needed to correct deficiencies. Administration of **IV hypertonic saline** (1–2 L of 7% NaCl/450 kg BW) will improve cardiovascular function for several hours.

In horses with severe (<4 g/dL) hypoproteinemia, administration of **colloidal solutions** is necessary to maintain oncotic pressure for adequate circulation volume. Fresh or thawed frozen **plasma** (6–10 L/450 kg BW) is ideal to restore oncotic pressure and provide functional proteins beneficial for clotting, immunity and modulation of the systemic inflammatory process. Alternatively, administration of synthetic solutions (**hetastarch** 6%, 5–10 mL/kg) may result in adequate transient volume expansion.

Horses with ischemic damage to intestinal segments generally absorb large amounts of endotoxin, thereby causing further **cardiovascular deterioration**. Treatment to dampen the systemic inflammatory response associated with endotoxemia is frequently beneficial. Choice of treatment options is based on severity of disease, renal function and hydration status.

The most important strategy in management of endotoxemia is **aggressive management of the primary disease** process. Available are **immune sera** and plasma collected from donors inoculated with portions of endotoxin molecules derived from Gram-negative bacteria. The resulting antibodies may bind circulating endotoxin and render it inactive; however, results of experimental studies are not definitive. **Polymyxin B** is an aminoglycoside antibiotic that binds and neutralizes endotoxin and decreases the systemic effects of endotoxemia when administered at 2000 IU/kg t.i.d. Side effects include nephrotoxicity and neurotoxicity, and patients should be monitored closely accordingly, especially during use of other nephrotoxic medications, azotemia and dehydration.

Treatment of endotoxemia also involves inhibition of mediator synthesis. NSAIDs (especially **flunixin meglumine** 0.25 mg/kg t.i.d. or 1 mg/kg b.i.d. IV or IM) are most often employed for this purpose. **Pentoxifylline** (8 mg/kg PO t.i.d.) **combined with flunixin meglumine** may be slightly more beneficial than flunixin meglumine alone. Inactivation of oxygen-derived radicals is sometimes attempted with **dimethyl sulfoxide** (DMSO 0.1–1 g/kg/day IV as a 10% solution).

Because **laminitis** (*q.v.*) is a common complication associated with all inflammatory and ischemic disease in horses, **frog supports** are recommended preventatively in these patients. Digital pulses and signs of lameness should be monitored closely. Blood gases and serum electrolytes should be monitored and the IV solution adjusted to correct deficiencies. Moreover, as clostridial infection (*q.v.*) is one suspected etiology, treatment with penicillin

(potassium benzylpenicillin 22 000–44 000 IU/kg IV q 6 h) is recommended. Surgery should be avoided in these horses.

After the nasogastric reflux has decreased to 1–2 L over a 4 h period, small amounts of water can be offered. If the water is tolerated without recurrence of colic, small amounts of mash and grass can be fed frequently. Coarse roughage should be avoided for 48 h. Overly aggressive feeding can lead to distension of the small intestine, ileus and recurrence of colic and nasogastric reflux.

In patients with prolonged (⩾7–10 days) nasogastric reflux, parenteral nutrition may be necessary to provide nutritional support until the reflux resolves. **Parenteral nutrition** is administered IV and must provide a source of dextrose, lipids, amino acids and multivitamins.

Also in long-standing cases, surgery can be considered to augment medical therapy. Two approaches have been used. A standing right flank laparotomy may be used for exposure of the duodenum and cecal base to create a stoma between the duodenum and cecal base using a side-to-side anastomosis. This stoma may act as a shunt for fluid to decompress the small intestine. The stoma usually spontaneously closes. More often, a ventral midline celiotomy offers better exposure of the abdomen for examination and shunt formation. A side-to-side anastomosis can be formed between the diseased jejunum (as far proximal as can be easily exteriorized) and a segment of normal distal jejunum.

With appropriate management, the intestinal disease resolves in 95% of cases. Losses result from laminitis and intra-abdominal adhesions (*q.v.*). Without appropriate gastric decompression, death can result from **gastric rupture** (*q.v.*). Spontaneous nasogastric reflux, which leads to aspiration pneumonia, occurs in a very small percentage of horses with fluid distension of the stomach.

Non-strangulating infarction

Etiology and pathogenesis

Non-strangulating infarction describes infarction (**necrosis due to loss of blood supply**) of the intestine without a constricting or compressive lesion.

Post mortem examination of most horses with **intestinal infarction** reveals **thrombus formation** at the cranial mesenteric artery consistent with damage by migration of fourth and fifth stages of *Strongylus vulgaris* larvae (*q.v.*). However, thorough examination of the peripheral mesenteric vessels of these horses rarely reveals occlusive arterial lesions. It has been postulated, therefore, that infarction is most likely the result of **hypoxia** induced by **vasospasm**.

A large number of non-fatal cases of colic also have been attributed to infarction or ischemia due to **verminous arteritis** (*q.v.*). These can only be tentatively diagnosed because there are no specific clinical findings diagnostic of this condition.

Clinical findings and diagnosis

A **poor parasite control program** may predispose horses to develop non-strangulating ischemia and/or infarction. However, the disease also occurs in horses that are regularly treated with anthelmintics. The severity of the clinical

signs is variable, ranging from depression to moderately severe abdominal pain. Heart rate and respiratory rate may remain normal or may increase. Hyperemic mucous membranes may be present suggesting endotoxemia (*q.v.*). Body temperature may be normal or elevated due to either endotoxemia or the inflammation caused by migrating parasites. Rectal examination often is normal but may reveal distended small intestine, and pain, fremitus or thickening may be evident upon palpation of the mesenteric root.

Auscultation of the abdomen may reveal increased, normal or decreased borborygmal sounds. **Gastric reflux** may be present due to functional obstruction of the involved segment. PCV, total plasma protein and creatinine may increase due to dehydration. The peripheral blood may reveal decreased (neutropenia with a left shift due to endotoxemia), normal or increased WBC count (neutrophilia due to inflammation). Total protein may be increased due to the chronic inflammation caused by parasitism or decreased as a result of protein loss through damaged intestinal mucosa. Abdominal fluid may be normal or have tremendous elevation in protein content ($\geqslant$3.0 mg/dL) and WBC count (up to 200 000 cells/μL).

Treatment and prognosis

Supportive therapies (see duodenitis and proximal jejunitis, *q.v.*) as discussed above are necessary. If nasogastric reflux occurs, careful attention should be given to maintain **gastric decompression**. Broad-spectrum antimicrobial drugs (e.g. potassium benzylpenicillin G 22 000–44 000 IU/kg IV q 6 h and gentamicin sulfate 6.6 mg/kg IV once q 24 h, and metronidazole 15–25 mg/kg t.i.d. PO or per rectum) are recommended if peritonitis is present. Pre- and post-operative supportive therapies (see volvulus, *q.v.*) are necessary. Large dosages of aspirin (20 mg/kg daily PO) and heparin (40–100 IU/kg q 8 h SC or IM) have been suggested to reverse the process of thrombosis; however, these are not routinely used.

Surgery should be considered in patients that deteriorate despite medical therapy. The prognosis is poor for patients with intestinal infarction requiring surgery for intestinal resection. Extensive peritonitis (*q.v.*) may have already developed. Ischemia not obvious at the time of surgery may later progress to infarction. Ileus and adhesions (*q.v.*) are common postoperative complications. Large intestinal involvement may be too extensive for resection to be practical. However, identification and resection of involved segments of either small or large intestine sometimes is performed successfully.

DISEASES OF THE LARGE INTESTINE CAUSING COLIC

INTRODUCTION

Abnormalities of the equine large intestine may be broadly classified as either physical or functional obstructions. Simple **physical obstructions** may be caused by intraluminal masses, large colon displacements or compression by extramural masses. Strangulating obstructions can follow intussusception (*q.v.*) or a **twist >180°** of a segment of intestine on its longitudinal axis. **Functional obstruction**, commonly called **adynamic or paralytic ileus**, may

be related to dietary and management factors (tympany), non-strangulating infarction, peritonitis or colitis (*q.v.*).

Intestinal obstruction prevents the aboral movement of ingesta, gastrointestinal secretions and gas, resulting in **distension** of the intestine. As the distension increases, **venous drainage is impaired** and the mucosa becomes congested and edematous. If the obstruction persists for a prolonged period of time, significant compromise of intestinal vascular integrity may result in **mucosal ischemia**. **Hypovolemia** can result from decreased oral intake and accumulation of fluid in the intestinal lumen. In strangulating obstructions, ischemia of the affected segment leads to **necrosis** and transmural leakage of **bacteria and endotoxin**. Therefore, it is important that large intestinal lesions are identified early in the disease process.

Therapy for large intestinal lesions includes control of pain, maintenance of cardiovascular and metabolic status, and establishing a patent and functional intestine. Pain control is accomplished by **gastric decompression** (*q.v.*) via a nasogastric tube and administration of visceral and centrally acting analgesics (see Table 10.1). Maintenance and support of cardiovascular and metabolic status is achieved by IV administration of balanced, **isotonic fluids** (e.g. acetated Ringer's; 50–60 mL/kg/day). Most cases of impaction and tympany respond to medical therapy. Ventral midline exploratory celiotomy is necessary for identification and correction of displacements, strangulating lesions, impaction and **enterolith** (*q.v.*) removal.

NON-STRANGULATING OBSTRUCTIONS

Non-strangulating obstructions cause partial or complete luminal obstruction without significant compromise of the vascular integrity of the intestine. Intraluminal obstructions include cecum or colon impaction, enteroliths and neoplasia (*q.v.*). Extraluminal causes of obstructions include large colon displacements and adhesions (*q.v.*).

Impaction

Impaction involves accumulation and dehydration of ingesta within the intestinal lumen. Numerous factors may predispose to impaction, including **poor dentition**, ingestion of **coarse roughage**, **parasitic infestation** and **inadequate fluid intake**. In addition, **stress** associated with transportation or intense exercise may lead to hypomotility, inadequate water intake or excessive fluid losses through sweating.

Obstruction of the colon by adhesions or displacement may result in impaction. Many cases of impaction of the large and small colon are associated with positive *Salmonella* spp. (*q.v.*) fecal culture. Therefore, inflammatory conditions of the bowel may also predispose to colon impactions. In many cases of impaction, predisposing conditions are not identified.

Cecal impaction

Etiology and pathogenesis

In addition to the above predisposing factors, **cecal impaction** also occurs as a complication of other diseases, especially those associated with endotoxemia,

surgery or pain, such as septic metritis, septic arthritis, fractures and corneal diseases (*q.v.*). If the pain associated with these conditions is not controlled, the sympathetic component of the autonomic nervous system is upregulated, leading to a decrease in normal gastrointestinal motility. Other poorly defined causes of cecal dysfunction may play a role.

Clinical findings and diagnosis

Clinical findings include anorexia, decreased fecal passage and mild to severe abdominal pain. Heart rate varies with the degree of pain. Mucous membranes are usually pink, but may be tacky due to dehydration. There is usually no nasogastric reflux except when severe impaction results in ileus of the small intestine. PCV, plasma protein and creatinine may be elevated due to dehydration. In severe long-standing cases, damage to the cecal wall may result in transudation of protein. This can progress to **cecal perforation** leading to **peritonitis** (*q.v.*). In these cases, the peritoneal fluid protein content and/or WBC count may be increased.

Diagnosis is based upon finding cecal impaction on **transrectal examination**. The ventral cecal tenia will be taut and may be displaced ventral and medial. An excessive quantity of dry ingesta is palpable in the body and sometimes in the base of the cecum. The cecal base may be filled with moderate amounts of gas. The cecal distension may cause the dorsal and medial cecal teniae to be palpable. The left colon and small colon are usually empty.

Treatment and prognosis

Mild to moderately severe impactions of the cecum almost always respond favorably to medical therapy. All food should be withheld, but access to water may be allowed if there is no nasogastric reflux.

Large volumes of fluid (three times daily maintenance requirements) should be administered PO and IV to hydrate the impaction. Horses that do not develop nasogastric reflux usually respond to administration of **6 L of fluid (per 500 kg horse) q 2 h** via an indwelling nasogastric tube. Mild impactions require less aggressive fluid administration (one to two times maintenance requirements). **Laxative therapy** facilitates hydration of impacted ingesta: **docusate sodium** (10–20 mg/kg up to two doses 48 h apart), **magnesium sulfate** (450 g/500 kg BW) or **psyllium hydrophilic mucilloid** (400 g/500 kg BW q 6–12 h until the impaction resolves) can be used. **Mineral oil** can be administered to facilitate passage after the impaction begins to resolve; however, it is not useful to penetrate and hydrate the impacted mass.

After resolution of the impaction, feeding should be resumed **slowly** to avoid immediate recurrence. Grass, pellets softened to a mash with water, and bran mashes are preferable for the first 24–48 h. After this, feeding of hay and grain can be resumed slowly. Horses that have cecal dysfunction may experience recurrence despite these precautions.

The method of choice for treatment of severe cecal impactions has not been determined. Many horses with severe impactions respond to the aggressive fluid and laxative therapy outlined above. However, severe cecal impactions sometimes result in **cecal perforation** (*q.v.*).

Surgical management of cecal impactions should be considered in cases where the horse has intractable pain, the impaction is excessively large, medical therapy is unsuccessful, or peritoneal fluid analysis or transrectal examination indicates intestinal degeneration. A number of **surgical options** are described and include extraluminal massage, typhlotomy and evacuation, partial or complete typhlectomy, cecocolic anastomosis and ileocolic anastomosis. The surgical approach for these procedures is ventral midline celiotomy. Massage of the impaction with or without transmural injection of fluid may facilitate the passage of ingesta from the cecum and has the advantage that an enterotomy is not performed. **Typhlotomy** may be performed between the lateral and ventral cecal teniae, near the cecal apex, for evacuation of ingesta by use of a warm water hose. Extreme care must be taken during exteriorization of the impacted cecum to avoid **cecal rupture**. It is often difficult to fully exteriorize the cecal apex and, therefore, contamination at the enterotomy site may be excessive.

Cecocolic anastomosis may be created between the dorsal and lateral cecal teniae and the lateral and medial non-mesenteric teniae of the right ventral colon. Mild postoperative abdominal pain associated with gaseous distension of the cecum has been reported with this procedure. This may be due to inability of gas to exit through the cecocolic anastomosis or accumulation of reflux gas from the right ventral colon.

Jejunocolic or ileocolic anastomosis to bypass the cecum and redirect ingesta to the right ventral colon appears to be superior to cecocolic anastomosis. In this procedure the proximal ileum or distal jejunum is transected and the distal stump oversewn. An end-to-side or side-to-side anastomosis is then created between the ileum or jejunum and right ventral colon between the medial non-mesenteric tenia and the medial mesocolic tenia. Apparently, maintenance of a functional cecocolic orifice prevents reflux of gas from the right ventral colon into the cecum. If the procedure is done without terminating the ileum, continued passage of ingesta into the cecum may lead to recurrence of the impaction.

Complete typhlectomy and ileocolic anastomosis has been described but infrequently performed for management of cecal impaction. This surgical technique requires positioning in left lateral recumbency with a right lateral paralumbar fossa approach and resection of the eighteenth rib.

Prognosis for mild to moderate cecal impactions is good. Severe cecal impactions may result in death as a result of perforation. Severe cecal impactions may require surgical therapy, which can be complicated by adhesions or peritonitis. The prognosis with severe impactions is guarded.

Large colon impaction

Etiology and pathogenesis

Large colon impactions occur at three sites of the large colon: the **pelvic flexure, right dorsal colon** and **transverse colon**. These also are sites of origin of retropulsive contractions (those propagated in an oral direction), which retain ingesta for microbial digestion. These normal contractile patterns may contribute to worsening of impactions.

Clinical findings and diagnosis

Clinical findings include anorexia, decreased fecal passage and mild to severe abdominal pain. Initially the abdominal pain is mild and intermittent, but signs gradually worsen. Heart rate varies with the degree of pain. Mucous membranes are usually pink, but may be tacky due to dehydration or hyperemic due to endotoxemia when the colonic mucosa is compromised. There is usually no nasogastric reflux except when severe impaction results in ileus of the small intestine or compression of loops of small intestine. PCV, plasma protein and creatinine may be elevated due to dehydration.

Transrectal examination will reveal impacted ingesta and varying degrees of distension of the pelvic flexure and ventral colon. In severe cases, the impaction can involve the dorsal colon. The distension commonly pushes the colon to the **right side** of the abdomen and into the pelvic canal. Impactions in the right dorsal and transverse colon are usually beyond the reach of the veterinarian performing transrectal examination, but secondary tympany is usually palpated.

In severe long-standing cases, distension of the colonic wall may result in **transudation of protein**. This can progress to bowel necrosis leading to peritonitis, increasing the peritoneal fluid protein content and WBC count. Severe and unrelenting abdominal pain, systemic signs of toxemia (hyperemic or cyanotic mucous membranes), tachycardia and tachypnea often become apparent with the development of bowel degeneration and peritonitis.

Treatment and prognosis

All food should be withheld to prevent continued accumulation of impacted ingesta, but access to water may be allowed if there is no nasogastric reflux. Very mild impactions respond to administration of water and mineral oil via nasogastric tube. Fluid and laxative therapy for moderate to severe colon impactions is similar to that discussed for cecal impactions.

If medical management of large colon impaction is unsuccessful, **surgical intervention** is necessary to relieve the obstruction and re-establish normal gastrointestinal transit. The decision for surgery is based on unrelenting abdominal pain, failure of medical therapy, transrectal examination findings indicating concurrent large intestinal displacement, systemic cardiovascular deterioration, or changes in peritoneal fluid characteristics indicating intestinal degeneration. A ventral midline celiotomy is performed and thorough exploration of the abdomen performed to reveal the extent of the impaction and if a concurrent colon displacement exists. The pelvic flexure is located, and colon carefully exteriorized and placed on a colon tray. An enterotomy is performed at the pelvic flexure and, with the aid of a warm water hose, ingesta is evacuated from the colon. Systematic abdominal exploration is then performed to determine possible concurrent abnormalities.

The prognosis for medical management of mild to moderate large colon impaction is good. Prognosis for surgical correction of severe large colon impaction is good unless there is **necrosis of the intestinal wall** or colonic devitalization results in intestinal rupture during exteriorization of the colons.

Sand impaction

Etiology and pathogenesis

Horses may ingest sand while grazing or eating hay from the ground. Horses on closely grazed pastures in areas with a sandy soil are at greatest risk. The ingested sand settles to the bottom of the **large colon** where it may accumulate in large quantities and cause obstruction.

Clinical findings and diagnosis

The clinical signs are similar to those caused by large colon impaction (*q.v.*). As the sand accumulates, it may cause mild intermittent abdominal pain. In some cases, the signs of pain are acute. The sand may be felt with the fingers during **transrectal examination** and can be **detected in the feces** by placing in a container and adding water. The ingesta will float in the water and be washed away; sand will settle to the bottom of the container. The shifting of sand in the colon may be **audible**, said by some to sound like "*sand on a beach*", during abdominal auscultation.

The impaction will be palpable via transrectal examination in either the pelvic flexure or cecum. Impactions in the right dorsal or transverse colon occur less commonly and usually are out of the reach of the examiner. The sand may act as an irritant and cause **diarrhea**. Degeneration and necrosis of the bowel can occur under the weight of the sand and lead to endotoxemia and peritonitis. Abdominal radiographs have been used to identify sand accumulation in the large colon and may be beneficial in monitoring resolution of the sand impaction with medical therapy.

Treatment and prognosis

Horses with sand impaction sometimes respond to administration of fluids and laxatives as for large colon impaction. **Psyllium hydrophilic mucilloid** is a laxative used for removal of sand and should be administered at 400 g/500 kg BW q 6 h until the impaction resolves. Psyllium therapy should then be continued at 400 g/500 kg BW daily for 3 wk to remove the majority of the sand from the colon. However, thorough removal of sand from the colon cannot be confirmed, and a recent study suggests the use of psyllium hydrophilic mucilloid may not be beneficial in removing sand from the colon.

Surgery may be necessary in horses that exhibit **unrelenting pain**, develop peritoneal fluid changes indicating bowel degeneration or fail to respond to medical therapy. The sand must be removed via a **pelvic flexure enterotomy**. Postoperative complications include peritonitis and adhesion formation. Furthermore, the sand can cause **extensive damage** to the colon wall leading to postoperative ileus, endotoxemia, colitis or bowel degeneration, thereby causing peritonitis. Therefore, although the prognosis is usually good for horses with mild sand impactions, horses with severe sand impactions and damage to the colonic wall have a poor prognosis.

Owners that keep horses in **sandy environments** should be taught **preventative management**. Pastures should be managed so that grass is thick and not overgrazed. Hay should be supplemented when needed, but **not fed off the ground**. Although these management techniques are the most effective way to prevent sand impaction, anecdotally it is suggested that psyllium

therapy can be used as an adjunct to remove sand from the colon before impaction develops. Effective preventative dosages have not been determined, but 400 g/500 kg BW daily for 3 wk has been used. Many horses will eat this in their grain ration if it is divided into several feedings. Flavored or soluble forms of psyllium are more expensive but may be better tolerated. This therapy can be repeated every 4–12 mo depending upon the amount of sand exposure.

Small colon impaction and foreign bodies

Etiology and pathogenesis

The inciting factors for **large colon impaction** (*q.v.*) can also lead to small colon impaction. Small colon impaction can also occur without predisposing factors. Many cases of uncomplicated small colon impaction are associated with salmonellosis (*q.v.*). **Intraluminal obstruction** with inspissated feces (fecalith), concretions of plant material (phytobezoar), hair (trichobezoar), or a combination (phytotrichobezoar) also occurs (*q.v.*).

Foreign body obstruction of the small colon is caused by ingestion of fibrous non-digestible material such as nylon fibers from lead ropes, halters, hay nets, twine, synthetic fencing material, blankets, or pieces of rubber, carpet and feed sacks. The foreign material often becomes coated with mineral precipitate, increasing the size and diameter of the mass. The foreign body may be present in the colon for months before causing an obstruction. Animals <3 yr of age, because of their curious nature, seem to be at a higher risk.

Clinical findings and diagnosis

Clinical signs of small colon impaction and foreign body include abdominal discomfort and straining to defecate. Bilateral abdominal distension and nasogastric reflux develop as complete obstruction leads to distension of the proximal large colon with gas and ingesta. Decreased fluid intake leads to dehydration. **Transrectal examination** may reveal distended, ingesta-filled small colon in the caudal abdomen. Small colon impactions may be diagnosed rectally in approximately 87% of the cases. A **foreign body** may be palpable in the small colon. However, the limited mobility of the small colon, increased tension on the mesentery, and secondary large colon distension often hinder transrectal examination.

In long-standing cases, **pressure necrosis** of the mucosa leads to endotoxemia (*q.v.*), thereby causing fever, depression and hyperemic mucous membranes. This can progress to bowel rupture, thereby causing **lethal peritonitis** and shock. Peritoneal fluid remains normal except in cases of protracted duration, in which increases in protein concentration and nucleated cell count reflect intestinal necrosis. Endotoxemia due to bowel necrosis or concurrent salmonellosis may cause neutropenia and a degenerative left shift.

Treatment and prognosis

Medical therapy is often successful in the treatment of small colon impaction and includes IV and oral fluids, **oral laxatives** (psyllium hydrophilic mucilloid, 0.25–0.5 kg/500 kg horse in 4–8 L per nasogastric tube; docusate sodium,

120–240 mL of 5% solution in 2–4 L per 500 kg horse once daily for 2 days; and magnesium sulfate, 1 g/kg in 4–8 L of water once daily for 2 days) and **intestinal lubricants** (mineral oil; 1 L q 24–48 h). Mild, gravity flow, warm water enemas have been used, but should be avoided when there is marked colonic distension or rectal mucosal edema. Surgical intervention should be considered when there is systemic deterioration, nasogastric reflux, uncontrollable pain, severe abdominal distension, evidence of intestinal degeneration on peritoneal fluid examination, and/or lack of response to medical therapy.

Ventral midline celiotomy is the preferred surgical approach for manipulation of the small colon near the transverse colon or rectum. The preferred technique for removal of small colon impactions is to administer a gentle warm water enema by introduction of a lubricated nasogastric tube through the rectum. The surgeon then guides the tube through the small colon to the site of impaction. Alternatively, the impacted mass may be injected with fluid and massaged to encourage dissolution. The wall of the colon is often very **edematous and friable** and extreme care must be used in manipulating the bowel to avoid seromuscular tears or colonic rupture.

Severe impactions and foreign bodies require an **enterotomy** to relieve the obstruction. The area of the obstruction should be exteriorized and isolated from the abdominal incision and packed off with moist towels. The incision is most often made through the antimesenteric tenia. If possible, the incision should be made in an area of normal colon to minimize postoperative healing complications. This is often not possible due to the immobility of the impaction or foreign body within the colon. A pelvic flexure enterotomy (*q.v.*) and evacuation of the ascending colon is also performed to minimize the amount of ingesta passing the enterotomy site in the immediate postoperative period, thereby reducing the incidence of recurrence.

The prognosis for **small colon impaction** is good providing there is no intestinal devitalization and a small colon enterotomy is not performed. If a small colon enterotomy is performed, the prognosis is slightly worse. High small colon mural collagenase activity, poor blood supply, high bacterial counts, and firm, formed feces all contribute to a high incidence of enterotomy incisional complications that may lead to peritonitis.

Enteroliths

Etiology and pathogenesis

Enteroliths are concretions composed of magnesium ammonium phosphate salts ("**struvite**") that form slowly around **a nidus** such as a small metallic object or stone. Enteroliths may be single or multiple and usually do not cause a clinical problem until they become **lodged in the transverse or small colon**. Smaller enteroliths may be passed rectally with no associated clinical problems.

The specific geographic distribution of this condition has led to speculation that undetermined constituents in water and soil of these locations may be inciting factors in the disease. **Enterolithiasis** is most frequently seen in middle-aged horses, with Arabians, Morgans, Saddlebreds and miniature horses being somewhat over-represented. A large percentage of affected horses are on an **alfalfa diet** with a high magnesium and protein content. One

hypothesis in the pathogenesis of enterolithiasis is the increase in dietary magnesium increasing intraluminal pH, thereby favoring struvite formation.

Clinical findings and diagnosis

Affected horses may present with decreased fecal passage, colic, and weight loss. Incomplete obstruction may allow passage of soft mucus-covered feces, mineral oil and gas and lead to recurrent episodes of mild colic, making the diagnosis difficult.

If the enterolith is firmly encompassed by colonic mucosa, the obstruction is complete and gas and ingesta accumulate proximal to the obstruction. This manifests as **severe acute abdominal pain**, tachycardia, abdominal distension, and sometimes nasogastric reflux. Transrectal examination most often reveals moderate to severe distension of the large colon and cecum. Abdominal radiography may be helpful in the detection of enteroliths. Peritoneal fluid usually remains normal unless pressure necrosis of the bowel wall develops around the enterolith, when there may be an increased protein concentration and nucleated cell count.

A presumptive diagnosis is made by history, geographic location and physical examination findings. Abdominal radiography and/or exploratory laparotomy are used to confirm the presence of an enterolith.

Treatment and prognosis

Although some enteroliths may be passed rectally, conservative therapy is usually not successful. **Surgical intervention** via a ventral midline or flank laparotomy is necessary for systematic exploration of the abdomen and identification and removal of the enterolith. Obstructing enteroliths are most often located in the transverse or small colon. If possible, the area of the obstruction should be exteriorized and isolated from the abdominal incision and packed off with moist towels.

Surgical removal of enteroliths in the proximal small colon or transverse colon must be preceded by evacuation of ingesta from the large colon through a pelvic flexure enterotomy to minimize abdominal contamination. A warm water hose is then passed per rectum to facilitate removal of the enterolith by flushing it proximally into the transverse or right dorsal colon. Small enteroliths may be flushed back to the enterotomy site and removed. Larger enteroliths may necessitate a separate enterotomy in the right dorsal colon to facilitate removal. It is extremely important to check the entire large and small colon for **additional enteroliths**. If the enterolith has a flat side or the shape of a polyhedron, there is at least one more enterolith present. Complete exploration of the remainder of the abdomen should be performed before closure.

Frequently enteroliths of the small colon must be removed via an enterotomy in the involved section of bowel because of the inability to move the enterolith. An enterotomy incision long enough for easy removal of the enterolith is made through the antimesenteric teniae of the small colon. Pelvic flexure enterotomy and evacuation of the large colon should be performed in addition to the small colon enterotomy to minimize the transit of ingesta passing the enterotomy site in the immediate postoperative period.

The short- and long-term prognosis for uncomplicated enterolith removal is good providing the horse presents in **good cardiovascular condition** without intestinal devitalization. If a small colon enterotomy is performed, the prognosis is slightly worse. Increased small colon mural collagenase activity, poor blood supply, high bacterial counts and firm, formed feces all contribute to a high incidence of small colon enterotomy incisional complications that may lead to peritonitis (*q.v.*).

Large colon displacements

The equine left ventral and dorsal colons are freely movable in the abdominal cavity, thereby allowing for intestinal displacement and torsion. The cause of displacement is not known, however alterations in colonic motility, excessive gas production, and rolling secondary to abdominal pain have been incriminated. Dietary changes, excessive concentrate intake, grazing lush pastures and parasitism may initiate colonic displacement. However, in most cases no initiating factors are identified. Rotation of the colon less than 180° does not cause vascular occlusion, but will cause partial luminal obstruction and mural edema due to lymphatic obstruction.

Right dorsal displacement of the colon

Etiology and pathogenesis

Right dorsal displacement of the colon involves displacement of the left large colon to the right of the cecum, between the cecum and the right abdominal wall. Most commonly, the pelvic flexure migrates to the right, traversing the pelvic inlet cranial to the base of the cecum, and comes to rest at the sternum. Less commonly the pelvic flexure migrates from its normal position directly to the right, caudal to the base of the cecum, and again comes to rest at the sternum. Both of these displacements may be complicated by variable degrees of **volvulus** (*q.v.*).

Clinical findings and diagnosis

Clinical signs associated with colon displacement include abdominal pain and abdominal distension. The degree of clinical signs depends upon the duration and amount of colonic distension. Signs usually develop more rapidly and are more severe than with impaction because of tension on the mesentery and greater colon distension. The displacement often results in pressure on the duodenum, thereby resulting in **nasogastric reflux**. Peritoneal fluid usually remains normal in the early stages of displacement; however, in cases of long duration, increases in peritoneal protein concentration and nucleated cell count reflect compromise of the intestinal wall.

Transrectal palpation reveals mild to severe gas distension of the cecum or colon with large colon teniae often palpable lateral to the cecum or horizontally traversing the pelvic inlet. If the small intestine is secondarily obstructed, several loops of moderately distended small intestine may also be palpable. Following **gastric decompression** and rectal flatulence the horse may exhibit less pain, only to demonstrate recurrent moderate to severe pain when feeding is resumed.

Treatment and prognosis

Correction of right dorsal displacement requires **surgical intervention**. Exposure is best achieved through a ventral midline celiotomy. The pelvic flexure is located and the colons exteriorized. Decompression is often necessary to facilitate exteriorization and correction. The colon is examined for concurrent torsion and the colon is placed back into the abdomen in its proper anatomic position. Effective reduction is ascertained by being able to exteriorize the colon normally and visualize the entire cecocolic fold. Enterotomy is not necessary unless the colon is severely distended with ingesta. Prognosis for complete recovery is good. There is a low occurrence of complications such as adhesions and laminitis (*q.v.*) associated with right dorsal displacement.

If recurrence is a problem, colopexy or large colon resection should be discussed. **Colopexy** may be performed via ventral midline celiotomy or laparoscopically. However, these two procedures are not benign due to the potential postoperative complications, including dehiscence of the colopexy site, catastrophic rupture of the left ventral colon, fistulous tracts associated with sutures entering the lumen of the colon, and severe abdominal adhesions.

Left dorsal displacement of the colon

Etiology and pathogenesis

Left dorsal displacement of the colon involves displacement of variable portions of the left large colon to a position between the dorsal abdominal wall and the nephrosplenic ligament. The colon may pass through the **nephrosplenic space** from a cranial or caudal direction, or it may migrate dorsally when lateral to the spleen. The exact cause of this displacement is not known, but some horses that suffer from the condition have an excessively large nephrosplenic space.

Clinical findings and diagnosis

Clinical signs are similar to those found in horses with right dorsal displacement (*q.v.*). Initially, only a **partial obstruction** exists, thereby resulting in mild pain. However, ingesta and gas accumulate in the region of the pelvic flexure, thereby increasing the distension and the severity of the pain. In some cases obstruction of small intestine by the distended colon will result in **nasogastric reflux**.

Long-standing cases will develop **dehydration**. Peritoneal fluid usually remains normal in the early stages of displacement; however, in cases of longer duration, increases in peritoneal protein concentration and nucleated cell count reflect intestinal devitalization. **Transrectal palpation** reveals mild to severe gas distension of the cecum or colon with large colon teniae often palpable coursing cranial and to the left, over the nephrosplenic space.

The horse may demonstrate signs of discomfort when the nephrosplenic region is palpated. The spleen may be rotated caudally, away from the left body wall due to ventral tension on the nephrosplenic ligament. Transabdominal ultrasound examination of the nephrosplenic space is reported to be a valuable aid in the diagnosis of nephrosplenic entrapment of the colon.

Treatment and prognosis

Non-surgical correction of left dorsal displacement of the colon is often successful in cases in which an early and accurate diagnosis has been made. The first method involves administering the sympathomimetic drug **phenylephrine** IV (20 mg diluted in a 1 L balanced electrolyte solution) to **contract the spleen** and then **jog the horse** to release the entrapment.

The second technique requires **anesthesia** with the horse positioned in right lateral recumbency. **Phenylephrine** is administered prior to induction of general anesthesia to contract the spleen. Hobbles are placed on the hindlimbs and the horse is lifted into dorsal recumbency. As the hindlimbs are lifted to elevate the hind end of the horse off the ground, the abdomen is **vigorously balloted**. This allows the large colon to fall cranial and to the right. The horse is then rolled 360° back to right lateral recumbency, and allowed to recover.

Transrectal palpation to assess the position of the colon may be performed with the horse in lateral recumbency or after recovery. If the procedure is unsuccessful it may be repeated one or two more times. This procedure should not be performed when there is **severe colonic distension** or evidence of **intestinal devitalization,** due to the increased risk of intestinal rupture resulting in fatal peritonitis. The procedure is 70–90% successful in patients with a stable cardiovascular status without severe colonic distension or devitalization. Worsening or recurrence of the displacement, iatrogenic colonic or cecal torsion, and intestinal rupture are potential complications that must be considered before performing this procedure.

When non-surgical treatment is unsuccessful, surgery is necessary. Ventral midline celiotomy reveals the left colons to be located dorsal to the spleen with the pelvic flexure approximating its normal position or slightly flexed cranial or to the right. The entire colon should be located before exteriorizing the pelvic flexure to prevent excessive tension on the ligament. Correction is achieved by pushing the spleen medially and elevating the colon ventrally, lateral to the spleen.

Decompression may be required to assist reduction. Once the colon is free from the nephrosplenic space the pelvic flexure may be exteriorized and the colon placed in its normal position, medial to the spleen. A bruise may be evident on the serosal surface of the colon where it rested on the ligament. Ingesta should be manually redistributed within the colon, however enterotomy and evacuation of ingesta is seldom required. If the colon wall is not compromised, prognosis for complete recovery is good. If recurrence is a problem, colopexy, large colon resection and nephrosplenic space ablation could be discussed. Nephrosplenic space ablation is not associated with complications in athletic horses, unlike colopexy.

Displacements of the pelvic flexure and/or left colon

Etiology and pathogenesis

The most common displacement is **cranial flexion of the left colon** that causes the pelvic flexure to come to lie by the sternum. Displacement and entrapment of the pelvic flexure through a rent in the gastrosplenic ligament, diaphragm, or intra-abdominal mesoductus deferens have also been reported.

Clinical findings and diagnosis

Clinical signs associated with these lesions are similar to those found in horses with right and left dorsal displacement (*q.v.*). The pelvic flexure often cannot be located by transrectal examination.

Treatment and prognosis

Surgery is required for correction of the displacement and repair of the defect. Rents that are impossible to close due to inadequate surgical exposure must be left unrepaired in the hope that displacement will not recur. Diaphragmatic defects should be repaired because recurrence is probable with associated cardiovascular compromise. Prognosis is good if the rent can be closed and the intestine is not devitalized.

STRANGULATING OBSTRUCTIONS

Strangulating obstructions cause **complete luminal obstruction** combined with significant **compromise of the vascular integrity** of the intestine. Vascular occlusion can be either exclusively venous, resulting in hemorrhagic strangulation, or arterial and venous, resulting in ischemic strangulation. Hypoxia and ischemia cause **necrosis** of the involved segment of intestine, thereby leading to hypovolemic and endotoxic **shock**. Equine large intestinal strangulating obstructions include large intestinal torsion, intussusception and incarceration through mesenteric defects (*q.v.*).

Torsion of the large colon

Etiology and pathogenesis

Torsion of the large colon is one of the most **severe and rapidly fatal** abdominal conditions occurring in horses. The condition consists of rotation of the ventral and dorsal colons around their long axis at the origin of the large colon including the cecum, just distal to the cecum in the right colon, or in the middle of the colons. Viewing the horse in dorsal recumbency, the colon usually twists in a counter-clockwise direction with respect to the base of the cecum. The large colon and cecum can also rotate together about the vertical axis of the mesentery (volvulus, *q.v.*).

Rotations of 360° cause the colon to come to lie in an apparently normal position with the mesenteric root completely strangulated. After 4 h of ischemia resulting from vascular occlusion, the colonic mucosa becomes **completely necrotic**, with marked submucosal edema and hemorrhage. By 5 h there is hemorrhage, edema and necrosis at all levels of the bowel wall, often resulting in **intestinal rupture** (*q.v.*). These **time lines** do not always correlate well with clinical findings. The severity of the intestinal compromise may be substantially worse compared with the duration of colic signs.

The exact cause of colonic torsion is not known. **Hypomotility** secondary to dietary changes, electrolyte imbalances and stress may predispose to excessive gas accumulation and floating of the larger ventral colon lateral and dorsal to the smaller dorsal colon, thereby initiating twisting. There is a higher incidence of colon torsion in periparturient brood mares.

Clinical findings and diagnosis

Colon torsions cause an **acute onset** of severe, unrelenting abdominal pain that is either only mildly responsive to analgesic therapy or totally refractory. Both xylazine and detomidine alone or in combination with butorphanol may offer temporary relief. Tachycardia, tachypnea and blanched or congested mucous membranes are usually present. As distension progresses, respiratory function is impaired, resulting in **respiratory acidosis**. Serosanguineous peritoneal fluid with increased protein concentration and nucleated cell count reflects intestinal ischemia and necrosis. Transrectal palpation reveals severe colonic distension sometimes accompanied by mural and mesenteric thickening secondary to edema formation. Teniae may be palpable traversing the abdomen, however the severity of the distension often prevents complete transrectal examination.

Treatment and prognosis

Successful treatment requires an **early diagnosis** and expedient surgical correction. **Decompression** is often necessary to exteriorize the colon. The colon should be placed on a colon tray and an enterotomy performed at the pelvic flexure to evacuate the large colon. This removes endotoxin that can be potentially absorbed following detorsion, prevents further distension during manipulation of the bowel, and facilitates correction. The colonic mucosa should be evaluated during this procedure to assess the degree of **ischemic necrosis**. The direction of the torsion should be determined by palpation at the base of the cecum, and the exteriorized colon rotated in the opposite direction until the cecocolic ligament is visible, running from the lateral cecal tenia to the lateral tenia of the right ventral colon. The affected bowel typically appears blue gray initially and then becomes red to black.

Following correction, the color of the serosal surface of the colon usually improves; however, evaluation of mucosal integrity as well as of the intestinal circulation with fluorescein dye, ultrasound Doppler, tissue oximetry and frozen tissue biopsy can be performed to further assess intestinal viability.

Postoperative treatment of horses that retain sufficient viability of the colon should include **aggressive support therapies** (see volvulus, *q.v.*). If viable cells remain in the mucosal crypts, the epithelium should regenerate within 48–72 h. These horses usually remain endotoxic and pass dark hemorrhagic stools during this time. In some cases, the absorptive function of the colon is lost and diarrhea and protein loss develop. This may resolve after several weeks or be permanent.

If the affected colon is non-viable, colon resection or euthanasia are the only alternatives. Resection involves creating a 15–20 cm side-to-side anastomosis between the remaining viable juxtaparietal (lateral) aspects of the dorsal and ventral colons and resecting the non-viable dorsal and ventral colons. This may be performed by hand suturing techniques or with intestinal stapling equipment. The staple anastomosis minimizes surgical time and contamination at the surgical field, and is therefore recommended if the colonic wall is not excessively edematous. An end-to-end anastomosis has also been described 10–12 cm distal to the cecocolic fold between the dorsal and ventral colons. Approximately 95% of the large colon may be resected, but future colonic function may be compromised.

Colonic torsion recurs in approximately 20–30% of cases. **Colopexy** techniques, in which the lateral tenia of the left colon or the lateral teniae of both the left and right colons are sutured to the abdominal wall, have been used by some surgeons to reduce the incidence of recurrence. Release of the adhesion, suture failure and colonic tearing are potential complications that have been reported. Controlled studies have not been performed to determine the efficacy and safety of these procedures. Elective **colon resection** may also be performed to minimize recurrence.

Prognosis for recovery following colonic torsion is dependent on the interval between diagnosis and surgical correction. Irreversible intestinal ischemia and necrosis rapidly progress to hypovolemic, endotoxic shock and peritonitis. Therefore, the prognosis is poor unless surgery is performed within 2–3 h of the onset of clinical signs. The prognosis is also associated with the length of intestine resected. If >50% of the colon is removed the prognosis is guarded.

Cecocecal and cecocolic intussusception

Etiology and pathogenesis

Cecocecal and cecocolic intussusception are rare causes of intestinal obstruction in horses and result from **invagination** of the **apex of the cecum** into the base of the cecum, or a continuation of the invagination through the cecocolic orifice into the right ventral colon. Ultimately, the **entire cecum** may invaginate into the colon and become strangulated. The exact etiology of these intussusceptions is not known; however, conditions causing aberrant intestinal motility, such as parasitism (most commonly, *Anoplocephala perfoliata, q.v.*), changes in diet, impaction, intramural lesions, and motility altering drugs may predispose to the condition. Cecocolic intussusception appears to occur most frequently in horses <3 yr of age and Standardbreds are overrepresented.

Clinical findings and diagnosis

Horses with **strangulating intussusception** may exhibit signs of acute, severe abdominal **pain**. In cases of chronic non-strangulating intussusception clinical signs include intermittent mild to moderate abdominal pain associated with depression, weight loss and scant, soft feces. The intussusception may be palpable per rectum as a large mass in the right caudal abdomen. The cecum may be distended and palpable in cases of cecocecal intussusception, but is not palpable with cecocolic intussusception. If the ileum is involved in the intussusception, distended small intestine may be palpable. The intussusception may have a "**bulls-eye**" appearance on ultrasonographic examination of the right lower quadrant of the abdomen.

Inflammation and edema of the invaginated cecum cause increased peritoneal fluid protein concentration and nucleated cell count. These changes, however, are often not evident until late in the disease because the affected tissue is sequestered from the abdominal cavity by normal cecum or colon. Failure to respond to medical therapy often leads to surgical exploration, at which time a definitive diagnosis is made.

Treatment and prognosis

Treatment involves **surgical correction** through a ventral midline celiotomy. If the apex of the cecum cannot be located and there is a firm mass palpable in the cecal base and/or the right ventral colon, a cecocecal or cecocolic intussusception should be suspected. The distal ileum and ileocecal orifice are usually involved, and tracing of the ileum into the intussusception confirms the diagnosis.

Attempts to reduce the intussusception are often unsuccessful due to marked mural edema and adhesions that may form between the serosal surfaces. However, if reduction is successfully accomplished and the viability of the cecum is questionable, a **partial typhlectomy** should be performed. If external reduction is not possible, reduction and resection of the devitalized segment of cecum may be performed via an enterotomy in the right ventral colon. If only the apex of the cecum is involved and external reduction is possible, the prognosis is good.

If reduction necessitates an enterotomy, or the entire cecum is involved in the intussusception, the prognosis depends on intestinal viability and degree of contamination at the surgical site, thereby causing peritonitis. A retrospective study on cecocolic intussusceptions suggested that even cases with a partial typhlectomy via a right ventral colon enterotomy with minimal intra-operative contamination should have a good prognosis. Successful management requires aggressive pre- and postoperative supportive therapies (see volvulus, *q.v.*).

Colocolic intussusception

Etiology and pathogenesis

Colocolic intussusception is a rare cause of intestinal obstruction in horses. The left ventral, pelvic flexure or left dorsal colons are most frequently involved. The exact etiology of **colocolic intussusception** is unknown; however, aberrant intestinal motility secondary to parasitism, changes in diet, impaction, intramural lesions and motility altering drugs may initiate intussusception. Colocolic intussusception appears to occur most frequently in **younger horses**.

Clinical findings and diagnosis

Initially, clinical signs include periods of mild to moderate **abdominal pain**. As the disease progresses, the pain becomes more persistent and is only mildly responsive to analgesics. Tachycardia, dehydration and depressed borborygmal sounds gradually develop. Nasogastric reflux may also be present. **Transrectal examination** may reveal a firm viscus within the large colon but, more commonly, distension of the large colon with gas and ingesta is the only abnormal finding. Increases in peritoneal fluid protein concentration and nucleated cell count reflect intestinal compromise, however these changes are often not evident until late in the disease due to sequestration of the affected tissue within the intussusceptum. **Progressive abdominal distension** and persistence of abdominal pain support the diagnosis of large bowel obstruction and the need for surgical exploration.

Treatment and prognosis

Treatment involves **ventral midline celiotomy** with decompression and exteriorization of the ascending colon. Manual reduction of the intussusception is

attempted and may be successful. If reduction is not possible or the intestine is devitalized, colon resection and anastomosis is indicated. If the colon is not markedly edematous, surgical stapling equipment may be used for the resection and anastomosis to minimize surgical time and contamination. End-to-end or side-to-side anastomosis may be performed depending on the location of the intussusceptum and the preference of the surgeon. The prognosis following manual reduction and surgical resection is fair. If resection and anastomosis is performed, successful outcome is dependent on the amount of intestine resected and the degree of peritoneal contamination.

Small colon strangulation

Etiology and pathogenesis

Strangulation of the small colon may occur when a segment of the small colon becomes entrapped in either an internal or external **hernia** (*q.v.*) or incarcerated by **pedunculated lipomas** (*q.v.*). Potential sites of **internal herniation** include the omentum, mesentery of the small or large intestine, and tears in the broad ligament of the uterus, gastrosplenic ligament, uterus or vagina. Potential sites of **external herniation** include the inguinal ring and umbilicus. Small colon volvulus (*q.v.*) is a rare cause of obstruction and strangulation that is usually associated with intra-abdominal adhesions.

Clinical findings and diagnosis

Small colon strangulation presents as acute, severe abdominal **pain** with alterations in cardiovascular and hydration status dependent on the duration of the strangulation. Nasogastric reflux may develop as the disease progresses. Fecal production is reduced or absent and complete transrectal examination is not possible due to small colon distension and tension on the mesentery. Distended loops of small colon are usually palpable, and the caudal mesenteric root may be palpable and extremely taut. The exact site of the strangulation is not discernible, and **exploratory celiotomy** is often necessary for definitive diagnosis.

Treatment and prognosis

Treatment involves ventral midline celiotomy to locate the site of entrapment or volvulus. The hernia is reduced or volvulus corrected and, when possible, defects in the mesentery, omentum or broad ligament are repaired. The viability of the involved small colon is assessed and resection of the affected segment and end-to-end anastomosis of normal colon performed.

FUNCTIONAL OBSTRUCTIONS

Primary cecal and colonic tympany

Etiology and pathogenesis

Cecal and colonic tympany may result either from primary causes or secondary to cecal impaction and large or small colon obstruction. Although the exact etiology is unknown, **primary tympany** may result from **rapid bacterial**

fermentation and gas production and/or impaired motility. Some predisposing factors include abrupt dietary changes and feeding of readily digestible foodstuffs such as grain, lush grass and clover (*q.v.*). It also has been suggested that parasitism may alter motility, leading to gas distension.

Clinical findings and diagnosis

The severity of the abdominal pain associated with cecal tympany depends upon the degree of cecal distension and the presence of a primary disease. In most cases of **primary cecal tympany**, there is mild distension causing mild intermittent abdominal pain. However, in cases of **cecal tympany secondary to physical obstruction**, there is severe distension and abdominal pain. In these latter cases, the horse may develop abdominal distension, greatest in the right paralumbar fossa, and dyspnea due to thoracic compression. The heart rate will be mildly elevated during episodes of pain in mild cases and persistently elevated (up to 90 bpm) in more severe cases. Mucous membranes are pink, but may be tacky due to dehydration. Borborygmal sounds are usually audible, but may be decreased to absent during bouts of abdominal pain.

Percussion of the abdomen reveals areas of gaseous distension. There usually is no nasogastric reflux. **Transrectal examination** usually reveals gas distension of the cecum; however, in severe cases, the ventral tenia of the cecum feels very taut as it courses from the right dorsal quadrant to the left ventral quadrant and the medial and dorsal teniae may be palpable.

In cases of cecal tympany **secondary to physical obstruction** of the colon, distension and/or displacement of the large colon may be evident on transrectal examination. There are usually no remarkable laboratory changes. Clinical examination often may not reveal differences between horses with primary cecal tympany and those with cecal tympany secondary to colonic obstruction.

Treatment and prognosis

Mild to moderate cases often respond to **analgesic drugs** (see Table 10.1). Administration of **mineral oil** (4 L to a 500 kg horse) may decrease fermentation and retard gas production. Mineral oil should not be administered to horses with nasogastric reflux. Cases in which cecal or colonic distension is secondary to a more distal obstruction usually require **exploratory celiotomy**. Cases of **colonic tympany** in which increases in heart rate, alterations in mucous membrane color, and recurrence of pain after analgesic administration are noted may have a more serious condition and should be carefully examined and monitored.

In cases of **severe cecal distension** with risk of cecal rupture, cecal trocarization for decompression may be necessary. Because of the risk of causing **severe peritonitis** due to contamination and laceration of the cecal wall, this procedure should be performed with care. The paralumbar fossa should be clipped, aseptically prepared, and blocked with a subcutaneous bleb of 2% lidocaine. A 14 or 16 G 15 cm needle or catheter should be used. Many equine cecal or bovine trocars are **too large** and will leave a large puncture in the cecal wall that does not seal after withdrawal. After the gas is removed, an antimicrobial agent may be flushed through the catheter just before it is

withdrawn to avoid leaving cecal contents in the peritoneum or abdominal wall. Even when the procedure is performed aseptically, trocarization will result in **peritonitis**, which usually resolves without consequence, but occasionally is severe with secondary abscessation. Therefore, **systemic broad-spectrum antimicrobial therapy** is indicated.

Non-strangulating infarction

Etiology and pathogenesis

Non-strangulating infarction describes **infarction** (*q.v.*) of the intestine without a constricting or compressive lesion. It has been postulated that such infarction is most likely induced by **vasospasm** associated with **verminous arteritis** (*q.v.*). Although lesions occur in both the small and large intestine, lesions of the cecum and colon are most common.

Clinical findings and diagnosis

A **poor parasite control program** may predispose horses to develop non-strangulating ischemia and/or infarction. However, the disease also occurs in horses that are regularly treated with anthelmintics. The severity of the clinical signs is variable, ranging from depression to severe abdominal pain. Heart rate and respiratory rate may remain normal or may increase. Hyperemic mucous membranes may be present suggesting endotoxemia (*q.v.*). Body temperature may be elevated due to either endotoxemia or the inflammation caused by migrating parasites. Lesions of the cecum and large intestine may cause mild or moderate cecal or colonic **tympany** (*q.v.*). Pain, fremitus or thickening may be evident upon palpation of the mesenteric root. Auscultation of the abdomen may reveal increased, normal or decreased borborygmal sounds. PCV, total plasma protein and creatinine may increase due to dehydration.

The peripheral blood may reveal decreased (neutropenia with a left shift), normal or increased WBC count. Total protein may be increased due to the chronic inflammation caused by parasitism or decreased as a result of protein loss through damaged intestinal mucosa. Abdominal fluid may be normal or have tremendous elevation in protein content (≥3.0 mg/dL) and WBC count (up to 200 000 cells/μL).

Treatment and prognosis

Balanced polyionic IV fluids (e.g. acetated Ringer's; 50–100 mL/kg/day) are an important part of therapy to correct dehydration and encourage reperfusion of the involved intestinal segments. If nasogastric reflux is obtained, careful attention should be given to maintain gastric decompression. **Broad-spectrum antimicrobials** (e.g. potassium benzylpenicillin G 22 000–44 000 mg/kg IV q 6 h and gentamicin sulfate 6.6 mg/kg IV q 24 h) should be administered if peritonitis (*q.v.*) is present. **Flunixin meglumine** (0.25 mg/kg q 8 h) may reduce thromboxane production, which causes or contributes to **mesenteric vasoconstriction**. **Dimethyl sulfoxide** (10 mg/kg q 8 h) diluted to a 10% solution in a balanced electrolyte solution and administered IV may help decrease some of the superoxide radical damage that occurs during reperfusion. Large dosages of aspirin (20 mg/kg PO daily) and heparin (40–100 IU/kg PO q 8 h) have been suggested to prevent thrombogenesis, however these are not routinely used.

Surgery should be considered in patients that deteriorate despite medical therapy. However, the prognosis is poor for patients with intestinal infarction requiring surgical resection. Extensive peritonitis may have already developed. Ischemia not obvious at the time of surgery may later progress to infarction. Ileus and adhesions (*q.v.*) are common postoperative complications. Large intestinal involvement may be too extensive for resection to be practical. However, identification and resection of involved segments of either small or large intestine is sometimes performed successfully.

LARGE COLON DISEASES CAUSING PERITONITIS

CECAL PERFORATION

Etiology and pathogenesis

The site of **cecal perforation** is usually the medial or caudal surface of the base. Excessive tension on the wall of the cecum as a result of **severe impaction** (*q.v.*) is the most common cause. Perforation of the cecum has also been associated with **late gestation** and **parturition**, but the pathogenesis of perforation in these animals is unknown. It has also been suggested that tapeworm infestation (*q.v.*) can cause perforation.

Clinical findings and diagnosis

Horses with cecal perforation usually have progressive signs of **cardiovascular shock** (*q.v.*) due to peritonitis. The rate of progression depends upon the rate of contamination of the peritoneal cavity. Transrectal examination may reveal enlargement of the cecum. However, after leakage of cecal contents into the peritoneal cavity, the distension may be reduced. **Emphysema** (*q.v.*) or roughening of the serosa at the base of the cecum may be palpable. The peritoneal fluid usually reveals an increased WBC count and protein content. Degenerative white cells and bacteria may also be present, depending upon the degree of leakage and the degree to which the resulting inflammation has sealed the perforation.

Treatment and prognosis

Therapy includes antimicrobials and supportive therapies (see duodenitis and proximal jejunitis, *q.v.*), which may result in temporary improvement of clinical signs. However, after fecal contamination of the peritoneal cavity has occurred, **death from shock** is imminent. Ventral midline celiotomy or a right flank laparotomy with resection of the eighteenth rib can be performed to repair the tear or remove the cecum and perform a bypass procedure. Open peritoneal lavage should also be performed. However, surgical correction after perforation is usually unsuccessful because the peritonitis continues to progress and the tear often cannot be completely exposed.

RECTAL TEARS

Etiology and pathogenesis

Rectal tears are most often **iatrogenic**, occurring during transrectal palpation for evaluation of the reproductive or gastrointestinal system. Other less

common causes include breeding accidents, pelvic fractures, dystocia, external trauma, perforation during enema administration and spontaneous rupture secondary to thromboembolism (*q.v.*). The rectum is the terminal 25–30 cm of the gastrointestinal tract, extending from the pelvic inlet to the anus. The peritoneum attaches 15–20 cm proximal to the anus, and therefore the proximal rectum is within the peritoneal cavity.

Most tears occur **dorsally**, between the 10 and 2 o'clock positions, in or near the site of **mesenteric attachment**. Those that occur more than 15–20 cm proximal to the anus are at a level beyond the peritoneal reflection and therefore at risk of extending into the peritoneal cavity.

Rectal tears are classified as grades I to IV according to the anatomic structures involved and **depth of mural perforation**. Grade I tears involve only the mucosa, or mucosa and submucosa. In grade II tears, only the muscular layers are separated and this results in a mucosal–submucosal diverticulum that rarely progresses to rupture. Grade IIIA tears involve perforation of the mucosa, submucosa and muscular layers, leaving the serosa as the only barrier between the peritoneal or pelvic cavity and the rectal lumen. Grade IIIB are similar to type A, but the tear is located dorsally so that only the mesorectum is left as the only barrier remaining. Both IIIA and B tears frequently progress to grade IV tears, in which all layers of the rectal wall are perforated, causing a communication between the peritoneal or pelvic cavity and the rectal lumen.

Although more common with inexperienced examiners, rectal tears may occur at all levels of experience. There appears to be a higher incidence of rectal tears in **Arabian** stallions and geldings. Regardless of the etiology, rectal tears should be considered an **emergency** and evaluated immediately to determine the degree of perforation in order to implement necessary supportive and therapeutic measures.

Clinical findings and diagnosis

In most cases the veterinarian is not aware that the tear has occurred until the arm is withdrawn and **fresh blood** is seen on the sleeve. The location of the blood on the sleeve may help indicate the depth at which the tear has occurred. A sudden release of rectal wall tension may be experienced during the tear, but is usually assumed to be a passage of a peristaltic contraction. The most common site of rectal tears is on the dorsal aspect approximately 15–55 cm from the anus.

Clinical signs will vary with the type of tear that is present. Horses with grade I and grade II tears rarely have any clinical signs associated with the tear. Horses with grade II tears may present for **rectal impaction** or **straining during defecation** at a later date. The diverticulum is identified during manual removal of feces from the rectum. Horses with grade III tears will develop fecal impaction within the **retroperitoneal space** of the pelvic cavity. Although there is no direct communication with the peritoneal cavity, **diffusion of bacteria and endotoxin** into the retroperitoneal cavity may cause ileus (*q.v.*), abdominal pain and increases in peritoneal fluid protein concentration and nucleated cell count.

The severity of clinical signs that follow is dependent on the degree of tissue involvement and the proximity of the lesion to the peritoneal cavity. If tissue dissection is extensive, the vascular supply to the mesocolon may be

damaged, leading to **infarction** (*q.v.*) of the affected segment of small colon and signs consistent with obstruction and strangulation (*q.v.*). If gross contamination of the peritoneal cavity occurs with grade IV tears, mild to severe abdominal pain is evident and endotoxemia (*q.v.*) and circulatory shock rapidly ensue. **Abdominocentesis** yields turbid fluid containing degenerative neutrophils, plant material and bacteria.

Diagnosis of rectal tears can be confirmed by careful digital examination of the rectum with a bare hand or visualization with a vaginal speculum or flexible endoscope. Tranquilization with **xylazine** (0.66 mg/kg IV) or acepromazine (0.06 mg/kg IV) and **caudal epidural anesthesia** (xylazine 0.017 mg/kg in 10 mL saline solution or 7–10 mL 2% mepivacaine in the first intercoccygeal space) greatly facilitates examination. The antimuscarinic **propantheline bromide** (0.014 mg/kg IV) can be used to induce **relaxation of the rectal wall**, and an **enema of 2% lidocaine hydrochloride** (30 mL mixed with **warm water**) will help desensitize the rectum. Fecal material is carefully removed and the tear is located. Once identified, the tear must be assessed for position, size, depth of penetration, and distance from the anus.

Treatment and prognosis

Medical therapy, including **stool softeners, a laxative diet, tetanus toxoid, IV broad-spectrum antimicrobial drugs** (e.g. metronidazole 15–25 mg/kg PO q.i.d., potassium benzylpenicillin G 22 000–44 000 mg/kg IV q 6 h and gentamicin sulfate 6.6 mg/kg IV q 24 h), and **flunixin** meglumine (see Table 10.1), should be initiated immediately for all rectal tears.

Supportive therapy for **shock** (see duodenitis and proximal jejunitis, *q.v.*) is necessary in some cases. **Mineral oil** (1 L PO) is the stool softener most commonly employed. Lush green pasture with controlled exercise is probably the best diet. Pelleted feeds may be used if green pasture is not available.

Small grade I or II tears usually heal spontaneously but should be monitored closely for 4–6 days and treated medically. Larger grade II tears should be treated with **manual evacuation of feces from the tear** in addition to medical therapy. With manual evacuation, care must be taken to prevent enlargement of the tear.

More severe grade II–IV tears are considered emergencies and should be transported to a **surgical referral** facility immediately. Following epidural anesthesia, the rectum should be gently packed proximal to the tear with cotton soaked in a non-irritating disinfectant such as dilute povidone-iodine. This will minimize contamination of the tear and peritoneum with fecal material during transport.

When possible, tears may be hand sutured through the rectum in standing or lateral recumbency or by ventral midline celiotomy. Transrectal suturing techniques may be performed by one-handed blind palpation and suturing, or with the aid of an expandable wire rectal speculum and specialized long surgical instruments. Stay sutures may be used to retract the tear into view. These transrectal techniques are often frustrating and difficult and carry the risk of making the tear worse or causing further tissue trauma. The success of these techniques depends on the skill and experience of the surgeon, temperament and condition of the horse, mobility of the rectum, and location of the tear. Hourly manual evacuation has also been reported to be successful in

treating grade II–III rectal tears with adjunctive stool softeners and appropriate medical therapy.

A **rectal liner** can also be used to protect the tear from contamination during healing. A ventral midline celiotomy is performed and the large colon evacuated through a pelvic flexure enterotomy. A small colon enterotomy is then performed and a rigid plastic ring with a rectal liner attached is sutured in the lumen of the colon proximal to the tear. These sutures are placed in a manner to cause necrosis and sloughing of that portion of the bowel. The colon segments oral and aboral are sutured together over the ring, resulting in an anastomosis once the inner portion of bowel sloughs. The rectal tear heals before the inner portion sloughs. Fecal material passes into the ring and through the liner, which exits outside the anal sphincter. Difficulty of passage of fecal material through the ring and premature sloughing of the ring are reported problems of this technique.

In grade III or IV tears, a temporary diverting **colostomy** may be performed to avoid continual contamination at the perforation site and allow the tear to heal by secondary intention. Either a loop or end-on technique is performed through a left flank laparotomy. Closure of the colostomy can be a very difficult and time-consuming procedure and is best done as early as possible (2–5 wk after the initial surgery). The end-on technique produces fewer adhesions, but results in atrophy of the distal segment causing a large discrepancy in luminal diameter between the proximal and distal segments, thereby making anastomosis more difficult. The loop colostomy prevents this problem but does allow some fecal material to pass the colostomy site, thereby serving as a source for continual contamination at the tear. This is minimized by careful placement of the loop colostomy to ensure that the proximal segment of bowel is dependent.

The **prognosis for grade I and II tears is good** with early detection and immediate and proper therapy. Grade III tears have a fair to guarded prognosis and grade IV tears have a grave prognosis. Complications associated with rectal tears and surgical repair include breakdown of the suture line, peritonitis, pelvic abscess formation, impactions, prolapse of the colon (colostomy) and laminitis (*q.v.*). If fecal contamination of the peritoneal cavity is generalized, fatal peritonitis (*q.v.*) or extensive intra-abdominal adhesion formation leads to the demise of the animal.

GASTROINTESTINAL DISEASES CAUSING CHRONIC WEIGHT LOSS

INTRODUCTION

Chronic weight loss is a relatively common complaint among horses presented to the equine practitioner. While the etiologies of chronic weight loss can be numerous and varied (Box 10.1), the majority of cases are caused by one of a much smaller group of diseases. With the exception of decreased feed intake and malnutrition, gastrointestinal diseases are among the most common causes of chronic weight loss.

Clinical evaluation of a horse with chronic weight loss requires consideration of the potential underlying mechanisms. **Decreased feed intake** or malnutrition may result from inadequate feed intake, feeding poor quality

Box 10.1 Differential diagnosis of chronic weight loss in the horse

Conditions resulting in decreased feed intake or malnutrition

- Inadequate diet
- Dental and jaw abnormalities
- Oral and pharyngeal abnormalities
- Esophageal abnormalities
- Any disease causing anorexia

Conditions resulting in increased nutrient loss

- Urinary loss of nutrients
  - Pituitary dysfunction
  - Renal disease
- Gastrointestinal loss of nutrients
  - Parasitism
  - Granulomatous, eosinophilic, lymphocytic and basophilic enteritis
  - Squamous cell carcinoma
  - Lymphosarcoma
  - Non-steroidal anti-inflammatory drug toxicity

Conditions resulting in maldigestion/malabsorption

- Maldigestion
  - Liver disease
- Malabsorption
  - Intestinal resection
  - Congestive heart failure
  - Parasitism
  - Granulomatous, eosinophilic, lymphocytic and basophilic enteritis
  - Sand-induced enteritis
  - Lymphosarcoma
  - Salmonellosis
  - Abdominal abscessation
  - Partial chronic bowel obstruction

Conditions resulting in increased energy requirements

- Abdominal abscessation
- Parasitism
- Recurrent airway obstruction
- Equine infectious anemia
- Equine viral arteritis
- Peritonitis
- Endocarditis/pleuritis
- Renal disease
- Neoplasia

foods, a failure to separate animals adequately at feeding time (thereby resulting in inadequate intake by non-dominant horses), poor dentition, oral and pharyngeal abnormalities, other causes of painful mastication and swallowing, and diseases causing anorexia.

Nutrient losses can occur in a number of conditions. For example, several diseases can cause significant loss of protein and/or glucose through the kidney or gastrointestinal tract.

Many diseases cause weight loss by impairing nutrient absorption. **Malabsorption** (*q.v.*) is a condition resulting from the impaired digestion and absorption of dietary components. It can result from structural or functional abnormalities of the large or small intestine, pancreas, liver or biliary tract. **Chronic diarrhea** due to large bowel malabsorption of water and electrolytes may or may not occur in horses with small intestinal malabsorption. **Large intestinal malabsorption** (*q.v.*) may result either from osmotic imbalances secondary to the passage of malabsorbed carbohydrates into the large intestine or from structural damage to the large intestine. Diseases causing malabsorption include disruption of the intestinal mucosa, intestinal inflammation and/or infiltration, lymphatic obstruction, abnormalities of the intestinal circulation (e.g. heart failure) and abnormalities of intestinal motility. Furthermore, impaired nutrient digestion and absorption can result from **chronic liver disease** (*q.v.*).

Increased energy demand not compensated by nutrient intake will result in weight loss. **Anxiety** or **increased exercise** may not be compensated by increases in feed ration. Chronic infection and **neoplasia** are common causes of increased energy utilization. Recurrent airway obstruction (RAO) (*q.v.*) can result in energy depletion through increased respiratory effort.

Several mechanisms may be involved in some causes of weight loss. For example, parasite infestation may result in both increased energy loss through **fecal protein exudation** and decreased absorption through damage to the intestinal absorptive surface.

DIAGNOSIS OF CHRONIC WEIGHT LOSS

History is a vital element in the diagnostic protocol for chronic weight loss. The owner should be questioned closely about the presence of additional localizing signs such as diarrhea, abdominal pain, pyrexia, exercise intolerance, coughing, dyspnea, dysphagia and polyuria (*q.v.*). If possible, the weight loss should be **quantified**. Because intermittent elevations of body temperature may be noted with some chronic infections, body temperature should be monitored periodically (e.g. twice daily). Owners can be instructed in the use of a "weigh tape" (*q.v.*) to provide a rough estimate of weight change.

Parasite control and feeding management practices should be evaluated. Knowledge of the frequency and type of anthelmintic treatment for all horses on the farm and number of horses pastured together is needed. The amount (by weight) and nature of feed consumed per day should be defined. Information about the location of feeding (group or individual) should be sought, pasture should be examined for quality, and the feed should be assessed for signs of spoilage. Analysis of the specific crude energy and protein content of the hay is useful to estimate quality.

A **complete physical examination** with close attention to the oral cavity should be made. The horse should be observed while eating for difficulty in prehension, mastication or swallowing. The presence of dyspnea, coughing, tachycardia, icterus, oral abnormalities or dysphagia may signal the presence

of respiratory, cardiovascular, liver or oropharyngeal diseases (*q.v.*) causing weight loss. If any question arises regarding quality or quantity of feeding, feed analysis is essential, and nutrient intake (*q.v.*) should be compared to estimated requirements for the individual.

Laboratory analyses should include fecal examination for parasites and blood, a complete blood count, serum chemistry (creatinine, total protein, albumin, liver enzymes, bilirubin, glucose and serum electrolytes), plasma fibrinogen concentration and urinalysis. Chronic anemia (*q.v.*) may be the result of chronic disease or diseases of the hemolymphatic system (*q.v.*) causing weight loss. Leukocytosis, neutrophilia, leukopenia, neutropenia, hyperfibrinogenemia, decreased plasma protein to fibrinogen ratio (≤10), or normal hematology and serum chemistry may be noted in horses with **chronic inflammatory diseases**. Elevated serum and urinary glucose concentrations may suggest an **endocrine abnormality** (*q.v.*). Elevated serum creatinine concentration, isosthenuria and proteinuria may be suggestive of **renal disease** (*q.v.*). Hypoalbuminemia may be associated with malnutrition, liver disease, renal disease or protein-losing enteropathy.

After it is determined that the horse has easy access to adequate nutrients and there is no historical, physical or laboratory evidence of diseases of other body systems, a thorough examination of the **gastrointestinal tract** is indicated. History of either intermittent abdominal pain or diarrhea is supportive of gastrointestinal disease; however, weight loss due to gastrointestinal diseases is frequently not accompanied by any other signs. For example, diseases causing **small intestinal malabsorption** can result in significant weight loss (e.g. **granulomatous enteritis**, *q.v.*). However, water absorption in the large colon, and therefore fecal character, are frequently normal in horses with small intestinal malabsorption.

Carbohydrate absorption tests should be used when intestinal malabsorption is suspected. The **glucose** and **D-xylose absorption tests** are the most widely used in horses (Box 10.2). The D-xylose absorption test is more expensive to perform due to the higher cost of xylose. However, because the results of glucose absorption tests are affected by endogenous factors (e.g. insulin and glucocorticoids), xylose absorption tests provide a more accurate indicator of small intestinal malabsorption. Both glucose and D-xylose absorption

Box 10.2 Oral glucose and D-xylose absorption test protocols

1. Fast the horse for 18–24 h
2. Administer a 10% solution of glucose or D-xylose via nasogastric tube at a rate of 1 g/kg BW
3. For the glucose assay, blood is collected in sodium fluoride tubes; for D-xylose, blood is collected in heparinized tubes
4. Blood samples are taken at 0, 30, 60, 90, 120, 150, 180, 210, and 240 min post administration
5. Peak concentration (D-xylose 20–25 mg/dL) occurs at 60–120 min post administration and is normally double the resting concentration
6. Concentration should return to normal at 6 h

tests are affected by delayed gastric emptying and increased intestinal transit time. Therefore, horses with abnormal results should be retested to eliminate the effects of these influences.

CHRONIC WEIGHT LOSS

Granulomatous, eosinophilic, lymphocytic and basophilic enteritis

Etiology and pathogenesis

These conditions are marked by a granulomatous, eosinophilic, basophilic or lymphocytic infiltration in the gut wall, with diffuse and patchy infiltrates and distinct granulomas composed of epithelioid, lymphoid and occasional giant cells and macrophages. Lymphoid hyperplasia, perilymphatic and transmural inflammation, lymphangiectasia, villous atrophy, mucosal ulceration, fibrosis, crypt abscesses and serosal fibrosis (*q.v.*) are often present. **Small intestinal lesions** are most common, thereby resulting in enteric protein loss and carbohydrate malabsorption. Protein loss may result from active protein secretion by mucosal cells, exudation through inflamed and ulcerated mucosa, disordered mucosal cell metabolism and rupture of dilated mucosal lymph vessels.

As the disease progresses, lesions develop in the large intestine **disrupting fluid absorption** and causing **diarrhea**. The etiology of these conditions is unknown but they are more prevalent in Standardbreds <5 yr of age than in other breeds. Rare cases of enterocolitis have been associated with infectious agents (e.g. *Histoplasma* and *Mycobacterium paratuberculosis*, *q.v.*).

Clinical findings and diagnosis

Chronic weight loss is the most common clinical sign associated with granulomatous, eosinophilic, basophilic and lymphocytic enteritis (*q.v.*). Appetite remains normal. Peripheral edema and diarrhea may be seen, especially in later stages of the disease. Anemia, hypoproteinemia and hypoalbuminemia are common laboratory findings. Small intestinal lesions result in malabsorption of glucose and xylose, while large bowel lesions cause diarrhea.

Hypoproteinemia in the absence of proteinuria, liver disease or malnutrition implicates the intestine as the site of protein loss. Demonstration of xylose and glucose malabsorption provides further support for the presence of an inflammatory or infiltrative disorder of the small intestine. A presumptive diagnosis can be made by ruling out other causes of malabsorption (see Box 10.1). Definitive diagnosis can only be made by **histologic examination** of intestinal sections obtained via **laparoscopy**, exploratory laparotomy or post mortem examination.

Treatment and prognosis

There is no effective treatment for these diseases. Reported treatments include administration of anthelmintic drugs, anabolic steroids, antibiotics, clioquinol, sulfasalazine and methylsulfonylmethane without efficacy. These medications may transiently alter **fecal consistency** without correcting weight loss. Temporary improvement has sometimes been associated with prolonged administration of corticosteroids. However, the weight loss and

hypoproteinemia eventually result in severe debilitation necessitating euthanasia.

Intestinal neoplasia

Etiology and pathogenesis

A number of intestinal neoplasms have been reported in the horse although the general incidence is ≤0.1%. Of the recognized intestinal neoplasms, **lymphosarcoma** (*q.v.*) is most common and affects horses of all ages. Other organ systems in addition to the gastrointestinal tract may be affected by lymphosarcoma. Other relatively common neoplasms of the equine gastrointestinal tract include gastric squamous cell carcinoma and adenocarcinoma (*q.v.*).

In horses with **intestinal lymphosarcoma**, infiltration of the intestinal wall by tumor cells can result in protein exudation and carbohydrate malabsorption. Chronic weight loss also results from increased energy requirements for tumor growth ("**cancer cachexia**"). **Gastric squamous cell carcinoma** and **adenocarcinoma** can also result in obstruction.

Clinical findings and diagnosis

Chronic weight loss is the most common early clinical sign. More specific signs vary with the location and type of tumor. Additional features may include **dysphagia** (gastric squamous cell carcinoma), acute abdominal pain, chronic abdominal pain secondary to adhesion formation, or chronic diarrhea secondary to neoplastic infiltration of the colonic wall.

As with other intestinal inflammatory or infiltrative diseases, **laboratory evaluation** may reflect intestinal protein loss (hypoproteinemia or hypoalbuminemia) and xylose and glucose malabsorption. Inflammatory responses to the tumor can also cause hyperproteinemia or hypergammaglobulinemia. Definitive diagnosis can occasionally be based on the cytologic evaluation of peritoneal fluid. With **multicentric disease**, peripheral lymph node biopsy or pleural fluid cytology may be diagnostic. Abdominal ultrasound occasionally reveals masses accessible by percutaneous biopsy. If this is unrewarding, histologic examination of intestinal tissues obtained at laparoscopy, exploratory laparotomy or post mortem may be required to provide a definitive diagnosis.

Treatment and prognosis

There is no effective treatment and euthanasia is eventually necessary due to severe debilitation.

Parasitism

Etiology and pathogenesis

Parasitic disease is the **most common cause of weight loss** in the horse (see also page 95). However, the frequency of disease has decreased with availability of newer anthelmintics. A range of deleterious effects may be ascribed to each type of parasitic infestation. Specific pathogenesis will depend on host, environment and parasite factors. Stress, immune suppression or concurrent diseases will all predispose to an increased severity of infection. Furthermore,

an intense inflammatory response to parasites may increase the severity of the intestinal lesions. As a result of the **complex interaction** of these factors, horses managed in the same environment and with identical anthelmintic therapy rarely demonstrate similar clinical signs due to parasitism.

Parasite transmission (*q.v.*) is determined by a number of factors. Heavily populated pastures with warm, moist environmental conditions promote environmental contamination, development of eggs into infective larvae, and ingestion of larvae. Parasite eggs are generally very hardy and survive for several years on pasture. Infective larvae survive for 6–10 wk in warm, moist conditions. They are relatively resistant to cold temperatures, but are rapidly destroyed by heat and desiccation.

Strongylus vulgaris (*q.v.*) larvae may cause a severe inflammatory reaction in the submucosa of the small intestine, cecum and ventral colon during their migration to the **ileocecocolic artery**. Lesions caused by the larvae in the mesenteric arteries may cause **bowel ischemia** and damage the adjacent mesenteric plexus. Gut motility and autonomic control may be disturbed. Ischemia may progress to infarction with mucosal necrosis and thus **malabsorption.** Extensive infarction can lead to **necrosis** of the entire bowel wall. Adult strongyles feed by digesting mucosal plugs in the glandular mucosa of the large intestine. This results in **ulceration**, which may extend into the muscularis and adjacent blood vessels. Absorptive and digestive functions are therefore impaired causing a malabsorptive, maldigestive weight loss. Protein exudation into the intestinal lumen infrequently occurs in horses with intestinal ulceration due to parasitism.

There has been an increased awareness of disease caused by **small strongyles** (**cyathostomes** *q.v.*) as a result of decreased incidence of disease due to large strongyles and increased prevalence of benzimidazole-resistant cyathostomes. Adult cyathostomes cause weight loss by causing intestinal wall inflammation and ulceration. In their larval stages, these parasites can migrate and become encapsulated in the mucosa of the large colon and cecum. These cysts damage the submucosal glands and generate an inflammatory infiltrate of neutrophils, fibroblasts and eosinophils. The fibrinous enteritis resulting from mucosal disruption also causes malabsorption and maldigestion.

Clinical signs and diagnosis

Acute clinical disease can be seen with large and small strongyle infestation. **Massive, sudden exposure** to infective larvae can result in a syndrome characterized by fever, endotoxemia, inappetence, lethargy, colic and weight loss due to massive intestinal ulceration and inflammation and/or intestinal infarction.

More commonly, subacute infestations result in chronic weight loss. Concurrent signs sometimes include dullness, poor haircoat, diarrhea and mild intermittent colic. Infestations with large and small strongyles may cause acute severe colitis or chronic weight loss due to **maldigestion/malabsorption** with or without diarrhea.

History is important in the diagnosis of parasite infestations. A horse that is presented for chronic weight loss, coming from a **crowded pasture** and with a poor or **unreliable deworming history**, should be considered at high risk for parasitic disease. Observation of the other members of the group with other

manifestations of parasite infestation may support such a suspicion. However, because there is individual variation in sensitivity to parasite infestation, disease may be restricted to one horse in a population. Weight loss due to parasitism can also occur in horses on a seemingly adequate parasite control program. **Ova counts** from fecal samples obtained from several horses in the same pasture can be used to help assess the adequacy of parasite control.

Clinicopathologic examination may reveal anemia, hyperglobulinemia, hypoalbuminemia and hypo- or hyperproteinemia. Horses do not commonly develop eosinophilia due to parasitism. Examination of feces may reveal a high ova count consistent with inadequate parasite control. However, if the disease is due to larval stages of *Strongylus vulgaris* or cyathostomes, fecal examination for ova can be negative. Peritoneal fluid may be normal or reflect mild inflammation with or without increased numbers of eosinophils.

Treatment and prognosis

The symptomatic animal should be treated with larvicidal dosages of anthelmintics (*q.v.*). Some clinicians prefer treatment with a non-larvicidal anthelmintic 2–3 days before larvicidal therapy. If severe bowel inflammation secondary to rapid parasite death is of concern, treatment with NSAIDs (e.g. **flunixin** meglumine at 0.25–1.1 mg/kg) at the time of anthelmintic administration may be warranted. **Larvicidal alternatives** include: **ivermectin** 200 μg/kg PO (single dose); **moxidectin** 400 μg/kg PO single dose; **fenbendazole** 50 mg/kg PO q 24 h for 3 days or 10 mg/kg PO q 24 h for 5 days. If improvement is not noticed in approximately 4 wk, larvicidal anthelmintic therapy should be repeated.

After larvicidal therapy, the **parasite control program** should be evaluated and improved if necessary. The frequency and type of anthelmintic treatments are important factors in a parasite control program. Commonly used anthelmintics are listed in Table 10.2. Slow rotational programs involve changing the class of anthelmintic on a yearly basis, while fast rotational programs use more frequent anthelmintic changes. **Conflicting results** have been reported as to which rotational strategy is more likely to minimize the development of resistance.

Each horse in a group should be treated **on the same day**. The **frequency** of anthelmintic therapy should be based on stocking rate, climate and pasture management. **Long-term evaluation** of a parasite control program is most easily obtained by monitoring fecal egg counts among herd members. Herd average fecal egg counts should be kept to <200 eggs per gram (EPG) at all times. Anthelmintic efficacy may be monitored by performing pre- and post-treatment fecal egg counts. A 90% decrease in EPG should be obtained for at least 3 wk post treatment.

Other parasite control measures include **rotation** to an uncontaminated pasture after anthelmintic treatment and **manure removal**, chain harrowing, or **cross grazing** of contaminated pastures with other species (e.g. cattle or sheep).

Abdominal abscessation

Etiology and pathogenesis

The diagnosis of chronic weight loss caused by **abdominal abscessation** is often difficult due to the insidious and non-specific nature of the disease.

Table 10.2 Dosage, safety and efficacy of commonly used equine anthelmintics

	Dosage (mg/kg)	Larvicidal	Worms affected
Non-benzimidazoles			
Ivermectin	0.2	Yes	*Parascaris equorum*, large strongyles, cyathostomes, bots, *Oxyuris equi*
Moxidectin	0.4	Yes	*Parascaris equorum*, large strongyles, cyathostomes, bots, *Oxyuris equi*
Pyrantel pamoate	6.6	No	*Parascaris equorum*, large strongyles, cyathostomes, *Oxyuris equi*
Pyrantel pamoate	13–20	No	*Parascaris equorum*, large strongyles, cyathostomes, *Oxyuris equi*, tapeworms[1]
Pyrantel tartrate	2.5 daily	No	*Parascaris equorum*, large strongyles, cyathostomes, *Oxyuris equi*
Praziquantel	1.5	No	Tapeworms
Ivermectin w/praziquantel	0.2 1.5	Yes	*Parascaris equorum*, strongyles, cyathostomes, bots, *Oxyuris equi*, tapeworms
Moxidectin w/praziquantel	0.4 2.5	Yes	*Parascaris equorum*, strongyles, cyathostomes, bots, *Oxyuris equi*, tapeworms
Benzimidazoles			
Fenbendazole	5–10	No	*Parascaris equorum*, large strongyles, cyathostomes, *Oxyuris equi*
Fenbendazole	10 s.i.d. × 5	Yes	*Parascaris equorum*, large strongyles, cyathostomes, *Oxyuris equi*
Fenbendazole	50 s.i.d. × 3	Yes	*Parascaris equorum*, large strongyles, cyathostomes, *Oxyuris equi*
Oxfendazole	10	No	*Parascaris equorum*, large strongyles, cyathostomes, *Oxyuris equi*
Oxibendazole	10–15	No	*Parascaris equorum*, large strongyles, cyathostomes, *Oxyuris equi*
Mebendazole	8.8	No	*Parascaris equorum*, large strongyles, cyathostomes, *Oxyuris equi*
Probenzimidazoles			
Febantel	6	No	*Parascaris equorum*, large strongyles, cyathostomes, *Oxyuris equi*

[1] *Commonly recommended for tapeworms but quantitative assessment of efficacy not available.*

Intra-abdominal abscesses may result from **dissemination of bacteria via the bloodstream** or **lymphatic system**, thereby resulting in abscessation of mesenteric lymph nodes. **Perforation of the intestine** (e.g. by a foreign body) or **penetration of the abdominal wall** may also result in local peritonitis and abscess formation. Specific etiologies include *Streptococcus equi equi*, *Strep. equi zooepidemicus*, *Rhodococcus equi* (foals), Gram-negative enteric bacteria (e.g. *Escherichia coli*, *Klebsiella* spp.) and anaerobic bacteria (*q.v.*).

Weight loss in horses with abdominal abscesses may result from several causes. Metabolic rate, and thus energy requirement, is increased as the body attempts to **resolve the infection**. Obstruction of the **mesenteric venous vasculature** may result in intestinal vascular congestion, and thus **malabsorption**. Compression of the intestine or adhesion formation may result in partial

or complete obstruction. Recurrent abdominal pain may result in inappetence. Recurrent fever may also cause depression and anorexia.

Clinical findings and diagnosis

Mesenteric abscessation may result in chronic weight loss, intermittent or low-grade fever, depression and inappetence. If the lesion results in partial or complete intestinal stricture, mild recurrent or severe acute colic may be seen. Colic may also result from a large abscess in the mesentery or secondary to peritonitis. Heart and respiratory rates may be increased.

Weight loss with an **intermittent fever** is consistent with abdominal abscessation. Hematologic abnormalities may include mild anemia, neutrophilia or neutropenia with a left shift, and elevated plasma fibrinogen concentration. Total plasma protein concentration is often elevated, with increased globulins and decreased albumin. Peritoneal fluid may be normal in the case of a walled-off abscess, however more commonly the fluid is cloudy with an increased nucleated cell count and protein concentration. Occasionally, intracellular bacteria are seen on cytologic examination of the peritoneal fluid. **Abdominal fluid should be cultured**, although the findings are often negative. The abscess may be palpable via rectal examination but may be out of the reach. Ultrasonographic evaluation may also be helpful.

Treatment and prognosis

Long-term treatment (for weeks to months) with an appropriate antimicrobial drug is usually necessary. If a positive culture is obtained, treatment should be based on antimicrobial sensitivity testing. *Streptococcus equi equi* and *Strep. equi zooepidemicus* are generally susceptible to penicillin. **Procaine benzylpenicillin** (22 000–44 000 IU/kg IM b.i.d.) or **potassium benzylpenicillin** (22 000–44 000 IU/kg IV q.i.d.) is commonly used. *Streptococcus* spp. are often sensitive to **erythromycin** (25 mg/kg PO t.i.d. or q.i.d.), but commonly resistant to potentiated sulfonamides. The combination of **clarithromycin** (7.5 mg/kg PO b.i.d.) and **rifampicin** (5 mg/kg PO b.i.d.) is the treatment of choice for abscessation due to *Rhodococcus equi*.

If the specific etiology is unknown, broad-spectrum antimicrobial therapy is indicated (potassium benzylpenicillin 22 000–44 000 IU/kg IV q 6 h or procaine benzylpenicillin G 22 000–44 000 IU/kg q 12 h with gentamicin 6.6 mg/kg once daily IV or IM and metronidazole 15 mg/kg q 8 h PO or 20 mg/kg per rectum q 8 h). Anti-inflammatory drugs such as **phenylbutazone** (4–8 mg/kg/day IV or PO) or **flunixin** meglumine (1.1 mg/kg/day IV, PO or IM) may be used to reduce fever and inappetence.

Response to therapy may be monitored by evaluating shrinking of the abscess by rectal examination or ultrasonography. Resolution or improvement of peritonitis, fever, colic and abnormal serum protein and fibrinogen is also evidence of response to therapy.

The prognosis with prolonged antimicrobial therapy is fair to good, provided there is no intestinal obstruction (*q.v.*). **Intestinal obstruction** can, however, occur during healing due to adhesion formation. In cases of abscessation with significant bowel obstruction, the prognosis is very poor. **Surgical exploration** may be indicated. The abscesses and affected bowel should be resected

if possible. If resection is not feasible, **marsupialization** of the abscess may permit flushing and drainage. An obstructed bowel that cannot be resected may be surgically bypassed, however there is risk of re-obstruction due to adhesion formation.

Sand-induced enterocolitis

Etiology and pathogenesis

Chronic weight loss can result from accumulation of **geosediment** in the colon.

Clinical findings and diagnosis

Chronic weight loss due to **sand** usually is accompanied by **diarrhea**. Rectal examination can reveal **soft stools** and **sand in the rectum**, however the presence of sand is not always obvious. The remaining physical examination and laboratory findings are usually normal. Diagnosis is made by evaluation of the environment, presence of diarrhea, absence of evidence of other diseases causing weight loss, and response to treatment for sand accumulation.

Treatment and prognosis

Specific treatment is psyllium **hydrophilic mucilloid** (see sand impaction, *q.v.*).

Non-steroidal anti-inflammatory drug toxicity

Etiology and pathogenesis

Mucosal ulcerations of the gingiva, hard palate, tongue, stomach, small intestine and large intestine can result from non-steroidal anti-inflammatory drug (NSAID) toxicity (see also Chapter 4, page 267). Right dorsal colitis also sometimes occurs in horses with NSAID toxicity. Although **high dosages of phenylbutazone** and other NSAIDs for several days are required experimentally in normal horses, mucosal ulceration has developed in clinical cases given standard dosage regimens. This implies that **clinical compromise** increases the susceptibility of horses to the adverse effects of NSAIDs. Bacterial invasion of the submucosa after damage to the mucosal barrier may be important in the pathogenesis of the ulcerative lesions. **Mucosal ulceration** allows exudation of protein into the intestinal lumen and absorption of bacterial endotoxin into the systemic circulation.

Clinical findings and diagnosis

Clinical signs include chronic weight loss, intermittent colic, diarrhea, anorexia and depression. Some horses with NSAID toxicity develop ulceration of the **gingival mucosa**. Hypoproteinemia may result in dependent edema. Hypoproteinemia due to hypoalbuminemia and hypoglobulinemia is the most consistent laboratory finding. Proteinuria (due to renal papillary necrosis) and neutropenia with a left shift (due to endotoxemia) are inconsistent laboratory findings in horses with NSAID toxicity. Peritonitis (*q.v.*) occurs rarely in horses with NSAID toxicity and results in increased concentration of WBCs and protein in peritoneal fluid. Diagnosis is based on a **history of NSAID administration** in horses with consistent clinical and laboratory findings.

Treatment and prognosis

NSAID therapy should be **withdrawn** whenever possible. There is no specific therapy for horses with NSAID-induced intestinal ulceration. **Proton pump antagonists** (**omeprazole** 4 mg/kg PO s.i.d.) or histamine receptor antagonists (**cimetidine** 4.4–6.6 mg/kg IV q.i.d. or 20 mg/kg PO t.i.d. or **ranitidine** 6.6 mg/kg IV or PO b.i.d.) and local protectants (**sucralfate** 20 mg/kg PO q.i.d.) may accelerate the healing of **gastric ulcers** (*q.v.*) due to NSAID toxicity. These medications provide minimal benefit to horses with colonic ulceration or right dorsal colitis.

The cornerstone of therapy is **reduction of stress**, correction of fluid and protein deficits (see supportive therapy in duodenitis and proximal jejunitis, *q.v.*) and feeding a low residue diet provided in an all pelleted ration with minimum of 25% fiber content. Hay and corn based diets should be specifically avoided. Transfusion with **plasma** (3–10 L) may help offset the effects of hypoproteinemia. This is usually not necessary until the plasma protein decreases <4 g/dL, however clinical signs and the rapidity of protein loss aid the clinician in choosing the patient that will benefit from plasma transfusion.

Treatment with appropriate dosages of **antimicrobials** may hasten resolution of right dorsal colitis and healing of colonic ulceration; antimicrobials also are indicated if abdominocentesis reflects peritonitis. The more commonly used antimicrobials include **potentiated sulfonamides** (15 mg/kg IV or PO b.i.d.), chloramphenicol (50 mg/kg PO q.i.d.), cephalosporins (25 mg/kg IV or PO q.i.d.), and gentamicin (2.2 mg/kg IV or IM t.i.d.) and amikacin (6.6 mg/kg IV or IM t.i.d.) combined with either **procaine benzylpenicillin** (22 000–44 000 IU/kg IM b.i.d.) or **potassium benzylpenicillin** (22 000–44 000 IU/kg IV q.i.d.).

Exploratory celiotomy may be necessary in horses with recurrent abdominal pain due to right dorsal colitis to rule out other causes of abdominal pain. Surgical treatment via resection of the right dorsal colon has been performed successfully in several cases, however the number of cases is not sufficient to conclude whether medical or surgical therapy is best.

Horses with recurrent abdominal pain due to right dorsal colitis have a guarded to poor prognosis. The prognosis is fair to guarded in horses with ulceration.

Salmonellosis

Salmonellosis (*q.v.*) rarely causes chronic weight loss in horses, except as a complication of acute salmonellosis. Chronic damage to the intestinal tract can result in malabsorption and protein-losing enteropathy, thereby causing weight loss, hypoproteinemia and diarrhea.

GASTROINTESTINAL DISEASES CAUSING ACUTE DIARRHEA

SALMONELLOSIS

Etiology and pathogenesis

Infection with *Salmonella* spp. (*q.v.*) is the most common cause of **acute toxic colitis**, an **inflammatory disease of the large colon** characterized by clinical

signs of endotoxemia (*q.v.*). The environment becomes contaminated as a result of **fecal shedding** of the bacteria by symptomatic or asymptomatic animals, including horses, rodents, birds, dogs, cats and goats. Salmonellae can survive in the environment for months to years and are not killed by freezing. Drying and exposure to sunlight will kill the organism.

Horses often become infected with *Salmonella* spp. without developing clinical signs and frequently shed organisms for weeks to months after infection. Conflicting evidence exists over whether a **chronic carrier state** with persistent tissue infection occurs in horses. The frequency of fecal shedding of salmonellae by horses in the general population is 0.8–17%. Upon infection with salmonellae, the dose, virulence and host immunity all interplay to determine whether clinical signs develop. **Stressors** associated with salmonellosis include transportation, antimicrobial treatment, surgery, colic and stable management changes.

After ingestion, organisms establish themselves on the intestinal villous surface and then invade the mucosa of the lower small intestine, cecum and large colon. **Virulence factors** that may be associated with *Salmonella* spp. include endotoxin, enterotoxin and cytotoxin. The resultant local inflammatory response leads to the production of prostaglandins, leukotrienes, bradykinins and oxygen radicals. **Diarrhea** is most likely due to a combination of motility changes, increased secretion and malabsorption. Clinical signs of shock (tachycardia, hyperemic and/or cyanotic mucous membranes, depression, weakness) result from hypovolemia and endotoxemia. Endotoxemia (*q.v.*) also causes fever and changes in the leukogram (neutropenia and left shift).

Clinical findings and diagnosis

Clinical signs of salmonellosis include fever, tachycardia, hyperemic and/or cyanotic mucous membranes, partial to complete anorexia, moderate to severe depression, various degrees of abdominal pain, increased or decreased borborygmal sounds and diarrhea. Initial signs usually include fever, depression, anorexia and, sometimes, abdominal pain and distension.

Careful **rectal examination** may reveal soft feces in the rectum with more fluid ingesta in the large colon. Occasionally the rectum will feel edematous. Diarrhea begins 1–7 days after these initial signs. After the onset of diarrhea, any abdominal distension and pain usually resolves. The duration of the diarrhea may vary from one day to several weeks. Hypoproteinemia may result in edema in the legs, ventral abdomen, throat, intestine and lungs.

Laboratory findings include leukopenia with neutropenia (degenerative left shift may or may not be present) and sometimes lymphopenia. This may be followed by rebound leukocytosis with WBC counts up to 28 000 cells/μL. Gastrointestinal losses of electrolytes, anorexia and intake of large quantities of fresh water often lead to hyponatremia, hypochloremia, hypokalemia and metabolic acidosis. Because large colon secretion of fluid and electrolytes may begin before the onset of diarrhea, these serum electrolyte abnormalities can occur without diarrhea. However, serum electrolytes are variable and must be monitored so that fluid therapy can be adjusted appropriately. Azotemia (*q.v.*) may be present and is usually pre-renal (urine specific gravity ⩾1.020 without increased blood, protein or abnormal sediment). However, renal azotemia can

result from tubular necrosis due to hypovolemia and endotoxemia. Hypoproteinemia is common as a result of protein-losing enteropathy.

Horses with severe endotoxic shock due to **colitis** may develop laboratory and clinical evidence of **disseminated intravascular coagulation** (thrombocytopenia, prolonged clotting times, increased fibrinogen degradation products and evidence of hemorrhage or thrombosis). **Abdominocentesis** may be normal or consistent with a transudate due to bowel inflammation. In rare cases, the integrity of the intestinal wall is compromised resulting in bacterial leakage into the peritoneal cavity and exudative peritonitis.

A presumptive diagnosis of **acute toxic colitis** can usually be made based on physical and laboratory findings. Culture of *Salmonella* spp. from the feces, rectal mucosa biopsy, or from tissues collected at necropsy of animals with clinical signs of colitis results in a diagnosis of salmonellosis. The best fecal sample is 10–30 g of feces collected either before profuse watery diarrhea develops or during the recovery period when the feces become more formed. It often takes up to **five cultures** before the organism is recovered. The mucosal sample can be placed in 5 mL 0.9% saline solution or enrichment medium before transferring to a laboratory.

If the animal dies or is euthanatized, samples of ileum, cecum, large colon and mesenteric lymph nodes should be submitted for culture. Testing of fecal samples with polymerase chain reaction (PCR) is also commonly employed, possibly providing increased sensitivity. The specificity and rate of false positives of PCR for clinical diagnosis of salmonellosis are difficult to assess.

In some cases, it is difficult to distinguish the early stages of acute toxic colitis from other causes of colic. Careful rectal examination, resolution of the abdominal pain and the onset of **profuse watery diarrhea** aid in making a diagnosis.

Treatment and prognosis

The cornerstone of therapy is **correction of fluid deficits**, acid-base imbalances and electrolyte disturbances while the gut is healing. Fluid therapy is aimed toward correcting deficiencies and meeting ongoing losses. Not all cases will require IV therapy; however, if oral intake is not sufficient, IV supplementation will be necessary. In horses with severe profuse watery diarrhea, treatment with **IV volumes exceeding 100 L/24 h** may be necessary. The serum electrolytes and bicarbonate equivalent should be evaluated so that the oral and IV therapy will be specific to the individual metabolic disturbances. IV fluid administration is usually necessary if azotemia is present.

Fresh water and water containing electrolytes should be offered. **Specific electrolytes** added to the drinking water can be tailored according to the serum electrolyte analysis. Oral isotonic saline contains 9 g sodium chloride per liter of water and isotonic sodium bicarbonate contains 12.5 g sodium bicarbonate per liter of water. Because hypokalemia is common, these solutions should be supplemented with potassium. However, supplementation with potassium >1.5–2 g/L water decreases palatability. Fifty grams of glucose can be added to each liter of water to increase palatability and absorption of electrolytes. Either potassium chloride (30 g/4 L water/454 kg BW) or sodium bicarbonate (50 g/4 L water/454 kg BW) can be given by stomach tube twice daily to aid in correction of acidosis and hypokalemia. Correction

of acidosis can lead to **hypokalemia**, and therefore it is almost always necessary to supplement with potassium (1.5–3 g/L) when administering sodium bicarbonate. Serial evaluation of PCV and plasma proteins will help determine the adequacy of fluid therapy.

The indications for **antimicrobial therapy** during salmonellosis are controversial. Treatment with appropriate dosages of antimicrobials that demonstrate in vitro efficacy against *Salmonella* spp. does not seem to hasten recovery from diarrhea or the gastrointestinal disease. Antimicrobials are sometimes used as prophylaxis during severe leukopenia and IV catheterization to prevent septic complications associated with *Salmonella* spp. or other enteric bacteria. Antimicrobials are indicated if abdominocentesis reflects **peritonitis**. The rebound leukocytosis that may occur during the recovery phase should not be taken as an indication for antimicrobial therapy.

Because bacteremia occurs more frequently in **foals**, prophylactic antimicrobial therapy is almost always indicated in animals <9 mo of age.

The more commonly used antimicrobials include **trimethoprim—sulfonamide** (22 mg/kg IV or PO q 12 h), chloramphenicol (50 mg/kg PO q 6 h), cephalosporins (25 mg/kg IV or PO q 6 h), and gentamicin (6.6 mg/kg IV s.i.d.) and amikacin (20 mg/kg IV s.i.d.) combined with penicillin. Whenever possible, antimicrobial selection should be based upon **culture and sensitivity** of the *Salmonella* spp.

The main **contraindication for antimicrobial administration** is destruction of the normal intestinal flora, thereby allowing proliferation of the *Salmonella* spp. Therefore, antimicrobials to which *Salmonella* spp. are frequently resistant and that remain in the intestinal tract in high concentrations (e.g. **tetracyclines** and **neomycin**) are contraindicated.

Oral astringents and protectants such as **bismuth subsalicylate, activated charcoal** or **kaolin** products may be helpful. **Bismuth subsalicylate** can be given at the rate of 2–4 L/500 kg BW by nasogastric tube three to four times daily. If no improvement in the character of the stool is seen within 72 h, its use can be discontinued. **Activated charcoal** may act by adsorbing toxins, but seems less effective than bismuth subsalicylate. Kaolin products can have the appearance of improving the character of the stool, however they **do not decrease** the water content of the stool or decrease water losses. **Ditrioctahedral smectite** (1.36 kg [3 lb]/500 kg BW loading dose followed by 1 g/500 kg BW q.i.d.) is an organomineral that absorbs endotoxins, exotoxins and organic vapors and appears effective in reducing symptoms of equine salmonellosis.

Supportive therapy is of the utmost importance in the management of acute diarrheal disease. In horses with severe (<4 g/dL) hypoproteinemia, administration of **colloidal solutions** is necessary to maintain oncotic pressure for adequate circulation volume. Fresh or thawed frozen **plasma** (6–10 L/450 kg BW) is ideal to restore oncotic pressure and provide functional proteins beneficial for clotting, immunity and modulation of the systemic inflammatory process. Alternatively, administration of synthetic solutions (**hetastarch** 6%, 5–10 mL/kg) may result in adequate transient volume expansion. There are anecdotal reports of increased death rate among foals after administration of some hyperimmune plasma preparations.

Horses with **ischemic damage** to intestinal segments generally absorb large amounts of endotoxin, thereby causing further **cardiovascular**

deterioration. Treatment to dampen the systemic inflammatory response associated with endotoxemia is frequently beneficial. Choice of treatment options is based on severity of disease, renal function and hydration status. The most important strategy in management of endotoxemia is aggressive management of the primary disease process.

Also available are **immune sera and plasma** collected from donors inoculated with portions of endotoxin molecules derived from Gram-negative bacteria. The resulting antibodies may bind circulating endotoxin and render it inactive; however, results of experimental studies are not definitive.

Polymyxin B is an aminoglycoside antibiotic that binds and neutralizes endotoxin and decreases the systemic effects of endotoxemia when administered at 1000–5000 IU/kg t.i.d. Side effects include nephrotoxicity and neurotoxicity. Patients should be monitored closely, especially during use of other nephrotoxic medications, azotemia and dehydration. Treatment of endotoxemia also involves inhibition of mediator synthesis. NSAIDs are most often employed for this purpose. **Flunixin** meglumine (0.25 mg/kg IV or IM q 8 h) may help by decreasing the production of thromboxanes and prostacyclins from arachidonic acid, thereby preventing some of the metabolic, cardiovascular and pulmonary effects of endotoxin. Furthermore, if these products of arachidonic acid contribute to the pathogenesis of laminitis, flunixin may help to reduce the incidence of this side effect in horses with salmonellosis. Higher dosages of flunixin meglumine (up to 1.1 mg/kg IV or IM q 12 h) may be needed to provide analgesia to horses with abdominal pain. Administration of flunixin to hypovolemic horses or at excessive dosages may decrease synthesis of protective prostaglandins, thereby contributing to intestinal ulceration, protein loss and renal disease. **Pentoxifylline** (8 mg/kg PO t.i.d.) **combined with flunixin** meglumine may be slightly more beneficial than flunixin meglumine alone. Inactivation of oxygen-derived radicals is sometimes attempted with dimethyl sulfoxide (DMSO 0.1–1 g/kg/day IV as a 10% solution).

Because **laminitis** (*q.v.*) is a common complication associated with all inflammatory and ischemic disease in horses, **frog supports** are recommended preventatively in these patients. Digital pulses and signs of lameness should be monitored closely.

The prognosis for *Salmonella*-induced colitis is **extremely variable**. Horses that continue to be alert and responsive with fair to good appetites tend to have a good prognosis. Clearly if a horse is presented with a PCV ⩾55% the prognosis is guarded and if ⩾60% the prognosis is poor. Horses with purple mucous membranes, severe tachycardia (⩾110 bpm) and renal azotemia also have a guarded to poor prognosis. The occurrence of thrombophlebitis (*q.v.*), whether septic or sterile, can also reduce the prognosis as fluid administration becomes difficult. The presence of exudative peritonitis is a reflection of severe compromise to the bowel wall indicating a poor to grave prognosis.

Horses that develop profuse diarrhea followed by scant or absent stool production, abdominal distension and pain have a poor prognosis. These horses often have irreversible intestinal ileus and pooling of fluid within the intestinal lumen that progresses to death or necessitates euthanasia.

POTOMAC HORSE FEVER (*EHRLICHIA* COLITIS, EQUINE MONOCYTIC EHRLICHIOSIS)

Etiology and pathogenesis

Neorickettsia risticii (previously *Ehrlichia risticii*) (*q.v.*) is a rickettsial organism responsible for an **acute enterotyphlocolitis**. This disease should be considered as a differential diagnosis in any case of acute toxic colitis in an area enzootic for *N. risticii*. The disease tends to occur mostly in the summer months in 43 of the United States, Canada, France, Italy, Venezuela, India and Australia. This rickettsia has been detected in several species of snails and aquatic insects (e.g. mayflies and caddis flies) and disease has been produced by feeding infected flies.

The pathogenesis is unknown. Once the organism gains access to the host, it is believed that infection of macrophages and peripheral blood monocytes occurs followed by **colonization** of the colonic and small intestinal epithelial cells and colonic mast cells.

Clinical findings and diagnosis

Clinical and laboratory findings of Potomac horse fever (*q.v.*) are indistinguishable from those found with other causes of **acute toxic colitis** in the horse (see salmonellosis, *q.v.*). Clinical signs include fever, complete or partial anorexia, and mild to severe depression. The fever may precede other clinical signs by 2–7 days. Most horses will exhibit depression with hyperemic and/or cyanotic mucous membranes. Approximately 50% of horses will exhibit some degree of abdominal pain, decreased borborygmi, and mild to moderate abdominal distension. **Diarrhea** occurs in 60–70% of the cases and varies in consistency and volume. Rectal examination may be normal or may reveal some degree of gas and fluid accumulation in the cecum and large colon. **Laminitis** (*q.v.*) can be a complication of Potomac horse fever.

Unfortunately, there is no quick method of definitively diagnosing Potomac horse fever, but the disease should be suspected in horses with clinical signs consistent with acute toxic enterocolitis in **endemic areas**. The most commonly used diagnostic test is paired serum indirect fluorescent antibody titers taken 7–10 days apart. A dramatic (4-fold) increase or decrease in the titer is consistent with a diagnosis of Potomac horse fever. Several problems with testing make diagnosis challenging. Paired serology does not allow diagnosis before initiation of therapy. A single high titer indicates previous exposure to *N. risticii* that may or may not be related to the current disease. Many horses will seroconvert by the time clinical signs become apparent. Previous vaccination for Potomac horse fever will also cause positive titer.

Treatment and prognosis

As with salmonellosis, the chief therapeutic goal in cases of Potomac horse fever is to **maintain adequate hydration** and correct any acid-base or electrolyte abnormalities. The use of an NSAID (e.g. **flunixin** meglumine at 0.25 mg/kg IV or IM q 8 h) and **bismuth subsalicylate** (2–4 L/500 kg BW) is recommended. Guidelines for plasma administration are the same as those discussed for salmonellosis (*q.v.*). Pre-renal and renal azotemia must be treated via fluid therapy. Antimicrobial therapy (oxytetracycline 6.6 mg/kg

q 24 h for 5 days) reduces the severity of the disease and results in a more rapid return of appetite. Resolution of diarrhea after antimicrobial therapy may lag behind improvement of other clinical signs. Occasionally, clinical signs recur after oxytetracycline therapy has been discontinued, necessitating therapy for another 5–7 days.

If improvement is not noted within 12–36 h, another etiology should be suspected.

If **oxytetracycline** is administered during the incubation period, the onset of clinical signs is delayed but not prevented. The occurrence of laminitis (*q.v.*) does not seem to be affected by treatment with oxytetracycline. Oxytetracycline administration will not prevent the development of antibody titer. Most *Salmonella* spp. are **resistant** to oxytetracycline. Furthermore, high concentrations of oxytetracycline are present within the intestinal lumen after parenteral administration as a result of enterohepatic circulation. This results in significant disruption of the intestinal flora, and therefore administration of oxytetracycline may worsen **salmonellosis** (*q.v.*). It is recommended, therefore, that oxytetracycline therapy should be restricted to those cases of enterocolitis in which the epidemiology is consistent with Potomac horse fever.

The prognosis varies from good to grave depending upon the severity of clinical signs and laboratory changes. In general, horses that remain alert with an appetite and those treated with oxytetracycline before the onset of the diarrhea have a fairly good prognosis. The occurrence of renal azotemia, laminitis and abdominal distension with cessation of diarrhea worsens the prognosis. A PCV ⩾55–60% at the onset of therapy is a reflection of poor tissue perfusion and is associated with a poor prognosis. Any horse with a PCV ⩾60% has a grave prognosis.

PARASITIC COLITIS

Etiology and pathogenesis

The adults and larvae of the common nematodes of the cecum and large colon, *Strongylus* spp. and *Cyathostoma* spp. (*q.v.*), may cause **acute diarrhea**. Although the exact mechanism for the colitis is unknown, it appears to result from either the inflammation in the bowel wall caused by **larval migration**, damage caused by feeding of **adult parasites** or local intramural **thromboembolism** resulting in local ischemia and/or infarcts or peritonitis (*q.v.*).

Clinical findings and diagnosis

Most commonly, parasitic enterocolitis causes **chronic weight loss** and/or **diarrhea**. In cases of heavy pasture contamination, a horse may ingest large numbers of larvae resulting in severe acute inflammation and diarrhea. Several clinical syndromes then may result:

1. Sudden onset of profuse watery diarrhea accompanied by hypovolemic or endotoxemic shock
2. Sudden onset of profuse watery diarrhea that persists for weeks to months thereby causing weight loss
3. Alternating bouts of watery diarrhea and cow-like manure that lead to weight loss.

All can be accompanied by fever, variable degrees of abdominal pain or colic, and variable appetite. The mucous membranes can be pale from blood loss anemia, icteric from anorexia, or hyperemic due to endotoxemia. Laboratory analysis can reveal neutropenia due to endotoxemia (*q.v.*). Eosinophilia is not a consistent finding in horses with parasitism. Occasionally there will be an increase in the number of neutrophils or eosinophils in the peritoneal fluid, however the absence of eosinophilic transudation does not rule out parasitic colitis. Hypoproteinemia and hypoalbuminemia may be present. Azotemia may result from hypovolemia. Horses with diarrhea due to parasitic colitis may develop hyponatremia, hypokalemia, hypochloridemia or metabolic acidosis.

The clinical diagnosis is largely speculative based on history (poor parasite control program or overpopulated pastures) and exclusion of the other causes of acute diarrhea. **Rectal examination** may indicate thickening of the cranial mesenteric artery, however this is a subjective finding. Serum protein electrophoresis may reveal an increase in the concentration of β_2-globulin due to inflammation but this is not specific for parasitism. Fecal worm egg counts are unreliable in the diagnosis of parasitic colitis, because the inflammation may be due to prepatent stages. The finding of eosinophils or cyathostome larvae in rectal biopsy samples taken with a uterine biopsy instrument is supportive of parasitic colitis, however the rectal wall is rarely involved in this disease.

Treatment and prognosis

Larvicidal anthelmintic therapy with several different anthelmintics has proven effective:

1. Fenbendazole at 10 mg/kg daily on 5 consecutive days
2. Fenbendazole at 50 mg/kg daily on 2 consecutive days
3. Oxfendazole at 10 mg/kg daily for 2 days
4. Ivermectin at 200 μg/kg for one treatment; and moxidectin 400 μg/kg for one treatment.

Prognosis is good provided the animal is not too debilitated at the time therapy begins. Several weeks to months may be required to regain body condition, normal serum protein concentration and optimum athletic performance.

ANTIMICROBIAL-ASSOCIATED DIARRHEA

Etiology and pathogenesis

Colitis may occur secondary to the use of **any antimicrobial**: those commonly incriminated include tetracycline, erythromycin, lincomycin, tylosin, potentiated sulfonamides, penicillin and ampicillin.

The antimicrobials may act to **alter the normal bacterial population**, thereby disrupting the critical intraluminal environment essential for normal digestion, absorption and secretion of fluid and nutrients, and maintenance of healthy epithelial cells. For example, these antimicrobials may depress volatile fatty acid absorption, which secondarily depresses sodium absorption and acidifies the colonic contents. Furthermore, removal of the normal bacterial flora may lead to **acute toxic colitis** caused by *Salmonella* (*q.v.*) and other pathogenic bacteria.

If a horse has a depressed appetite, the chance of these antimicrobials inducing diarrhea may be higher. The enterohepatic circulation of tetracycline, erythromycin, lincomycin and tylosin may increase enteric concentrations of these antimicrobials, making diarrhea more likely.

Clinical findings and diagnosis

Clinical signs and laboratory findings are as outlined for the other causes of **acute diarrhea** (*q.v.*).

Treatment and prognosis

The suspect drug should be discontinued and the use of any antimicrobial should be selected using sound medical judgment. Treatment and prognosis are as for salmonellosis (*q.v.*).

BLISTER BEETLE TOXICOSIS

Etiology and pathogenesis

Cantharidin-containing beetles belonging to the family Meloidae are responsible for the toxicosis. The **striped blister beetle** is the most common cause of toxicosis in the eastern USA; however, others (e.g. the black blister beetle) have also been identified as causes of toxicosis. **Cantharidin toxicosis** (*q.v.*) occurs when dead blister beetles that are killed in the harvesting of alfalfa are ingested. In the southeastern USA, toxicosis is uncommonly associated with harvesting of non-legume grasses.

After absorption, cantharidin induces **acantholysis** and **vesicle formation,** thereby disrupting cellular oxidative metabolism and leading to **cell death**. In addition, the normal transport systems for nutrients, water and electrolytes across the intestinal mucosa and renal tubules and collecting ducts are disrupted. Permeability changes and inflammation of the intestinal mucosa result in protein losses. Although the pathogenesis is unknown, **hypocalcemia and hypomagnesemia** occur commonly with blister beetle toxicosis.

Clinical findings and diagnosis

The severity of the clinical signs is proportional to the amount of toxin ingested. Common signs include abdominal pain, anorexia, depression, sweating, diarrhea and **frequent attempts at urination**. Some horses submerge their muzzles in **water** or frequently drink small amounts of water. Mucous membranes may be reddened with a prolonged capillary refill time. More variable signs include synchronous diaphragmatic flutter and a stiff, stilted gait (due to hypocalcemia), gingival and oral erosions, increased salivation and nasogastric reflux. Severe cases may progress to **shock** and death. Macroscopic hematuria and hematochezia sometimes occur. Azotemia may be pre-renal due to dehydration or renal due to toxin-induced tubular necrosis.

Laboratory abnormalities include hemoconcentration, neutropenia or neutrophilia, hypocalcemia, hypomagnesemia and azotemia. Serum protein concentration is usually normal to increased early in the disease, but hypoproteinemia develops later due to intestinal protein loss. Urinalysis often reveals dilute urine (specific gravity 1.008) and microscopic hematuria.

Peritoneal fluid analysis demonstrates an increased protein concentration. Acidosis or normal acid-base status may be present.

The clinical signs and **persistent hypocalcemia and hypomagnesemia** are suggestive of cantharidin toxicosis. Diagnosis is based upon finding blister beetles in the hay, feed or feed manger and toxin in stomach contents or urine. The optimum sample for toxicology is 500 mL of urine collected in the first 2 days of disease.

Treatment and prognosis

No specific antidote is available, therefore therapy is largely supportive (see salmonellosis, *q.v.*). **Fluid therapy** is essential to correct dehydration and promote diuresis to increase cantharidin excretion and treat azotemia. **Acetated isotonic balanced polyionic fluids** administered IV are preferred. The rate of fluid administration depends upon the amount that the horse drinks voluntarily and the amount of fluid losses in diarrhea or reflux. Maintenance fluid requirements for adult horses are approximately 50 mL/kg/day, and fluid losses can occur at the rate of 0.5 mL/lb/h (0.5 mL/450 g/h) to as high as 2 mL/lb/h (2 mL/450 g/h).

Severe hypoproteinemia may require colloidal support with administration of **plasma** (6–10 L/450 kg BW) or **hetastarch** (6%, 5–10 mL/kg). **Mineral oil** (2–4 quarts [1.9–3.8 L]/500 kg BW) may be administered via nasogastric tube to decrease absorption of the toxin and to help evacuate the intestinal contents, if nasogastric reflux is absent. Medication should not be given via nasogastric tube to animals with nasogastric reflux. NSAIDs should be used to control abdominal pain, however large dosages of these drugs may contribute to renal tubular and gastrointestinal disease.

Calcium (23% calcium gluconate) should be supplemented into the crystalloid fluid solution for slow IV infusion (2–4 mg/kg/h). Severe hypocalcemia sometimes requires treatment with calcium gluconate 23% at 6 mg/kg/h. Magnesium (magnesium sulfate or magnesium chloride) can be supplemented into the crystalloid solutions at a rate of 4–10 mg/kg/h. Serum or plasma calcium and magnesium concentration should be monitored during supplementation.

The prognosis is poor with a mortality rate near 60%. Therapy must be early and aggressive.

ARSENIC TOXICOSIS

Etiology and pathogenesis

The most common source of **arsenic** used to be fluids formerly used for the control of ectoparasites on farm animals. Poisoning may occur when horses accidentally gain access to **recently sprayed** areas or are fed grass clippings from lawns treated within 6 mo with **arsenical herbicides**. Wood preservatives containing arsenic may be a cause of poisoning when applied to fencing. Ashes from burned lumber or fence posts treated with arsenic compounds may be a cause of poisoning because of the **palatable salty** taste.

The clinical signs and pathology of arsenic toxicosis (*q.v.*) are due to the inactivation of sulfhydryl groups in tissue enzymes, thereby causing **necrosis**

of tissues rich in oxidative metabolism (e.g. gastrointestinal mucosa, neural tissue and renal tubular epithelium).

Clinical findings and diagnosis

Affected horses show signs of abdominal pain, watery diarrhea that may contain blood, depression, weakness and/or ataxia, and hyperemic mucous membranes. The heart rate is increased with a weakened pulse. Arsenic toxicity can result in polyuric or anuric renal failure. Azotemia, hypoproteinemia, hyponatremia, hypokalemia and hypochloremia are all possible laboratory findings with arsenic toxicity.

The attending veterinarian should be suspicious of arsenic toxicity in cases of **acute colitis** when the animal either has a history of exposure to arsenic, concurrent neurologic signs or bloody diarrhea. Diagnosis is made by finding high concentrations of arsenic in body fluids or tissues. Urine concentrations exceeding 16 mg/mL and liver and kidney concentrations >10–15 mg/kg are compatible with a diagnosis of arsenic toxicity.

Treatment and prognosis

Oral protectants such as mineral oil are suggested as well as oral sodium thiosulfate (20–30 g in 300–500 mL water). **Dimercaprol** is a specific antidote, although its use is frequently unsuccessful. Supportive therapy is as discussed for other causes of colitis. Mortality approaches 100% for cases of arsenic toxicosis.

MONENSIN TOXICOSIS

Etiology and pathogenesis

The use of monensin in the horse is contraindicated. Toxicosis occurs when feed containing this antimicrobial is inadvertently fed to horses. **Ionophores** disrupt membrane transport systems in the horse.

Clinical findings and diagnosis

Clinical signs resulting from altered gastrointestinal function include variable levels of abdominal pain and diarrhea. Diagnosis is based upon compatible clinical signs, history of possible exposure to cattle feed, and identification of the ionophore in the feed.

Treatment and prognosis

There is no specific antidote to the ionophores, and therefore therapy is supportive (see salmonellosis, *q.v.*). The prognosis is poor.

CLOSTRIDIUM PERFRINGENS TYPE A

Etiology and pathogenesis

Large numbers of *Clostridium perfringens* type A (*q.v.*) in the cecum and colon have been associated with **acute toxic colitis**. *C. perfringens* type A has been hypothesized to be a cause of what used to be called **colitis X**. Stress, dietary

factors (e.g. feed containing high protein and low cellulose) and antimicrobial therapy may predispose to overgrowth of *C. perfringens* type A. The disease has been reproduced experimentally by oral inoculation of bacterial culture and by administration of exotoxin IV. The cause of the diarrhea is probably the local release of mediators of inflammation and bacterial exotoxin.

Clinical findings and diagnosis

Clinical signs are similar to those associated with salmonellosis (*q.v.*) including depression, inappetence, fever, tachycardia, hyperemic and/or cyanotic mucous membranes and diarrhea. Abdominal pain and sweating are sometimes seen. Horses frequently die within 24 h. **Common complications** include laminitis and phlebitis (*q.v.*). Laboratory analysis may reveal leukopenia, hyponatremia, hypochloremia, hypokalemia, metabolic acidosis and azotemia (renal or pre-renal). PCV is increased and serum protein concentration is elevated or decreased depending on the degree of hemoconcentration and colonic protein loss. Evidence for **disseminated intravascular coagulation** (*q.v.*) may be present in rare cases.

Because *C. perfringens* can be cultured from feces of **healthy horses**, definitive diagnosis requires assay of clostridial exotoxin from intestinal contents obtained during post mortem examination. The assay is not readily available. Presumptive diagnosis is often made by culturing at least 10^3 colony-forming units of *C. perfringens* per gram of feces. However, other causes of diarrhea and colitis may result in **clostridial overgrowth**.

Treatment and prognosis

Therapy is largely supportive as described for horses with salmonellosis (*q.v.*). Type A antitoxin is not readily available. Without therapy the mortality rate approaches 100% and the mortality rate with intensive therapy is still very high.

CLOSTRIDIUM DIFFICILE

Etiology and pathogenesis

Clostridium difficile also inhabits the intestinal tract of normal horses, but increased numbers with enterotoxin production can lead to **enterocolitis.** The conditions resulting in clostridial growth and enterotoxin production are not understood but dietary changes, other intestinal diseases (e.g. colic) and antimicrobial use appear to be factors involved in the development of *C. difficile* diarrhea. *C. difficile* produces toxins A and B which induce an intestinal inflammatory response and fluid secretion leading to diarrhea.

Clinical findings and diagnosis

Clinical findings are similar to those associated with salmonellosis (*q.v.*) including depression, inappetence, fever, tachycardia, hyperemic and/or cyanotic mucous membranes and diarrhea. The clinical course may be peracute; however, it is also common to see a milder, more prolonged clinical course with *C. difficile*.

As for *C. perfringens* (*q.v.*), diagnosis is based on culture of organism from feces and identification of toxins. Bacterial culture of *C. difficile* may be difficult and may be an insensitive test. Diagnosis of disease due to *C. difficile* from culture depends on the ability to induce toxin production within the isolate. Due to availability and sensitivity, the preferred test for diagnosis of *C. difficile* is detection of toxins A and B in feces by use of a commercial ELISA test. PCR methods have also been developed for detection of the genes for toxins A and B.

Treatment and prognosis

Therapy is largely supportive as described for horses with salmonellosis (*q.v.*). The preferred treatment is metronidazole (15–25 mg/kg q 8 h PO or per rectum) and is effective in most cases. Metronidazole-resistant *C. difficile* appears to be rare in horses.

GRAIN OVERLOAD

Etiology and pathogenesis

The consumption of **readily fermentable carbohydrates** causes **colitis** (*q.v.*). Some starches are poorly digested in the small intestine of the horse. For example, 90% of oat starch is digested in the small intestine and only 30% of corn. The highly fermentable starch is then fermented in the cecum and large colon by *Lactobacillus* to form **lactic acid** in place of volatile fatty acids. This reduces the pH and increases the osmolality of colonic contents, thereby damaging the mucosal cells. Death of the Gram-negative bacteria results in release of **endotoxins** to interact with epithelial cells to initiate an inflammatory process and to be absorbed across the damaged mucosa causing endotoxemia. Changes in the concentration of volatile fatty acids in the colonic contents alter colonic motility. The osmotic changes, mucosal necrosis and inflammation, endotoxemia and altered motility result in diarrhea.

Clinical findings and diagnosis

The clinical signs vary with the quantity of fermentable feed ingested. The most common signs to be noted are variable degrees of **abdominal pain** and **diarrhea**. In more severe cases, hyperemic and/or cyanotic mucous membranes, fever or subnormal temperature resulting from shock, sweating and tachycardia develop. Laboratory findings include leukopenia resulting from endotoxemia, increased PCV and total plasma protein due to dehydration, metabolic acidosis resulting from shock and hypoperfusion, and renal or prerenal azotemia. **Laminitis** (*q.v.*) is a common complication. Diagnosis is based on physical examination and laboratory findings and history of exposure to quantities of concentrate, lush pasture or legume to which the horse is not accustomed.

Treatment and prognosis

Therapy is most rewarding when administered before the onset of clinical signs. **Mineral oil** (2–4 L/500 kg BW) is administered to decrease fermentation and to facilitate evacuation of colonic contents. **Fluid therapy** and other

supportive therapies are recommended (see salmonellosis, *q.v.*). **Frog supports** should be applied due to the high incidence of laminitis. The prognosis is guarded to poor due to the common occurrence of laminitis in cases of grain overload.

LIVER DISEASE IN HORSES

Hepatic disease, as determined by **increased liver enzymes** and **histopathologic changes in a liver biopsy**, is common in horses. The liver has **enormous reserve capacity** and **regenerative ability**, and disease does not result in insufficient function until 70% or more of the organ has been damaged.

Common causes of liver failure in horses and foals include pyrrolizidine alkaloid toxicosis, acute hepatitis and Tyzzer's disease (*q.v.*). Liver disease (and occasionally liver failure) sporadically is caused by mycotoxicosis, chronic active hepatitis, hepatic lipidosis, cholelithiasis, ferrous fumarate ingestion, hepatic neoplasia, hepatic abscessation, portosystemic shunts, perinatal equine herpesvirus 1, kleingrass intoxication, strangulating obstruction of the large colon, hypoxemia, septicemia and endotoxemia (*q.v.*).

CLINICAL FINDINGS AND DIAGNOSIS

Symptoms of liver failure can arise from an acute massive hepatic insult, or when chronic loss of hepatocytes and fibrotic infiltration reaches a critical threshold. The most common clinical signs of liver failure in horses are **icterus, neurologic abnormalities, anorexia, weight loss and photodermatitis**. Less common signs include colic, coagulopathy, pruritus and diarrhea.

Icterus (jaundice) is caused by accumulation of bilirubin within the blood (total bilirubin concentration of 3.5 mg/dL or greater) and tissues. Because conjugated bilirubin produces a more intense discoloration, icterus is most readily observed in association with cholestatic disorders.

Neurologic abnormalities (hepatoencephalopathy) arise from altered neurotransmission in the CNS. The severity of the clinical signs corresponds with the degree of hepatic insufficiency. Mildly affected horses may show subtle behavioral changes (*q.v.*). More severely affected horses exhibit varying degrees of mental depression, aggressive or violent behavior, head-pressing, circling, aimless propulsion and pronounced yawning. Other symptoms include mild proprioceptive deficits, dysphagia and inspiratory dyspnea caused by flaccid paralysis of the larynx and pharynx. Advanced cases of hepatoencephalopathy exhibit coma and terminal seizure activity.

The etiology of the neurologic dysfunction in hepatic insufficiency is only partially understood. Neurotoxic compounds that are produced in the gut and normally removed by the liver accumulate in the bloodstream and ultimately in the CNS. Examples of **neurotoxins** include ammonia, short-chain fatty acids, mercaptans and γ-aminobutyric acid. Neuroexcitatory transmission is further compromised by failure of the liver to remove aromatic amino acids (phenylalanine, tyrosine and tryptophan) from the systemic circulation. As a result, the ratio of aromatic to branched chain amino acids in the blood and CNS increases. Moderate to severe **hypoglycemia** secondary to impaired

gluconeogenesis can also contribute to signs of neurologic dysfunction (*q.v.*). Correction of hypoglycemia causes remission of neurologic signs in some cases of hepatoencephalopathy.

Horses with chronic hepatic insufficiency often present with **weight loss** (*q.v.*), which in some cases may be the only presenting complaint. Most horses with weight loss have a history of partial to complete anorexia for several weeks or more before examination.

Photodermatitis (*q.v.*) occurs fairly frequently in horses with liver failure. Crusty, erythematous lesions develop in unpigmented sparsely haired areas of the body such as the face (especially the muzzle) and the distal extremities as a result of **phylloerythrin accumulation** in the superficial layers of the skin. Phylloerythrin is a photodynamic by-product of chlorophyll digestion that is produced by microbes in the gastrointestinal tract. Normally it is removed from portal circulation by the liver and excreted in bile. Failure of the excretory mechanism allows phylloerythrin to enter the systemic circulation and become deposited in the skin. When phylloerythrin in the skin absorbs UV light, free radicals are generated that produce **cellular destruction**. Unpigmented skin is more vulnerable because it absorbs UV light more efficiently.

Hepatocellular swelling and obstruction of the biliary tract can cause signs of abdominal pain. For this reason, **hepatobiliary disease** should be an etiologic consideration for colic (*q.v.*), particularly if symptoms are recurrent and accompanied by icterus, fever and weight loss. Palpation of the abdomen caudal to the last rib on the right side may elicit a painful response in these cases.

The liver is the major site for synthesis of circulating hemostatic proteins. As a result, some horses with severe hepatic insufficiency manifest **increased bleeding tendencies**, particularly following trauma (venipuncture, nasogastric intubation, etc.). Spontaneous hemorrhage in the lungs and gastrointestinal tract is observed less frequently. Clotting factor VII has the shortest half-life, so prolongation of the prothrombin time may precede prolongation of the activated partial thromboplastin time in progressive cases of liver failure. Because absorption of fat-soluble vitamins is dependent on the presence of bile acids in the intestinal lumen, cholestasis can lead to increased bleeding tendencies by causing **vitamin K deficiency** (*q.v.*). Clotting factors (II, VII, IX and X) need vitamin K to complete hepatic modification into active clotting factors.

Pruritus, diarrhea and terminal hemolysis are infrequent manifestations of liver failure in horses. **Pruritus** arises from accumulation of bile salts within the skin. Causes of **diarrhea** include portal hypertension, hypoalbuminemia, maldigestion due to bile acid deficiency, and altered gastrointestinal microflora.

Hepatic integrity can be assessed through a variety of tests that reflect hepatocellular injury, cholestasis and reduced functional mass. In addition, the morphology of the liver can be assessed by ultrasonography and microscopic evaluation of a liver biopsy. Table 10.3 lists approximate normal ranges for liver diagnostic tests.

Enzymes normally confined within the cytosol are released into extracellular fluid following hepatocellular necrosis. The magnitude of the increase in serum enzyme concentration correlates directly with the magnitude of the injury, but not with the reversibility of the lesion. Cytosolic enzymes are most likely to be elevated in acute disorders when active cellular destruction is

Table 10.3 Diagnostic tests for equine liver disease

Test and reference range	Interpretation of results	Sample handling
Sorbitol dehydrogenase (SDH) 1–8 U/L	Increase indicates active hepatocellular necrosis (liver specific)	Serum sample. Refrigerate immediately and analyze within 12 h
Aspartate aminotransferase (AST)	Increase indicates active hepatocellular or muscle damage	Serum sample. Stable for several days at room temperature and for 1 wk in refrigerator
Gamma glutamyltransferase (GGT) 8–28 U/L	Increase indicates hepatobiliary disease (especially cholestasis; liver specific)	Serum sample. Stable for several days at room temperature and for 1 wk in refrigerator
Alkaline phosphatase (ALP)	Increase indicates hepatobiliary disease (especially cholestasis). Also elevated by bone growth and remodeling and intestinal epithelial damage	Serum sample. Stable for several days at room temperature and for 1 wk in refrigerator
Bilirubin Total: 0.2–2.0 mg/dL Conjugate: 0.0–0.4 mg/dL) Total bile acid <10 μmol/L	Total bilirubin increased by hepatobiliary disorders, hemolysis and fasting >20 μmol/L consistent with hepatobiliary disease	Serum sample. Stable for several days. Keep sample out of direct sunlight Serum or plasma
Blood ammonia 13–108 μg/dL	Increase indicates hepatic insufficiency or portosystemic shunting	Heparinized blood is collected and immediately placed on ice. Separate plasma from cells within 30 min and analyze within 1 h

occurring. In chronic liver disease and biliary tract disorders, concentrations of these enzymes may be normal or only slightly increased.

Clinically useful tests for hepatocellular necrosis in equine practice include **sorbitol (iditol) dehydrogenase** and **serum aspartate aminotransferase** (formally serum glutamic oxaloacetic transaminase). Sorbitol dehydrogenase (SDH) has the advantage of being a **liver-specific test**. SDH has a relatively short serum half-life (12 h), and returns to normal within 4–5 days after an acute hepatic insult. For this reason, it is useful for monitoring improvement following hepatic injury. Its major disadvantage is its poor stability in serum, particularly at room temperature. Analysis should be performed as soon as possible and within 12 h on a refrigerated (4°C) sample to obtain reliable results. Aspartate aminotransferase (AST) is more stable in serum, but is less liver specific. Elevations are noted in serum following muscle damage (cardiac and skeletal) and hemolysis. Foals, weanlings and yearlings have higher serum concentrations of AST than adults.

Gamma glutamyltransferase (GGT) and **alkaline phosphatase** (ALP) are clinically useful markers of **cholestasis**. Both enzymes are synthesized in increased quantities in response to hepatobiliary disorders. Intrahepatic cholestasis due to blockage of canaliculi by hepatocyte swelling commonly leads to increases in GGT in horses with hepatocellular disorders. Serum GGT concentration is elevated primarily by increased hepatocellular production

whereas serum ALP may reflect increased production by liver, bone, placenta and intestinal epithelium. As a result, serum GGT is more specific for liver disease than serum ALP. Because the reference range for GGT is much narrower than ALP, serum GGT results are easier to interpret. GGT is elevated in most cases of acute and chronic liver disease and is a good screening enzyme for liver disorders. Serum GGT has a long half-life, and may stay elevated for weeks after clinical signs and other laboratory findings are improving.

Some drugs (e.g. **corticosteroids**) secondarily cause transient elevations of serum concentrations of liver enzymes. These cases can be differentiated by history and by restoration of normal enzyme concentrations over time. **Persistent elevations** of liver enzymes in horses should be evaluated by other bile acids, liver ultrasound, and liver biopsy. Foals have higher serum concentrations of GGT and ALP than adults. Levels progressively decline and approximate adult concentrations by 3 mo of age.

Hepatic functional capacity is evaluated in various ways. The **serum bilirubin** concentration and **total bile acid concentration** reflect the liver's ability to remove endogenous anions from the blood, whereas the **sulfobromophthalein (BSP) clearance** test (*q.v.*) evaluates the liver's ability to remove exogenous anions from circulation. Blood glucose concentration, serum albumin concentration, clotting profile, serum urea nitrogen concentration and blood ammonia concentration also are useful indices of liver function.

Hyperbilirubinemia occurs most frequently in acute hepatic failure and biliary obstruction. **Total bilirubin concentration** may be normal or only slightly increased in cases of chronic liver failure. Horses with hepatic insufficiency characterized by impaired biliary excretion develop hyperbilirubinemia secondary to regurgitation of conjugated (direct reading) bilirubin from bile canaliculi into the bloodstream. Unconjugated (indirect reading) bilirubin increases in the blood due to impaired uptake and conjugation. In contrast to other species, horses with liver failure or obstruction of the bile duct develop relatively modest increases in the serum concentration of conjugated bilirubin.

Even with **complete obstruction of the common bile duct**, the conjugated fraction rarely exceeds 50% of the total. A conjugated (direct) bilirubin concentration of 25–50% of the total bilirubin concentration is indicative of significant cholestasis. Although an increase in the conjugated fraction is a useful parameter, a normal concentration does not rule out hepatic insufficiency in horses. Other causes of hyperbilirubinemia include fasting and hemolysis. The total bilirubin concentration can exceed 10.0 mg/dL in horses with normal hepatic function after 48 h of fasting. The increase is due to elevation of unconjugated bilirubin, and conjugated bilirubin remains normal during fasting.

The presence of **urobilinogen** in urine indicates that the bile duct is patent. If the common bile duct is completely obstructed, urobilinogen will not be detected on urine reagent strips. Urobilinogen concentration in urine is increased by **hemolysis** and **hepatic disease**. Conjugated bilirubin is normally absent from the urine, but it can be detected in some cases of hepatobiliary disease because regurgitated conjugated bilirubin is freely filtered by the kidney.

The urine can be screened in the **field** for the presence of conjugated bilirubin by **shaking fresh urine** until it foams. Normal urine creates a **white foam** whereas urine that contains conjugated bilirubin makes a **yellowish-green foam**.

Total serum bile acid determination is a relatively new clinical tool and is becoming more available on a commercial basis. Bile acids are produced by the liver from cholesterol and excreted in bile conjugated to either glycine or taurine. Approximately 86% of equine bile acids are conjugated to taurine. The bile acids are actively absorbed in the ileum and removed from portal circulation by the liver; only small quantities of bile acids reach systemic circulation. Normal horses have total serum bile acid concentrations of $<10\,\mu mol/L$. Elevations $>20\,\mu mol/L$ are highly associated with hepatic insufficiency, obstruction of the biliary tract and portosystemic shunting.

Bile acids are excreted into and absorbed from the gastrointestinal tract at a fairly constant rate in horses; total bile acid concentration can be measured at any point regardless of feeding time. Assays that only measure bile acids conjugated to glycine are not as useful in equine practice as assays that measure total bile acids because the glycine conjugates account for only 14% of the total in horses.

The clearance rate of **sulfobromophthalein (BSP)** dye from the bloodstream assesses the liver's ability to remove anions from circulation. The dye is injected IV at 2.2 mg/kg, and heparinized blood samples are collected at 6, 9, 12 and 15 min. The dye is very irritating, and perivascular injection should be avoided. The amount of dye cleared per unit time is reported as the half-life ($t_{1/2}$) for disappearance. Normal horses have a $t_{1/2}$ for BSP of 2.0–3.7 min. Because BSP dye is rarely available and measurement of serum concentrations of total bile acids provide a sensitive and specific test of liver function, BSP clearance is rarely assessed in horses.

Evaluation of other blood parameters can provide supportive evidence of hepatic insufficiency. Blood glucose can be normal, increased or decreased in horses with liver failure. **Hypoglycemia** is attributed to impaired gluconeogenesis and anorexia. **Hyperglycemia** may be observed post-prandially in horses with liver failure that are still eating.

In advanced cases of liver failure, inadequate protein synthesis can result in **hypoalbuminemia**. Because the half-life of albumin is >100 days, albumin concentration is usually normal in acute cases of hepatic insufficiency. Impaired production of proteins also can result in hemostatic abnormalities. When clotting factors reach plasma concentrations of <30% of normal, prolongation of fibrin endpoint tests such as the prothrombin time and activated partial thromboplastin time is observed. **Hypergammaglobulinemia** commonly occurs in patients with liver disease; gut toxins normally removed from portal circulation by the highly phagocytic Kupffer cells enter the systemic circulation and stimulate lymphocytic antibody production.

Because the failing liver is unable to convert ammonia to urea, the **serum urea nitrogen** concentration can be reduced and the plasma ammonia concentration elevated. Plasma ammonia determination is impractical for most field situations, however, because the heparinized sample must be chilled immediately, the plasma separated from cells within 30 min, and analysis performed within an hour of collection to prevent false increases.

Ultrasonography of the liver provides useful non-invasive information concerning the size of the liver and may detect soft tissue masses, choleliths, parenchymal changes and dilated bile ducts. It is important to realize, however, that a normal scan does not conclusively rule out the presence of liver

disease. Normally the liver has a homogeneous parenchyma with an echogenicity similar to or slightly greater than the renal cortex but less than the spleen. The liver can be imaged on the right side along the ventral lung margin from the 6th–15th intercostal space. Age-related atrophy of the right side of the liver may prevent visualization on this side. The liver can be viewed on the left side below the costochondral arch from the 8th–10th intercostal space; however, in some horses imaging from the left side is obscured by the spleen and colon. A 3.0 or 5.0 MHz scanner (linear or sector) is suitable for examination.

Microscopic examination of a **liver biopsy** can yield important etiologic and prognostic information. Since biopsy is not a benign procedure, its use should be reserved for patients with elevated liver enzymes in association with clinical signs of liver failure and/or abnormal liver function tests, and for horses with persistent, unexplained elevations in liver enzymes. Abnormal liver enzymes arising from secondary hepatic insults generally return to normal once the primary disease process resolves. Liver biopsy is most informative in disease processes that cause uniformly dispersed lesions.

Liver biopsy can be performed under **field conditions**. **Hemorrhage** is the major complication, and a **clotting profile** (*q.v.*) and **platelet count** should be assessed prior to biopsy to ensure hemostatic capabilities are adequate. Because of the potential for abdominal and thoracic contamination, a liver biopsy should not be performed in cases of suspected liver abscessation.

Liver biopsy is performed on the horse's **right side** through the 13th or 14th intercostal space at the height of a line drawn from the point of the shoulder to the tuber coxae. The site is clipped, surgically prepared and infiltrated with 2% lidocaine. Using sterile technique, a small stab incision is made through the skin with a number 15 scalpel blade, and a notch-cutting biopsy needle (Tru-Cut, Travenol, Deerfield, IL, USA) is then inserted in a slightly ventral direction. The needle passes through the caudal aspect of the thorax and the diaphragm, then into liver parenchyma.

Ultrasonography facilitates selective needle placement, and is especially helpful when the liver is small. In horses with decreased colonic filling due to anorexia and a large window of liver against the abdominal wall, ultrasound guided transabdominal liver biopsy can be safely performed without puncturing the colon. Some discomfort can be expected as the needle passes through the pleura and peritoneum, so the horse should be restrained to minimize the risk of injury. After the biopsy is obtained, the sample is placed in formalin and submitted for histopathology. Another sample can be placed in transport medium for culture and sensitivity. Hepatic lesions and their significance are described in Table 10.4.

The creatinine concentration, electrolyte, acid-base and hydration status should also be carefully assessed, since other abnormalities often arise in horses with liver failure. In addition, a complete blood count and serum fibrinogen concentration should be evaluated for evidence of inflammatory changes. These findings will help guide appropriate supportive therapy.

TREATMENT AND PROGNOSIS

When treating horses with liver failure, the goal is to provide **supportive care** while the liver regenerates to the point that function is restored. Treatment is

Table 10.4 Histology of hepatic lesions

Lesions	Causes	Clinical significance	Liver enzymes
Randomly dispersed focal areas of necrosis	Secondary to bacterial septicemia, salmonellosis, endotoxemia, EHV-1	Rarely associated with signs of liver failure	SDH, AST increased; GGT often increased
Centrilobular lesions	Hypoxic injury secondary to cardiac insufficiency, severe anemia, shock, monensin toxicity	Rarely associated with signs of liver failure	SDH, AST increased; GGT often increased
Acute massive necrosis	Acute, hepatic necrosis (Theiler's), aflatoxin, carbon tetrachloride, ferrous salts,	Clinical signs of hepatic insufficiency when >70% of functional mass affected	SDH, AST increased; GGT, ALP increased
Diffuse hepatic lipidosis	Negative energy balance, azotemia, and endotoxemia	Rarely associated with signs of liver failure in horses. Severely affected ponies can develop hepatic failure	SDH, AST increased; GGT, ALP sometimes increased
Focal hepatic lesions	Abscesses, neoplasia	Rarely associated with signs of hepatic failure	SDH, AST variable; GGT, ALP variable
Cholelithiasis (cholangiohepatitis)	Ascending bacterial infection, obstructed bile flow	Causes intermittent colic, inappetence, fever. Clinical signs of hepatic insufficiency when >70% of functional mass affected	SDH, AST variable; GGT, ALP disproportionately increased; conjugated bilirubin increased
Portal venous systemic shunts	Congenital or acquired (secondary to chronic fibrosis)	Clinical signs of hepatic insufficiency when >70% of functional mass affected	SDH, AST, GGT, ALP, normal; increased ammonia
Chronic progressive primary liver disease	Pyrrolizidine alkaloid toxicosis, aflatoxins, chronic active hepatitis	Clinical signs of hepatic insufficiency when >70% of functional mass affected	SDH, AST increased initially but can decline as disease progress; GGT, ALP increased

ALP, alkaline phosphatase; AST, aspartate aminotransferase; GGT, gamma glutamyltransferase; SDH, sorbitol dehydrogenase.

most successful in horses with **acute hepatic failure** because there is greater potential for hepatocyte renewal. The initial aim in patient management is to correct hydration, acid-base and electrolyte abnormalities. Acidosis should be corrected gradually, and overcorrection avoided. Alkalemia favors movement of ammonia into the CNS, thereby precipitating or worsening hepatoencephalopathy. Horses improve with **glucose administration** even if they are not hypoglycemic on presentation.

If hypoglycemia is detected, administer **10% glucose** IV to establish normoglycemia, then maintain therapy with 5% glucose at a rate of 2 mL/kg/h for the initial 24 h of hospitalization. The blood glucose should be monitored and the rate adjusted to maintain blood glucose between 80 and 110 mg/dL. Fluids containing balanced electrolyte solutions and glucose (**half-strength**

lactated Ringer's solution and **2.5% dextrose**) can be used at 4 mL/kg/h to provide fluid, electrolytes and glucose for maintenance.

Horses with signs of **hepatoencephalopathy** (*q.v.*) can be uncontrollable or abnormally agitated; sedation may be necessary. Small dosages of **xylazine** (0.2–0.5 mg/kg IV), chloral hydrate (50 mg/kg IV as a 5% solution) or detomidine (0.005–0.007 mg/kg IV) work well in these instances. Care should be taken when using sedatives since hepatic metabolism of the drugs will probably be impaired.

When signs of hepatoencephalopathy are noted, steps should be taken to reduce absorption of toxic metabolites from the gut. **Mineral oil** is a safe, cost-effective laxative, and can be administered by nasogastric tube at a rate of 2–4 L/500 kg horse s.i.d. Intubation should be conducted carefully since **impaired hemostasis** may result in prolonged bleeding after trauma. Other therapeutic modalities include oral administration of **lactulose syrup** (0.3 mL/kg q.i.d.) or **neomycin liquid** (50–100 mg/kg q.i.d.). Lactulose is digested by colonic bacteria into small organic acids that reduce luminal pH and create an osmotic diarrhea. Lactulose has been documented to decrease ammonia production without causing diarrhea. Neomycin decreases microbial production of toxic metabolites, but its negative impact on normal flora increases the risk for salmonellosis (*q.v.*), thus limiting its clinical usefulness.

Dietary management (*q.v.*) is an important therapeutic consideration. Frequent administration of small quantities of a diet low in protein and high in carbohydrates is recommended. Dietary restriction of protein decreases the amount of protein available for production of neurotoxic substances. **Legume hays should be avoided** and only **grass or oat hay** fed to horses with liver failure. An example of a useful maintenance diet for horses with compromised livers that are still eating is a mixture of one part cracked corn and two parts beet pulp in molasses. Sorghum, oat hay or grass hay can be used instead of beet pulp. Feed 2.5 kg/100 kg/day split into 4–6 meals.

Anorectic horses can be supplemented a gruel containing oral formulations of branched chain amino acids (24 g leucine, 18 g isoleucine, 18 g valine per day). Administer vitamin B_1 and folic acid parenterally on a weekly basis. Horses should be allowed to graze, but kept out of intense sunlight to avoid **photosensitization** (*q.v.*). Partial parenteral nutrition and treatment with IV preparations of branched chain amino acids is rarely utilized due to economics.

The prognosis for liver failure depends largely on the **regenerative capabilities** of the liver. Extensive fibrosis and impaired hepatocellular division warrant a poor to guarded prognosis.

INDIVIDUAL CAUSES OF LIVER FAILURE

Pyrrolizidine alkaloid toxicity

Etiology and pathogenesis

Pyrrolizidine alkaloid (*q.v.*) toxicity is a common cause of liver failure in horses. Although acute liver failure is occasionally noted, chronic liver failure is the most common presentation. Prolonged ingestion of small amounts of **toxic plants** generally precedes onset of clinical signs by weeks to months. More than 150 plants worldwide contain pyrrolizidine alkaloids toxic to grazing

animals. Most of them belong to the genera *Amsinckia, Crotalaria, Echium, Heliotropium, Senecio* and *Trichodesma.* Horses ingest the plants when forage is poor. **The plants retain their toxicity after drying**, and horses can be poisoned by contaminated hay and pelleted hay cubes.

Clinical findings and diagnosis

Gradual weight loss and decreased interest in food is noted by some owners for several weeks prior to development of hepatoencephalopathy, mild icterus and photodermatitis. **Inspiratory dyspnea** associated with hepatoencephalopathy is reported as a primary presenting complaint in some animals with pyrrolizidine-induced chronic liver failure.

The GGT, ALP, SDH, AST and serum bile acid concentration are generally increased. In long-standing cases SDH and AST may be normal or only slightly elevated. Histopathologic changes characteristic of **pyrrolizidine alkaloid toxicosis** are portal necrosis and fibrosis, biliary hyperplasia and megalocytosis. Pyrroles produced by hepatic metabolism of pyrrolizidine alkaloids produce an anti-mitotic effect by cross-linking DNA; megalocytes develop because hepatocytes cannot divide properly.

Ingestion of **kleingrass** (*Panicum coloratum*) sporadically causes **chronic hepatitis** in horses, characterized by bridging fibrosis, biliary hyperplasia, cholestasis and multifocal areas of necrosis. The absence of megalocytosis differentiates this plant toxicity from pyrrolizidine toxicosis.

Treatment and prognosis

Prognosis for advanced cases of chronic liver failure is poor, and most cases die within several weeks after clinical signs become apparent. Acute or mildly affected cases are more likely to respond to supportive therapy. Long-term prognosis depends on the ability of the liver to regenerate to a functional point, and the prevention of further hepatic insults.

Acute hepatitis

Etiology and pathogenesis

Acute hepatitis (**Theiler's disease**, **serum sickness**) is a common cause of liver failure in adult horses. Symptoms of acute liver failure can appear 1–2 mo after receiving an equine origin serum-derived product such as **tetanus antitoxin**. In some farm outbreaks, however, there is no history of horses receiving serum-derived biologicals. The seasonality and large number of animals affected during these outbreaks have prompted speculation that an infectious agent spread by **hematophagous insects** or direct contact may be involved.

Clinical findings and diagnosis

Horses with acute hepatitis typically exhibit intense **icterus**, signs of **hepatoencephalopathy** and **photodermatitis**. Laboratory findings include hyperbilirubinemia, elevated cytosolic leakage enzymes (SDH, AST), induced enzymes (GGT, ALP) and elevated bile acid. Marked diffuse hepatocellular necrosis, varying degrees of bile duct proliferation and inflammatory cellular

infiltration in the portal area are noted histologically. Grossly, the liver is either swollen or smaller than normal.

Treatment and prognosis

Supportive therapy is warranted in acute hepatitis, as most cases have a fair prognosis for survival. Most cases either die or recover within a week after the onset of clinical signs.

Tyzzer's disease

Etiology and pathogenesis

Tyzzer's disease is a sporadic and highly fatal disease of foals 9–45 days of age caused by *Clostridium piliformis* (*q.v.*). The bacterium is probably shed in the feces of clinically normal horses. Ingested bacteria gain access to the portal circulation and subsequently the liver of susceptible foals.

Clinical findings and diagnosis

The infection produces a **fulminant septicemia**, and death occurs 2–48 h after signs appear. Affected foals exhibit depression, fever, hypoglycemia, tachycardia and diarrhea. In more protracted cases, icterus may be observed. Terminally, foals become recumbent, hypothermic and comatose. An ante mortem diagnosis is difficult to achieve because signs are non-specific and the course of the disease peracute. Polymerase chain reaction has been used to identify the bacterial antigen in biopsy specimens of exotic animals. Many foals with Tyzzer's disease are **found dead**, and the diagnosis is made on post mortem examination of the liver. Necrotizing lesions are noted in the liver parenchyma, particularly in periportal regions. Necrotic areas are surrounded by a neutrophilic response, and bacteria are readily observed along the periphery of lesions with silver stains.

Treatment and prognosis

Treatment with broad-spectrum antibiotics such as a combination of **potassium benzylpenicillin** (44 000 IU/kg IV q.i.d.) and an **aminoglycoside** (e.g. gentamicin 6.6 mg/kg IV or IM s.i.d.) should be initiated promptly. Supportive therapy with **IV fluid** therapy (e.g. acetated Ringer's solution at 4–8 mg/kg/h) and an **NSAID** (flunixin meglumine 0.5–0.75 mg/kg IV s.i.d.) is also recommended to treat shock. The prognosis is grave.

Mycotoxicosis

Etiology and pathogenesis

Aflatoxins (*q.v.*) are the most common mycotoxins associated with liver disease (and occasionally liver failure) in horses and other domestic livestock. Aflatoxins are fungal metabolites produced by *Aspergillus flavus* and *A. parasiticus*. **Fumonisin**, a mycotoxin produced by *Fusarium moniliforme*, is associated with the development of **leukoencephalomalacia** (*q.v.*) and **hepatitis** in horses. Damaged **corn kernels** that are stored in a moist, warm environment provide optimal growth conditions for *A. flavus* and *F. moniliforme*.

Clinical findings and diagnosis

The signs depend on the dosage of mycotoxin ingested over time. Consumption of **large quantities** of aflatoxins or fumonisin can cause depression, neurologic signs (circling, head-pressing, blindness and ataxia), anorexia and death within 5 days (or more) of exposure. Hypoglycemia, elevated liver enzymes and abnormal liver function tests may be noted. Chronic low-grade exposure to aflatoxins is associated with immunosuppression, ill thrift and increased liver enzymes. The effect of chronic exposure to low levels of fumonisin is unknown.

Post mortem hepatic changes suggestive of **aflatoxicosis** and **fumonisin toxicosis** include fatty degeneration, biliary hyperplasia, periportal fibrosis and hepatocellular necrosis. Other changes associated with acute fatal aflatoxicosis in horse are encephalomalacia of the cerebrum, myocardial degeneration and fatty degeneration of the kidney. Liquefactive necrosis of the cerebral hemispheres (leukoencephalomalacia) is a prominent finding in horses poisoned by fumonisin ingestion.

Mycotoxicosis should be considered whenever more than one horse in a group demonstrates symptoms shortly after consumption of **feed recently introduced** to the group. The feed should be withdrawn and analyzed for mycotoxins. Although there are no safe levels of aflatoxins in feeds, levels >20 ppb are considered unsafe for consumption by people, dairy cattle and young animals. In several natural outbreaks of acute aflatoxicosis in horses, feedstuffs containing >400 ppb were being consumed at 0.5 mg/kg/day for 5 days or more prior to death. Levels of 72 ppm fumonisin have been measured in association with an outbreak of leukoencephalomalacia in horses.

Treatment and prognosis

Prognosis for advanced cases of chronic liver failure is poor, and most cases die within several weeks after clinical signs become apparent. Acute or mildly affected cases are more likely to respond to supportive therapy. Long-term prognosis depends on the ability of the liver to regenerate to a functional point, and the prevention of further hepatic insults.

Iron toxicity

Etiology and pathogenesis

Iron intoxication is an uncommon cause of hepatitis in adult horses and foals. Neonates are particularly susceptible to toxicosis prior to ingestion of colostrum. Ingestion of a single dose of an oral inoculant containing ferrous fumarate shortly after birth caused hepatitis and death in foals by 2–5 days of life; the product associated with the syndrome was removed from the market in 1983 and no subsequent cases occurred.

Consumption of vitamin supplements containing **ferrous fumarate** has been associated on several occasions with the development of hepatitis in adult horses. Normal daily iron intake for adult horses is 40 ppm. Iron is absorbed from the intestinal tract, and surplus iron is stored in high concentration in body tissues, particularly the liver and spleen. Ferrous iron is more soluble than ferric iron, and therefore more readily absorbed. If accumulation of iron within tissues becomes excessive, toxicosis can occur. The time to onset

of clinical signs is influenced by the daily dosage, the presence of underlying hepatic disease, and the antioxidant capacity of the liver. Vitamin E and selenium are important cofactors in the glutathione peroxidase antioxidant mechanism. If vitamin E or selenium concentrations are reduced, the liver is more vulnerable to damage.

Clinical signs and diagnosis

Icterus, hepatoencephalopathy and coagulopathy characterize iron toxicosis. Cholestasis and hepatic necrosis elevate the serum GGT and SDH concentrations, respectively. Serum bilirubin and plasma ammonia concentrations are typically elevated, and lymphopenia is noted on the hemogram. Clotting profile abnormalities (*q.v.*) include thrombocytopenia, prolongation of the prothrombin time and activated partial thromboplastin time, and increased fibrin degradation products. Serum iron concentration exceeds the normal equine reference range (73–140 μg/mL).

Histopathologic lesions consistent with iron toxicosis are periportal proliferation of bile ductules, necrosis and fibrosis of periportal and periductule hepatocytes, and infiltration of affected areas by a mixture of inflammatory cells. Lymphoid necrosis, particularly in the spleen, is a prominent finding.

Treatment and prognosis

Treatment consists of discontinuing iron supplementation and providing supportive care for liver failure. **Chelation therapy** with **ethylenediaminetetraacetic acid (EDTA)** or **desferrioxamine** has been used successfully in people and small animals with iron intoxication. As a rule, chelation therapy is reserved for patients whose total body iron stores exceed five times the upper limit of the reference range. Prognosis for foals and horses with iron intoxication is guarded. Most foals with hepatic failure caused by ferrous fumarate ingestion in the early 1980s did not recover.

Cholelithiasis

Etiology and pathogenesis

Cholelithiasis is defined as the presence of **calculi** (choleliths) in the hepatobiliary system, usually accompanied by biliary inflammation and infection. It is uncertain whether the association between cholangiohepatitis and cholelith formation is one of cause and effect. The isolation of **enteric bacteria** and anaerobes from equine cases suggests ascending infection from the proximal small intestine.

Equine **choleliths** are predominantly calcium bilirubinate and calcium phosphate, which are associated with ascending biliary infection in man. The calculi vary in size and are most often multiple. **Hepatolithiasis** refers to cholelithiasis of the intrahepatic biliary tracts, whereas **choledocholithiasis** refers to calculi in the common bile duct.

The cause of cholelithiasis is unknown, but **biliary stasis**, ascending Gram-negative bacterial infections and alteration in biliary composition are likely contributors to calculus formation. Furthermore, **ascarid ova** (*q.v.*) may serve as nidi for formation of calculi in the biliary tract.

Clinical findings and diagnosis

Cholelithiasis occurs most commonly in middle-aged horses (5–18 yr of age). Symptoms of biliary obstruction include icterus, fever, anorexia and abdominal pain. Clinical signs may be intermittent, and chronic cases generally develop weight loss. Hepatoencephalopathy and photosensitization develop in a small percentage of cases.

Marked elevation of induced cholestatic enzymes (GGT, ALP) and mild to moderate elevation of cytosolic enzymes (SDH, AST) characterize biliary tract obstructive disorders. Conjugated bilirubin concentration is often >25% of the total bilirubin concentration. Bilirubin can often be detected in the urine, and urinary urobilinogen is often undetectable. Total serum bile acids are generally increased. Inflammatory changes such as a neutrophilic leukocytosis with a left shift, hyperproteinemia and hyperfibrinogenemia are noted frequently in the leukogram. The prothrombin time and activated partial thromboplastin time may be prolonged if biliary obstruction is chronic enough to interfere with clotting factor synthesis.

Ultrasonography is an important adjunct diagnostic tool. Visualization of well-defined hyperechoic masses with acoustic shadows within dilated bile ducts confirms the diagnosis. However, not all choleliths are easily seen with ultrasonography so failure to observe them does not preclude a diagnosis of cholelithiasis. Other ultrasonographic findings highly supportive of a diagnosis of obstructive biliary disorders include hepatomegaly, increased echogenicity of liver parenchyma and bile duct dilatation.

A **liver biopsy** (*q.v.*) is necessary to help determine long-term prognosis, particularly when surgery is being contemplated. The biopsy typically reveals varying degrees of periportal and intralobular fibrosis, bile duct proliferation and foci of hepatocellular necrosis with infiltration of polymorphonuclear cells. A culture and sensitivity can be performed on a biopsy sample. Mixed populations of Gram-negative bacteria (*E. coli*) and anaerobes (*Clostridium* spp., *Bacillus* spp. and *Peptostreptococcus* spp.) (*q.v.*) are commonly isolated from the hepatic biopsies of horses with cholelithiasis.

Treatment and prognosis

The prognosis for horses with **symptomatic cholelithiasis** is guarded to poor. Conservative medical management alone is often unsuccessful and surgical management is associated with many risk factors. Supportive therapy, as described in the section covering treatment of horses with liver failure (*q.v.*), should be initiated along with broad-spectrum **antimicrobial therapy** for the accompanying cholangitis. Broad-spectrum antimicrobial therapy can be initiated with potassium benzylpenicillin (22 000–44 000 IU/kg IV q.i.d.) and gentamicin (6.6 mg/kg IV s.i.d.) and further therapy should be adjusted based on culture and sensitivity of liver biopsy and response. Antimicrobial therapy should be continued for several weeks to months until GGT concentrations in serum are normal.

Surgery is an option for horses with calculi in the common bile duct that do not have extensive fibrosis on liver biopsy. If the cholelith cannot be gently massaged into the duodenum, then gentle digital pressure should be applied to crush the concretion (**choledocholithotripsy**). The fragments can then be flushed into the duodenum with saline solution.

If these methods are unsuccessful, **choledochotomy** can be attempted. This procedure is risky, however, because the common bile duct is deep in the abdomen and difficult to isolate surgically. **Iatrogenic contamination** of the peritoneal cavity with bile results in life-threatening chemical and bacterial peritonitis. This complication, as well as failure to remove all calculi, warrants a guarded prognosis. Horses should be treated with appropriate antimicrobials. Broad-spectrum antimicrobial therapy can be initiated with potassium benzylpenicillin (22 000–44 000 IU/kg IV q.i.d.) and gentamicin (6.6 mg/kg IV s.i.d.) and further therapy should be adjusted based on culture and sensitivity of liver biopsy and response. Antimicrobial therapy should be continued for several weeks to months until GGT concentrations in serum are normal for treatment of cholangiohepatitis.

Chronic active hepatitis

Etiology and pathogenesis

Chronic active hepatitis (CAH) in horses is a chronic, progressive hepatopathy of unknown etiology. A similar syndrome in people has been linked to autoimmune disease, viral hepatitis, Wilson's disease, α_1-antitrypsin deficiency and drug allergy. Extrahepatic signs of autoimmune disease occur in some people including dermatitis, arthritis and glomerulonephritis.

Coronary dermatitis has been observed in some horses with CAH and could be a manifestation of autoimmune disease (*q.v.*); however, this has not been confirmed by immunohistologic staining. Viral hepatitis, Wilson's disease and α_1-antitrypsin deficiency have not been documented in horses. Therefore, immune mediated disease is commonly incriminated as a cause of CAH in horses. Although idiosyncratic drug hypersensitivity has been reported in a few cases in horses, this is not a consistent finding in horses with CAH.

In addition, CAH may result from **chronic cholangitis** in horses. Suppurative inflammation is documented histologically in some cases accompanied by culture of a coliform organism (*q.v.*) from biopsy samples. These horses often respond to antimicrobial treatment.

Clinical findings and diagnosis

Clinical signs of CAH are intermittent and insidious with minimal manifestation of illness until severe liver pathology and failure ensue. Signs of progressive liver failure include exercise intolerance, partial anorexia, **icterus** and fever.

Horses with CAH frequently have mild elevations of SDH and AST with more dramatic increases of GGT. Serum bile acid and bilirubin are normal until 70% of the liver is involved leading to liver failure. Total protein is generally elevated. Immunodiagnostics including antinuclear antibody titer and anti-immunoglobulin staining of skin lesions rarely confirm an autoimmune phenomenon.

Diagnosis is based on histologic lesions obtained from **liver biopsy** (*q.v.*) in the face of significant laboratory findings and, sometimes, clinical signs. The definitive diagnosis of CAH depends on the presence of periportal hepatocellular necrosis obscuring and distorting the limiting plate. This causes bridging necrosis, leading to fibrosis and cirrhosis. Mononuclear cells are the predominant

infiltrate; however, neutrophils predominate if **cholangiohepatitis** is the etiology and may be accompanied by biliary hyperplasia.

Treatment and prognosis

Supportive therapy is paramount in the treatment of CAH. Specific therapy depends on the histopathologic findings. If the liver biopsy reveals predominantly mononuclear cells, including plasma cells suggestive of an immune etiology, **corticosteroids** may be helpful. Treatment is commonly initiated with dexamethasone 0.05–0.1 mg/kg/day PO for 7 days followed by a gradual reduction in dose over 30 days. Additional treatment with prednisolone (1 mg/kg/day PO) for several weeks may be necessary.

When the liver biopsy contains large numbers of neutrophils supporting **cholangiohepatitis** or when **culture of liver biopsy is positive**, antimicrobial therapy instead of corticosteroids is indicated. Broad-spectrum antimicrobial therapy can be initiated with potassium benzylpenicillin (22 000–44 000 IU/kg IV q.i.d.) and gentamicin (6.6 mg/kg IV s.i.d.) and further therapy should be adjusted based on culture and sensitivity of liver biopsy and response. **Antimicrobial therapy** should be continued for several weeks to months until GGT concentrations in serum are normal for treatment of cholangiohepatitis. If GGT concentrations do not return to normal after 6 wk and liver biopsy reveals mononuclear CAH with resolution of the suppurative disease, corticosteroid therapy should be considered.

The duration of the disease greatly affects the prognosis in horses with CAH. **Hepatic cirrhosis** warrants a grave prognosis.

Other biliary tract disorders

Fibrotic obstruction of the common bile duct can occur in foals secondary to healing of duodenal ulcers. **Cholangiohepatitis** can result from ascension of enteric bacteria up the common bile duct; it generally occurs in association with **cholelithiasis** (*q.v.*) but occasionally occurs as a distinct disease. **Congenital atresia** of the common bile duct has been described in one foal.

Hepatic abscessation

Hepatic abscessation occasionally develops in horses. Bacteria gain access to the liver **hematogenously** through the portal vein, hepatic artery, the umbilical vein (neonates) and by ascending up the common bile duct from the bowel lumen. ***Clostridium* spp.** (*q.v.*) and enteric bacteria are the most common isolates. Non-specific symptoms include fever, intermittent signs of low-grade abdominal pain, and weight loss. Ultrasonography may identify a hypoechoic mass in the hepatobiliary tract. Biopsy of the abscess is not recommended because it can cause iatrogenic bacterial peritonitis and pleuritis. Treatment consists of supportive care and administration of long-term broad-spectrum antibiotics. The prognosis is guarded.

Hepatic neoplasia

Hepatic carcinoma, diffuse hepatic lymphosarcoma and biliary tract carcinomas (*q.v.*) have been sporadically identified in horses. Although neoplasias

arise more commonly in older horses, hepatic carcinomas have been reported in yearlings and young adults. Signs of liver failure arise if over 60–70% of the liver parenchyma is damaged, or if the neoplasia obstructs the common bile duct. Prognosis for horses with hepatobiliary neoplasia is extremely poor.

Portosystemic shunts

Etiology and pathogenesis

Portosystemic shunts are uncommon in horses. **Congenital vascular anomalies** involving shunts between the portal circulation and the caudal vena cava and the azygos vein have been described in horses under a year of age. Failure of portal blood to circulate through the liver in a normal fashion results in liver atrophy.

Clinical findings and diagnosis

Affected horses manifest symptoms of **intermittent neurologic disease** (hepatoencephalopathy) (*q.v.*) and stunted growth. Consistent laboratory findings include increased total bile acids and elevated plasma ammonia concentration. The blood urea nitrogen (BUN), glucose, clotting profile and albumin concentration findings are more variable. Liver enzymes are within normal ranges or only mildly elevated. Ultrasonography may reveal an undersized liver. Microscopically, hepatocytes are smaller than normal, especially in the centrilobular areas. **Mesenteric portography** is recommended for congenital cases in which surgical correction is being considered in order to determine the number and locations of shunts.

Treatment and prognosis

Surgical correction of a single shunt should theoretically be possible, based on success in people and small animals. However, reports of attempted surgeries in large animals are lacking. Most cases described in the literature were definitively diagnosed by post mortem examination.

PERITONITIS

ETIOLOGY AND PATHOGENESIS

Peritonitis is **inflammation of the mesothelial lining of the peritoneal cavity.** Types of peritonitis can be characterized according to onset (peracute, acute, chronic), region affected (diffuse, localized) and presence of bacteria (septic, non-septic).

Causes of **septic peritonitis** include gastrointestinal perforation, gastrointestinal inflammation or infarction with transmural migration of bacteria, abdominal abscessation, septicemia, omphalophlebitis, uterine perforation, surgical complications, enterocentesis, complications associated with castration, and penetrating abdominal wounds (*q.v.*).

Causes of **non-septic peritonitis** include gastrointestinal inflammation without transmural migration of bacteria, hemoperitoneum, neoplasia, urinary

tract perforation or rupture, cholelithiasis, abdominocentesis, and abdominal surgery (*q.v.*). Parasite larval migration, verminous arteritis and systemic diseases such as equine influenza, equine viral arteritis, equine infectious anemia and African horse sickness (*q.v.*) can also cause peritonitis.

Peritoneal inflammation results in release of inflammatory mediators, increases in vascular and peritoneal permeability, vasodilatation, chemotaxis of inflammatory cells, fibrin deposition on the peritoneal surface, and disruption of gastrointestinal motility. **Bacterial toxins** within the peritoneal cavity easily enter the systemic circulation causing endotoxemia (*q.v.*). Hypovolemia may result from leakage of fluid into the peritoneal cavity.

CLINICAL SIGNS AND DIAGNOSIS

Peracute septic peritonitis can result in hyperemic or cyanotic mucous membranes, tachycardia, weakness, depression, tachypnea, weak peripheral pulse, nasogastric reflux, colic and rapid deterioration to death. Rectal examination may reveal emphysema or roughening of the serosa. **Acute peritonitis** often causes reluctance to move and splinting of the abdomen due to parietal pain. Tachycardia, tachypnea, sweating, pawing, kicking at the abdomen and other signs of abdominal pain may be present. In severe cases, nasogastric reflux and clinical signs of shock may be present.

Horses with **localized peritonitis** often present with intermittent fever, weight loss, depression and anorexia. If present, abdominal pain is low grade. Heart rate and respiratory rate are normal or slightly increased. Decreased water intake may result in dehydration.

Laboratory findings may include increased PCV due to dehydration and reduced total protein due to leakage of large quantities of protein into the peritoneal cavity. When the duration of peritoneal inflammation is >48 h, hyperfibrinogenemia often occurs. The acute inflammatory process and/or endotoxemia associated with peritonitis often result in neutropenia and a left shift. **Metabolic acidosis** may occur in horses with shock.

The diagnosis of peritonitis is confirmed with **peritoneal fluid analysis**. The volume of peritoneal fluid and ease of collection are variable and cannot be used as a basis for diagnosis of peritonitis. During inflammation, peritoneal fluid usually is turbid and may become either bloody or serosanguineous. Clinicopathologic examination of the fluid reveals elevation of the WBC count and total protein. **Biochemical analysis** of peritoneal fluid may be useful in detecting sepsis when cytologic examination and culture are equivocal. Peritoneal fluid pH and glucose are significantly lower (pH < 7.3 and glucose <30 mg/dL) in horses with septic peritonitis than in horses with non-septic peritonitis and healthy horses. Differences in serum and peritoneal glucose concentration >50 mg/dL are most predictive of septic peritonitis.

In **acute peritonitis**, either degenerative or non-degenerative neutrophils are the predominant cell type, whereas in chronic peritonitis the majority of the cells are either macrophages or neutrophils. **Degenerative neutrophils** are more likely to be present in cases of septic peritonitis or peritonitis due to tissue necrosis. In cases of septic peritonitis, cytologic evaluation of the peritoneal fluid may reveal bacteria free or phagocytosed in leukocytes. Gram stain may help to identify the types of bacteria present, thereby assisting with

antimicrobial choices. Bacterial cultures are sometimes negative in cases of septic peritonitis. Furthermore, the absence of bacteria on cytologic examination does not rule out septic peritonitis.

TREATMENT AND PROGNOSIS

Therapy involves correction of the **primary disease process**, broad-spectrum antimicrobial agents (see antimicrobial therapy below, *q.v.*) and therapy for hypovolemia and endotoxemia (see salmonellosis, *q.v.*). In some cases, abdominal surgery is necessary to correct the primary disease. Because it is often not possible to differentiate septic and non-septic peritonitis, antimicrobial therapy should be initiated whenever peritonitis is diagnosed or suspected.

It is preferable to obtain an **abdominal fluid sample** for cytology and culture before initiating antimicrobial therapy. Aerobic (*Escherichia coli, Streptococcus zooepidemicus, Strep. equi, Pseudomonas* spp., *Klebsiella* spp., etc.) and anaerobic bacteria are often involved in peritoneal infections; therefore, broad-spectrum antimicrobial therapy is indicated until results of culture and sensitivity are available.

IV antimicrobial therapy provides higher plasma levels and is therefore more effective in cases of acute peritonitis. **Penicillin** is effective against *Streptococcus* spp. and non-β-lactamase-producing anaerobic bacteria. Unless the presence of Gram-negative bacteria has been ruled out, penicillin should be **combined with an aminoglycoside or potentiated sulfonamide**. **Metronidazole** is often effective against β-lactamase-producing anaerobic bacteria. Chloramphenicol has efficacy against aerobic and anaerobic bacteria. However, plasma concentrations achieved with chloramphenicol administration in horses are low. Therefore, chloramphenicol is more effective for chronic therapy after penicillin and an aminoglycoside or potentiated sulfonamide have been administered in the acute stages. The minimum duration of antimicrobial therapy for peritonitis usually is 3 wk. Treatment of abdominal abscessation sometimes requires months.

Peritoneal lavage is sometimes attempted by placing 14 G catheters in each paralumbar fossa by use of aseptic techniques for infusion of large volumes (>20 L) of sterile polyionic fluid solutions. A Foley catheter (30 F) is placed in the ventral abdominal wall for drainage of lavage fluid. Successful drainage of infused fluids rarely occurs. Complications of peritoneal lavage include further introduction of bacterial organisms and adhesions.

Prognosis is at best guarded. The most common complication is **adhesion formation** leading to future **bowel obstruction**. Failure of antimicrobial cure due to resistance of bacterial organisms and failure of antimicrobial penetration can occur. Laminitis (*q.v.*) is a potential life threatening complication.

Chapter 11

The endocrine system

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Chapter contents

INTRODUCTION

The endocrine system comprises a complex and integrated system of glands and chemical substances (**hormones**) that function, along with the nervous system, to maintain homeostasis. Hormones have considerable influences on many of the **metabolic processes** of the body, and are involved not only in diseases that are commonly regarded as endocrine in nature, but also in such processes as growth and pregnancy, the response of the body to infection and trauma, and the development of neoplasms.

Much of the endocrine system is related developmentally, anatomically or functionally to the **nervous system**. The **hypothalamus** is part of the brain and is a most important part of the endocrine system. It controls directly the adenohypophysis (anterior pituitary gland), and indirectly (via the pituitary) several other glands, including the adrenal cortex, the gonads and the major part of the thyroid. Part of the hypothalamus extends into the neurohypophysis (posterior pituitary) to form a single anatomic and functional unit. Nuclei within the hypothalamus control the **sympathetic nervous system**, which includes the adrenal medulla.

Another group of endocrine tissues are derived embryologically from the **neural crest**, and are present as cells or clusters of cells within other organs; these include the parafollicular cells of the thyroid, the endocrine cells of the alimentary tract and the islet cells of the pancreas. Finally, there is a group of endocrine cells and tissues that is apparently **independent of the nervous system**; this includes the parathyroids, part of the adrenal cortex, and parts of other organs, tissues and blood. It is often said that the alimentary tract represents "the largest endocrine organ of the body", and the complex endocrine and neural enteric systems have essential roles in the coordination of gut function, including motility, mucosal transport and local blood flow. The principal hormones and their sites of actions are summarized in Table 11.1.

Clinical endocrinology involves the study of how the body behaves in endocrine disorders and the application of the results to prevent, alleviate or cure endocrine disease. Unfortunately, the amounts of hormones usually present in the blood (especially the pituitary hormones) are extremely small, and the difficulty of measuring them has hindered the study of endocrine disorders. However, recent improvements in analytical techniques and in specificity and sensitivity of hormone assays have led, and continue to lead, to dramatic advances in the understanding of the normal and pathologic processes of endocrinology.

Diseases of the endocrine system often cause **dysfunction** of one or more of its parts. Hormones may be secreted in excess, causing syndromes of glandular hyperfunction, or in deficient amounts, causing syndromes of hypofunction. The overactivity or underactivity of one gland may adversely affect the function of another. Disorders may also arise because of a defect in the metabolism or breakdown of hormones, or the target tissues may become insensitive to the action of a hormone.

THE PITUITARY GLAND

INTRODUCTION

The equine pituitary gland measures approximately 2 cm × 1 cm and weighs from 1 to 3 g. The terms anterior and posterior lobes are anatomically incorrect in horses, since the **neurohypophysis** (equivalent to the posterior lobe in primates) is embedded in and lies dorsal to the **adenohypophysis** (equivalent to the anterior lobe of primates). The adenohypophysis (80–85% of the total weight of the gland) is composed of endocrine cells derived from ectoderm. The neurohypophysis (15–20% of the total weight of the gland) consists of

Table 11.1 Principal endocrine glands and hormones

	Anterior pituitary hormones	Target glands/tissues	Main hormones
Hypothalamus and dependent glands			
1. Hypothalamic nuclei secreting trophic hormones			
(a) Releasing hormones (RH)			
Growth hormone RH	GH	All tissues	—
Thyrotropin RH	TSH	Thyroid (follicular)	Thyroxine Triiodothyronine
Corticotropin RH	ACTH	Adrenal cortex	Cortisol Androgens Estrogens
Follicle stimulating hormone RH	FSH	Ovary	Estrogens
		Testis (tubules)	—
Luteinizing hormone RH	LH	Ovary	Progesterone
		Testis (Leydig cells)	Testosterone
(b) Inhibiting hormones (IH)			
Prolactin releasing IH	Prolactin	Mammary gland	—
Melanocyte stimulating IH		MSH Melanocytes	—
2. Hypothalamic nuclei related to posterior pituitary			
Antidiuretic hormone (ADH)		Renal tubes	—
Oxytocin		Uterus	—
		Mammary gland	—
3. Hypothalamic nuclei controlling sympathetic nervous system			
Adrenal medulla and sympathetic nervous tissue	Catecholamines		
Endocrine glands and tissues derived from neural crest			
Thyroid (parafollicular cells)		Calcitonin	
Alimentary tract (endocrine cells)		Gastrin	
		Secretin	
		Cholecystokinin	
		Enteroglucagon	
		Enterogastrone	
		5-Hydroxytryptamine	
Pancreatic islet cells		Insulin	
		Glucagon	
Endocrine glands and tissues independent of nervous system			
Parathyroids		Parathormone	
Skin		Vitamin D	
Adrenal cortex (zona glomerulosa)		Aldosterone	
Kidney		Renin	
		Vitamin D	
		Erythropoietin	
Blood		Angiotensin II	
		Kinins	
Liver		Gonadotropin	
		Lactogen	
		Thyrotropin	
		Progesterone	
		Estrogens	
		Relaxin	
Other tissues		Histamine	
		Prostaglandins	
		Leukotrienes	

modified glial cells and axonal processes extending from nerve cell bodies in the supraoptic and paraventricular nuclei of the hypothalamus.

The adenohypophysis consists of three parts: the pars distalis, the pars intermedia and the pars tuberalis. Control of secretion from the pars distalis and pars tuberalis is by means of hypothalamus-derived releasing and inhibiting factors which are transported to the pituitary gland by local circulatory pathways. Control of secretion of the pars intermedia is by hypothalamus-derived neurotransmitters that are transported by axons directly into the pars intermedia.

The **pars distalis** is responsible for the secretion of numerous hormones, including growth hormone, prolactin, the gonadotropins luteinizing hormone (LH) and follicle stimulating hormone (FSH), pro-opiomelanocortin (POMC), adrenocorticotropic hormone (ACTH), corticotropin-like intermediate lobe peptide (CLIP), β-endorphin (β-END), thyrotropin (TSH) and melanocyte stimulating hormone (MSH). The **pars intermedia** is associated primarily with the synthesis of MSH and β-END.

The **circadian rhythm** of ACTH release arises mainly from **corticotropin** in the pars distalis. Increases in plasma ACTH lead to increases in circulating **cortisol** concentration. A diurnal pattern of ACTH and cortisol release occurs, with cortisol surges lasting 1–2 h starting between 02.00 and 04.00 h, resulting in peak plasma cortisol concentrations between 06.00 and 09.00 h. Circulating cortisol is largely bound to cortisol-binding globulin and has a half-life of 2–3 h.

The **neurohypophysis** comprises the pars nervosa, infundibular stalk and the pituicytes. Oxytocin and antidiuretic hormone (ADH) (also known as arginine vasopressin, AVP) are secreted by hypothalamic neurons arising in these nuclei, and are stored in the neurohypophysis.

The most common malfunction of the equine pituitary gland is associated with functional adenomas or adenomatous hyperplasia of the pars intermedia resulting in **Cushing's disease** (*q.v.*).

DIABETES INSIPIDUS

Diabetes insipidus (*q.v.*) results from the decreased release of **antidiuretic hormone** (ADH) from the posterior pituitary (**central diabetes insipidus**) or lack of sensitivity of the kidney to actions of ADH (**nephrogenic diabetes insipidus**). The disease is most commonly associated with destruction of the posterior pituitary by compression from a tumor of the pars intermedia; however, rare cases of **idiopathic diabetes insipidus** have been recorded. The clinical signs include polydipsia and polyuria, with urine specific gravity <1.010 that fails to increase after a **water deprivation test** (*q.v.*). Serum ADH levels are low and remain unaltered by water deprivation.

Diagnosis may be achieved by using a water deprivation test and ADH response test. In the **water deprivation test**, access to all feed and water is denied and the bladder is emptied by **catheterization**. Urine specific gravity, body weight, blood urea and creatinine levels are monitored every 4 h for a maximum of 20 h. Water deprivation should be terminated if urine specific gravity rises >1.020, or if blood urea or creatinine levels increase above normal, or if there is **clinical dehydration** or a loss of more than 5% body weight.

Horses in which urine specific gravity fails to exceed 1.020 during 20 h water deprivation are deficient in, or lack sensitivity to ADH. The **ADH response test** is performed by the IM injection of 40–60 U **pitressin** (*q.v.*) following bladder evacuation and recording of urine specific gravity. Urine samples are collected 8, 12, 16 and 20 h post injection, and should exhibit maximal concentrations. Restoration of the ability to concentrate urine after ADH administration in an animal that failed to concentrate urine after water deprivation confirms **central diabetes insipidus**.

Treatment is by IM injections of **desmopressin** s.i.d. or b.i.d.; the dose must be adjusted to the individual requirements of the patient.

Failure to concentrate urine after water deprivation and ADH administration confirms **nephrogenic diabetes insipidus**, which may occur secondary to renal infection such as **pyelonephritis** (*q.v.*). This condition must be differentiated from the more common **medullary washout** that occurs in association with **psychogenic water drinking**. Animals affected by the latter condition are expected to show a normal urine concentrating response to water deprivation, although this may take the full 20 h or even slightly longer.

THE ADRENAL CORTEX

INTRODUCTION

The paired adrenal glands contain two anatomically and functionally distinct parts—the cortex and the medulla. The outer cortex, comprising 90% of the gland, surrounds the central medulla. The cortex is a zoned structure and is covered by a thin capsule, below which are isolated groups of glomerulosa cells. Most of the cortex is made up of the zona fasciculata and the zona reticularis, the latter adjoining the medulla.

The **adrenal cortex** produces three major types of steroid hormones: **mineralocorticoids, glucocorticoids and androgens**. The source of mineralocorticoids, aldosterone and in part deoxycorticosterone, is the glomerulosa cells. Aldosterone is involved in the regulation of sodium and potassium balance, and is under the control of the **renin–angiotensin system** (*q.v.*). Cortisol and the adrenal androgens (estrogens and progesterone) are derived from the fasciculata and reticularis cells. The only known important control mechanism is by means of **ACTH**. This adenohypophysis-derived hormone regulates adrenocortical growth; it also mediates the rate at which steroid biosynthesis occurs.

Cortisol and **corticosterone** are the principal glucocorticoids of horses. As with many other species, there is a **circadian rhythm** of adrenal activity, with peak secretion of glucocorticoids occurring in the morning. Levels of cortisol can be increased by **stress** (such as transport and surgery) and **exercise**. Normal term foals have a high plasma cortisol concentration and have a maximum response to exogenous ACTH during the first day of life. Premature foals have decreased adrenocortical function and the adrenal gland appears to be refractory to ACTH. Low cortisol levels have also been reported in **chronic infections**.

The most commonly recognized abnormality of the adrenal cortex in the adult horse is hyperadrenocorticalism (**Cushing's disease**, *q.v.*) secondary to pituitary **pars intermedia dysfunction**. Hypoadrenocorticalism secondary to synthetic steroid administration also occurs, but there are few well-documented cases.

ADRENAL EXHAUSTION AND THE ACTH STIMULATION TEST

Adrenal insufficiency (also known as hypoadrenocorticalism or "steroid let-down syndrome") is a poorly defined syndrome, sometimes associated with stress or poor performance syndrome (*q.v.*). Low circulating cortisol levels have been reported in **endurance ride horses** following a 100 mile (161 km) ride, but abnormal responses to ACTH have not been determined and no deficiency in cortisol levels in racehorses affected by poor performance has ever been recorded. In fact, adrenal gland hypertrophy is more commonly observed at necropsy of racehorses than adrenal atrophy.

The adrenal glands are **shock organs** and can be damaged during endotoxemia, colic and anaphylaxis (*q.v.*). **Long-term administration** of exogenous corticosteroids or anabolic steroids can also lead to adrenal insufficiency if treatment is suddenly discontinued. The steroids suppress production of **pro-opiomelanocortin** (POMC) peptides by pituitary corticotropins, and the adrenal gland atrophies due to lack of ACTH stimulation. As little as 4 mg of dexamethasone may suppress the pituitary–adrenal axis for 18–24 h.

Clinical features of adrenal insufficiency include depression, anorexia, weight loss, poor haircoat and lameness. Serum biochemistry may be normal or show variable degrees of reduced levels of sodium and chloride, hyperkalemia and hypoglycemia.

Laboratory confirmation of adrenal insufficiency depends on an abnormal response to **ACTH challenge**; this may be performed using either ACTH gel or cosyntropin (synthetic ACTH). The test should be performed early in the morning. The protocols are summarized in Box 11.1.

Treatment of adrenal insufficiency includes rest and steroid supplementation.

Box 11.1 Protocols for ACTH challenge

ACTH Gel

1. Obtain pre-challenge plasma sample for cortisol estimation
2. Administer 1 U/kg ACTH gel IM
3. Obtain plasma samples at 2 and 4 h

In the normal horse, plasma cortisol should increase by 100–200% over basal levels after stimulation.

Cosyntropin

1. Obtain pre-challenge plasma sample for cortisol estimation
2. Administer 100 IU (1 mg) cosyntropin IV
3. Obtain plasma sample at 2 h

In the normal animal, plasma cortisol should increase by 100% after challenge.

CUSHING'S DISEASE

Introduction

Cushing's disease (hyperadrenocorticalism) (*q.v.*) arises as a result of prolonged exposure to excess glucocorticoids, produced as a consequence of hyperplasia of the adrenal cortex. In the horse, this condition is almost exclusively associated with **pituitary pars intermedia dysfunction**, usually due to a functional tumor (**adenoma**).

The abnormal pituitary glands usually weigh 2–3 times the normal weight. The tumors cause varying degrees of **compression** of the pars distalis and occasionally infiltrate the neurohypophysis. Dorsal expansion of the tumor through the diaphragma sella can also lead to compression of the hypothalamus and optic chiasm, resulting in blindness and other neurologic deficits. The tumor cells have not been reported to metastasize.

Pars intermedia adenomas in horses contain markedly reduced amounts of **dopamine** (approximately 10% of normal), and it has been suggested that hyperplasia may arise as a result of loss of hypothalamic dopaminergic innervation. Currently, it is uncertain whether pituitary pars intermedia dysfunction in horses is the result of spontaneous pituitary disease (neoplasia) or the result of loss of dopaminergic innervation and thereby a primary hypothalamic disorder. If the latter mechanism is important, then there is justification for considering treating clinical cases with compounds with **dopamine agonist** action in order to limit the secretion of the active pituitary products.

Conventionally, and simplistically, it has been presumed that neoplastic pituitary glands secrete high levels of ACTH that result in hyperplasia of the adrenal cortices. However, the pathogenesis of equine Cushing's disease is more **complex**, involving alterations in metabolism of other endocrine substances derived from the pituitary gland, including β-END, MSH and CLIP.

Although there are only limited data on the incidence of equine Cushing's disease, it is recognized that the condition has a pronounced age distribution: essentially this is a disease of **aged ponies and horses**. The mean age of affected horses in a number of case series has ranged from 18 to 23 yr. The condition is very rare in horses <10 yr old, and the youngest recorded age is 7 yr.

The frequency of diagnosis of the condition has increased significantly over the past decade, but this is probably due to greater awareness and a larger population of older horses, rather than to an increasing prevalence. All breeds and types of equids (including donkeys) can be affected by Cushing's disease, but ponies and Morgan horses may be at greatest risk. There is no apparent sex predisposition to the disease.

Clinical signs

Cases of equine Cushing's disease may be presented for investigation of a fairly **diverse range** of complaints, including lethargy, dullness, weight loss, excessive thirst, chronic infections, abnormal haircoat, persistent sweating and chronic, refractory laminitis (*q.v.*). The classic clinical sign of Cushing's disease is generally considered to be **hirsutism** (a long, curly haircoat that fails to shed). Despite the characteristic appearance of "classical" **cushingoid**

ponies or horses, it is not uncommon for owners to have accepted many, or all, of these features as normal aging processes.

Most of the clinical signs of equine Cushing's disease are explicable by the presence of increased amounts of **plasma cortisol**. For example, chronic, intractable infections are consequent upon **prolonged immunosuppression**, and **laminitis** (*q.v.*) arises from the effects of endogenous cortisol on the laminae of the foot. Commonly recognized infections include skin infections, recurrent subsolar abscesses, conjunctivitis, sinusitis, gingivitis and alveolar periostitis. **Chronic insidious onset laminitis** is seen in >50% of affected horses and is a common reason for euthanasia. The precise mechanisms by which hypercortisolism results in laminitis is poorly understood, but might relate to hyperinsulinemia and decreased glucose uptake by the laminar tissues.

High levels of plasma cortisol also stimulate **protein catabolism**, resulting in loss of body weight. Typically this is most pronounced in the **epaxial and lumbar musculature** such that affected animals appear dip-backed and/or pot-bellied. Despite the weight loss, the appetite of affected animals is usually normal, or may even be increased. However, dental abnormalities (*q.v.*) are common and can lead to painful mastication and quidding; this results in reduced feed intake that can also contribute to weight loss.

Other cortisol effects, seen less consistently, include **oral ulceration** and **redistribution of fat**. Deposition of fat occurs along the crest of the neck, over the tail head, and in the sheath of male horses. Another common site of fat deposition is above the eyes, producing prominent, bulging supraorbital fat pads.

Excessive thirst, or polydipsia, with increased urine output, is present in approximately one third of animals with Cushing's disease. A number of different disease mechanisms may contribute to this **polyuria–polydipsia** (PU/PD) (*q.v.*). The enlarged pars intermedia may destroy the neurohypophysis by expansion resulting in partial neurogenic diabetes insipidus. Hypercortisolism may also result in central stimulation of thirst. In addition, PU/PD can arise through direct effects of cortisol on renal function causing increased glomerular filtration or antagonism of ADH at the collecting ducts. Cortisol also indirectly contributes to PU/PD via the osmotic diuresis effects of glucosuria, inevitable in hyperglycemic horses. The hyperglycemia of equine Cushing's disease arises from the inhibition of the action of insulin to lower plasma glucose. Thus, PU/PD in equine Cushing's disease may be a consequence of secondary diabetes insipidus (*q.v.*) and secondary diabetes mellitus (*q.v.*) within the same animal. Another possible urinary complication of Cushing's disease is urinary tract infection, which may result in dysuria (*q.v.*).

Clinically, the most distinctive feature of cases of equine Cushing's disease is the **abnormal hair growth pattern** which presents as an extremely long haircoat (hirsutism), frequently with a very curly appearance, and which is often retained for prolonged periods including into the summer months. During the first few years of the disease, the abnormal haircoat may be restricted to the lower jaw, base of neck and palmar/plantar aspects of the distal limbs. Later, **generalized hirsutism** may develop, and in some cases a dark haircoat may turn lighter in color. In some animals, the haircoat may be found to be matted and wet due to persistent sweating (**hyperhidrosis**) unrelated to exercise. The pathogenesis of hirsutism and hyperhidrosis (*q.v.*) is unclear but

it has been suggested that it may be related to elevated POMC peptides or possibly due to the physical effect of the tumor causing pressure on the adjacent hypothalamus, thereby affecting the **thermoregulatory center**.

In a small proportion of cases, other clinical effects may arise from physical expansion of the neoplastic pituitary gland such as ataxia, seizures or blindness due to pressure on the optic nerves and/or their blood supply. Although interpretation of clinical findings such as lethargy or dullness must be somewhat subjective, it is not infrequent for these cases to appear **abnormally docile**, stoical or even somnolescent. It is possible that this changed behavior arises from raised levels of β-endorphins in plasma and cerebrospinal fluid (CSF).

Other clinical signs that have been reported in horses with Cushing's disease include persistent lactation and infertility. These effects could be due to abnormal release of prolactin and gonadotropic hormones. Hypertrophic osteopathy has been reported in one pony with a pituitary adenoma. Breakdown of the suspensory apparatus and spontaneous fractures have also been described.

Diagnosis

In many instances, the clinical presentation and physical findings are virtually pathognomonic of equine Cushing's disease. However, some cases may not manifest typical signs such that the diagnosis will require confirmation. The most consistent **laboratory findings** are hyperglycemia, glucosuria, raised plasma liver enzymes, mild anemia, absolute or relative neutrophilia and lymphopenia. Neutrophils may appear hypersegmented. On occasions, blood samples will appear lipemic due to raised levels of plasma triglycerides and cholesterol.

In principle, assessment of endocrine function in equine Cushing's disease is appropriate in order to reach a definitive diagnosis, which may be particularly important prior to initiating treatment. In fact, the usefulness of **endocrine function tests** in horses is compromised to some extent by apparent **wide variation in responses** between individual animals, and a lack of studies that compare different tests or validate the results of tests with pathologic findings. The endocrine investigation is directed toward the assessment of function of the adrenal glands and the pituitary gland.

Adrenal cortical dysfunction may be assessed by the following:

1. Resting plasma levels of cortisol
2. Diurnal rhythm of plasma cortisol
3. Adrenocorticotropin stimulation test
4. Dexamethasone suppression test (DST)
5. Combined DST/ACTH stimulation test
6. Urinary corticoid-to-creatinine ratio
7. Salivary cortisol concentration.

Resting plasma levels of cortisol

Although hyperadrenocorticalism may be accompanied by elevated plasma cortisol concentration, resting plasma cortisol levels are not routinely elevated in horses with Cushing's disease. Therefore, measurement of plasma cortisol concentration alone is not a reliable diagnostic test for the disease.

Diurnal rhythm of plasma cortisol

Loss of the normal diurnal rhythm of plasma cortisol concentration has been described as a screening test for Cushing's disease. A variance of <30% between plasma cortisol concentrations measured in samples collected in the morning and the evening has been suggested to indicate loss of normal diurnal variation. There are, however, few published data to validate this test.

Adrenocorticotropin stimulation test

Administration of exogenous ACTH produces an exaggerated cortisol response in animals with adrenocortical hyperplasia. This test is commonly used to confirm hyperadrenocorticalism in other species. However, in the horse, only about 20% of animals with Cushing's disease actually have adrenocortical hyperplasia. This test is therefore considered unreliable for the diagnosis of equine Cushing's disease. It might, however, be helpful in identifying those cases with adrenocortical hyperplasia (*q.v.*), prior to treatment with drugs that inhibit cortisol secretion from the adrenal cortex.

Dexamethasone suppression test

The dexamethasone suppression test (DST) is considered to be the "**gold standard**" endocrinologic test for the diagnosis of equine Cushing's disease by many workers. There is concern, however, that the administration of dexamethasone could exacerbate or induce **laminitis** (*q.v.*) although this complication appears to be extremely rare.

Several different protocols for the DST have been proposed, and two are summarized in Box 11.2. The overnight protocol is useful as a screening test, but the standard protocol allows more detailed assessment of the degree of loss of pituitary function.

In normal horses, the plasma cortisol will fall to 1 μg/dL or less 19–24 h after the administration of dexamethasone. In affected horses, the cortisol levels show only a slight fall from basal levels.

Although the overnight DST is the most useful diagnostic test for Cushing's disease in practice, both **false positive and false negative results** sometimes occur. Results always need to be interpreted along with clinical and other information.

Box 11.2 Protocols for the dexamethasone suppression test

Overnight protocol

1. Obtain plasma sample for baseline cortisol between 16.00 and 18.00 h
2. Administer dexamethasone IM (40 μg/kg or 2 mg/50 kg)
3. Obtain plasma sample for cortisol estimation at 12.00 h the following day (i.e. 19 h post dexamethasone)

Standard protocol

1. Obtain plasma sample for baseline cortisol at 24.00 h
2. Administer dexamethasone IM (40 μg/kg or 2 mg/50 kg)
3. Obtain plasma samples for cortisol estimation at 08.00, 12.00, 16.00, 20.00 and 24.00 h

Combined DST/ACTH stimulation test

The protocol for this test involves collection of a resting plasma sample and IM administration of 10 mg dexamethasone. A second plasma sample is collected 3 h later, followed by IV administration of 100 IU of synthetic ACTH. A third blood sample is collected 2 h later.

The reason for performing the combined test is to **suppress endogenous cortisol** concentration in cushingoid horses to a value similar to normal horses before ACTH administration, and then to document an exaggerated response to exogenous ACTH. However, the combined DST/ACTH stimulation test is **not recommended**, since it does not allow evaluation of the rebound of cortisol seen in affected horses 24 h after dexamethasone administration. Also, adrenocortical hyperplasia is not a common feature of equine Cushing's disease.

Urinary corticoid–to–creatinine ratio

Measurement of urinary corticoids is commonly undertaken in other species and might be valuable in the assessment of equine Cushing's disease. However, few studies have investigated the value of this test. Currently, a urinary corticoid–creatinine ratio $>20 \times 10^{-6}$ is considered consistent with Cushing's disease.

Salivary cortisol concentration

Salivary cortisol concentration may be useful in the investigation of Cushing's disease, but has received only limited assessment to date.

Insulin resistance

Indirect evidence of hyperadrenocorticalism can be obtained by demonstrating **insulin resistance** on the basis of the following tests:

1. Resting serum insulin concentration
2. Glucose tolerance test
3. Failure to increase plasma insulin in response to glucose loading
4. Insulin tolerance test.

Resting serum insulin concentration

The frequency of **hyperinsulinemia** (*q.v.*) in equine Cushing's disease appears to be greater than the incidence of hyperglycemia. Increased serum insulin levels may be due to the antagonistic metabolic effects of excess circulating cortisol, or due to secretory effects of increased CLIP levels. Measurement of fasting serum insulin concentration can therefore be used as a **screening test** for Cushing's disease.

Although hyperinsulinemia ($>57\ \mu U/mL$) is commonly present, it is not specific for Cushing's disease and can occur for other reasons, including **peripheral Cushing's syndrome** (excessive cortisol activity in peripheral tissues due to altered activity of 11-β-hydroxysteroid dehydrogenase, *q.v.*). The measurement of serum insulin concentration should not, therefore, be used as the sole test to confirm Cushing's disease.

Glucose tolerance test and serum insulin response to glucose challenge

The protocols for glucose tolerance tests are described in the section on diabetes mellitus (*q.v.*). Many of the limitations that affect the sensitivity and specificity of single measurement of serum insulin also affect these tests.

Insulin tolerance test

The insulin tolerance test is performed by administering 0.05 U/kg crystalline insulin IV; blood samples for glucose estimation are obtained before insulin challenge, and at 15 min, 30 min, 1 h, 2 h and 4 h post challenge. In the normal horse the plasma glucose falls by 30–45% at 15 min, 60% at 30 min, and returns to normal by 2 h. Failure to lower resting hyperglycemia by administration of exogenous insulin is expected in Cushing's disease. However, caution should be exercised when interpreting insulin tolerance test results because **pony breeds** are known to be inherently **less sensitive to insulin** and this may be further exacerbated by the presence of obesity and/or laminitis.

Pituitary gland dysfunction

Pituitary gland dysfunction is best demonstrated by:

1. Thyrotropin-releasing hormone (TRH) stimulation test
2. Combined DST/TRH stimulation test
3 Plasma ACTH concentration.

TRH stimulation test

Plasma samples for cortisol estimation are obtained before and 15, 30, 60, 90 and 120 min after IV administration of 1 mg TRH. Although TRH normally causes release of thyroid-stimulating hormone and prolactin, it is known that when given to animals with pituitary disorders it gives rise to elevations in plasma cortisol via release of ACTH.

In equine Cushing's disease, there is a consistent increase in plasma cortisol soon after TRH administration that is not seen in normal animals. A 30% increase in plasma cortisol concentration between 15 and 90 min after administration of TRH is considered supportive of Cushing's disease. However, interpretation of the results can be complicated if the initial basal cortisol concentration is high.

Combined DST/TRH stimulation test

The combined DST/TRH stimulation test is used to try to overcome the problem of variable initial cortisol concentration that can complicate interpretation of the TRH stimulation test. Dexamethasone (40 μg/kg) is administered 3 h before TRH to suppress cortisol concentration to similar values in both Cushing's-affected and normal horses. Cortisol concentration is measured before and 30 min after TRH administration. Horses with Cushing's disease show an increase in cortisol, whereas normal horses do not.

Plasma ACTH concentration

Horses with Cushing's disease usually have elevated amounts of ACTH in the pars intermedia and release increased amounts of ACTH into the circulation.

Measurement of plasma concentration of ACTH can therefore be helpful diagnostically. However, many of the assays currently used to measure ACTH have not been validated for equine plasma. In addition, sample handling is difficult. ACTH can be adsorbed onto glass and can be degraded by proteolytic enzymes in whole blood and plasma. Therefore, collection into plastic tubes prefilled with enzyme inhibitors, rapid separation from red blood cells, and freezing the plasma prior to shipment are recommended. The use of a laboratory that runs an assay that has been validated as specific for ACTH in equine plasma is recommended.

An alternative approach to confirming pituitary dysfunction is by measurement of plasma levels of other pituitary peptides such as β-END or MSH. However, at present, assays for these substances are not widely available in clinical practice.

Diagnostic imaging

Diagnostic imaging using computed tomography (CT) or magnetic resonance imaging (MRI) has been described in horses with Cushing's disease, but the sensitivity and specificity of the techniques are currently unknown. In view of the fact that some horses with pituitary pars intermedia dysfunction do not have gross enlargement of the pituitary gland, it seems unlikely that these imaging techniques will be useful for routine diagnosis. They may, however, become important if surgical treatment should be considered.

Definitive confirmation of equine Cushing's disease is only possible by post mortem identification of a pituitary tumor together with hyperplasia of the adrenal cortices. The tumors are usually clearly delineated white or yellow masses within the pars intermedia with variable compression of the adjacent pars distalis, hypothalamus or optic chiasm. Other pathologic features that may be present include hepatopathy, laminitis and septic foci. Very rarely, clinical signs might arise from a primary adrenal disease such as an adrenal tumor, but the strict classification of such an animal would be equine Cushing's syndrome.

Treatment

Management of cases is affected by the severity of signs and financial considerations. For example, in some animals there may be unacceptable **pain** from laminitis or marked debilitation from protracted muscle wasting such that euthanasia is the humane decision. Other cases may be managed by **supportive therapy** such as treating respiratory or skin infections, maintaining a high plane of nutrition, and hoof care for mild laminitis (*q.v.*). **Clipping** to remove long hair may be beneficial. Such conservatively managed cases may have a life of acceptable quality for several years.

Successful treatment, in terms of diminution of clinical signs, has been achieved by medication with several compounds that modify the secretion of the active peptide substances of the pituitary tumor. Drugs that have been used for this purpose include cyproheptadine, bromocriptine and pergolide. Drugs that target steroidogenesis (such as trilostane) have also been used.

Cyproheptadine

Oral **cyproheptadine**, a serotonin antagonist that also has anticholinergic and antihistaminic effects, was one of the first drugs used to treat equine Cushing's disease. Serotonin has been shown to be a potent secretagogue of ACTH in laboratory animals. The suggested dosage regimen is 0.25 mg/kg s.i.d. for 8 wk increasing to 0.50 mg/kg divided twice daily for a further 4–8 wk if no improvement is seen. Although this treatment has been reported to result in improvement in some clinical cases, the response appears to be variable and it can be difficult to separate clinical improvement due to the drug from that attributable to improved management and nutrition.

Bromocriptine mesilate

Since loss of dopaminergic innervation appears to be important in the pathogenesis of pituitary pars intermedia dysfunction, treatment with **dopaminergic agonists** is a rational approach. Beneficial effects have been obtained using oral, subcutaneous, IM or IV **bromocriptine mesilate** (5–100 mg b.i.d.), which is a dopaminergic drug. However, the bioavailability of this drug is low, and it is not readily available.

Pergolide

The **therapy of choice** is probably oral medication with the **dopamine agonist, pergolide** (0.01 mg/kg daily). Clinical improvement is generally more apparent than normalization of blood glucose concentration or endocrinologic test results. A low-dose regimen (0.002 mg/kg PO q 24 h) (1 mg/500 kg horse) appears to be effective in approximately 80% of cases.

If no improvement is noted within 4–8 wk of "low-dose" pergolide treatment, the daily dose can be increased by 0.002 mg/kg monthly up to a total dose of 0.01 mg/kg. Side effects of the drug can include anorexia, diarrhea and colic, but these are more likely at the higher dose rates. The drug is an ergot alkaloid and may have vasoconstrictive effects; this has led to concern that it might exacerbate laminitis, although this problem has not been described in clinical cases.

Concurrent administration of pergolide and cyproheptadine (0.3–0.5 mg/kg) might be beneficial in refractory cases; however, few data supporting this approach are available.

Trilostane

Trilostane is a competitive inhibitor of 3-β-hydroxysteroid dehydrogenase. This drug has been used in an attempt to block endogenous cortisol production by the adrenal gland, and has been demonstrated to reverse both the clinical signs and abnormal endocrinologic test results in one series of equine Cushing's disease cases. The recommended dose rate is 0.4–1.0 mg/kg once a day given in the feed.

These treatments are expensive and there is no regression of the pituitary neoplasia such that lifelong medication is required. Response to treatment, by improvement of clinical and laboratory findings, should be evident within about 4 wk. Nutritional supplementation and complementary therapies (such

as acupuncture, homeopathy and herbal remedies) are commonly employed. Both magnesium and chromium supplementation have been advocated.

PERIPHERAL CUSHING'S DISEASE ("EQUINE METABOLIC SYNDROME")

The term "peripheral Cushing's disease" refers to the syndrome of **mature, adult horses** that develop **laminitis in the face of obesity**. Abnormal regulation of glucocorticoids at the cellular level in the laminae of the feet may play an important role in this condition. By comparison with similar human diseases, the term "**equine metabolic disease**" is probably a more appropriate term.

Obesity results in **insulin insensitivity**, also known as insulin refractory state. Multiple metabolically active factors are secreted by adipocytes and exert their actions locally through paracrine and autocrine mechanisms, and systemically through endocrine mechanisms. These factors inhibit the action of insulin in central (hepatic) and peripheral (skeletal muscle and adipocytes) tissues. Inhibited insulin responsiveness leads to the development of **glucose intolerance**. Hyperglycemia that occurs as a result of insulin insensitivity can have a toxic effect on certain tissues, including endothelial cells, and this may play a role in the development of laminitis (*q.v.*).

Horses affected by the metabolic syndrome are usually obese and tend to be aged between 8 and 18 yr. These horses are commonly described as being "easy-keepers". Affected horses may present with signs of laminitis, or may have evidence of chronic subclinical laminitis (convex sole, divergent hoof lines, widening of the white line).

Diagnosis of equine metabolic syndrome is based on the characteristic clinical signs, ruling out other endocrinopathies with specific tests, and demonstrating **hyperinsulinemia**. Hyperinsulinemia in the presence of a normal or slightly elevated blood glucose concentration in the fasted animal supports the diagnosis of peripheral Cushing's syndrome. Serum free fatty acid levels are also commonly elevated. Glucose intolerance can be confirmed using an intravenous glucose tolerance test.

Treatment of this syndrome consists of increasing physical activity and reducing body weight by dietary modification. Although thyroid supplementation has been widely used in the management of obesity-associated laminitis, there is no evidence to support the concept that hypothyroidism occurs in this condition.

THE ADRENAL MEDULLA

INTRODUCTION

The adrenal medulla, like the sympathetic neurons, is derived from ectodermal cells of the neural crest. These chromaffin cells, so called because they stain brown with chromium salts, have a central position in the gland. The adrenal medulla secretes the **catecholamines**: noradrenaline (norepinephrine), adrenaline (epinephrine) and dopamine. Compared with other species,

relatively little is known about adrenal medullary function and dysfunction in the horse.

The biologic effects of catecholamines released into the circulation depend on the amount fixed in the tissue, which is related to its blood supply and sympathetic innervation, and also on the sensitivity of the tissue receptor binding sites. α-Adrenergic receptors cause smooth muscle contraction, for example in the skin and dilator muscles of the iris. The β-adrenergic receptors mediate smooth muscle relaxation, for example in the bronchi. Adrenaline/epinephrine acts on both α- and β-receptors, whereas noradrenaline/norepinephrine acts mainly on α-receptors.

Of the three major catecholamines, it is most appropriate to measure adrenaline/epinephrine in cases of suspected **adrenal medullary dysfunction**. However, care must be exercised in the interpretation of catecholamine data due to **physiologic variability**. Stressful conditions and acidosis or hypoxia will result in increased catecholamine levels.

CATECHOLAMINE LEVELS IN THE NEONATE

It has been suggested that premature foals have depressed adrenocortical and medullary function, but wide variations in catecholamine levels are seen in the newborn foal and these variations are probably related more to the degree of **stress at parturition** than to the maturity of the foal.

There is an inverse relationship between plasma catecholamine levels and blood pH around the time of birth, although hypoxemia appears to be more important than low blood pH in stimulating adrenal medullary secretion. The catecholamine concentrations are higher in stressed foals than in non-stressed foals. The proportions of adrenaline/epinephrine and noradrenaline/norepinephrine vary with maturity of the foal at birth; in full-term foals, adrenaline/epinephrine predominates, whereas in premature foals noradrenaline/norepinephrine predominates.

CATECHOLAMINE LEVELS IN THE ADULT

High adrenaline/epinephrine levels are expected to occur during stressful events. For example, elevated levels (4–6 ng/mL) have been recorded during second stage labor, but these subsequently fall to 1–3 ng/mL soon after delivery.

Elevated levels of plasma catecholamines (along with ACTH and cortisol) have been detected in cases of **grass sickness** (*q.v.*). These levels are higher than those seen in other cases of colic (*q.v.*), but the precise role of sympathoadrenal activation in grass sickness is unknown.

PHEOCHROMOCYTOMAS

Pheochromocytomas are **tumors of the chromaffin cells** of the adrenal medulla. A small number of cases have been reported in aged horses, usually as an incidental post mortem finding. The tumors may be functional (i.e. they secrete excessive quantities of catecholamines) or non-functional. **Functional pheochromocytomas** result in increased catecholamine production which in turn produces varied clinical effects including anxiety, sweating, trembling, ileus, tachycardia, tachypnea and mydriasis (with intact pupillary light

reflex). **Compromised renal function** and acidosis, resulting from the vasoconstrictive action of noradrenaline/norepinephrine, may also result. Myocardial degeneration secondary to hypertension and cardiovascular collapse are common terminal events in human patients.

A few cases of functional pheochromocytomas have been recorded in horses. Most of these have had **non-responsive colic** as the predominant presenting clinical sign. The signs are generally acute and rapidly progressive, and may be confused with those seen in other more common acute conditions including intestinal obstruction, rhabdomyolysis, acute laminitis and impending colitis (*q.v.*). One horse had no other sign except chronic, watery diarrhea. Increased hematocrit and a "stress leukogram" may be identified. Azotemia, metabolic acidosis, hyperglycemia and hyperkalemia are the most consistent clinicopathologic findings.

Documentation of high serum concentrations of catecholamines or their metabolites in urine is difficult to achieve because of the labile nature of these substances and technical difficulties involved with their measurement.

Attempted treatment of pheochromocytomas in the horse has not been recorded; adrenalectomy might be attempted, but surgical access and the risk of fatal arrhythmias would make this treatment extremely difficult.

THE OVARY AND REPRODUCTIVE HORMONES IN THE MARE

INTRODUCTION

The ovaries (*q.v.*) of the mare are bean-shaped organs of variable size that contain the female gametes. The ovary is an intraperitoneal structure that is attached to the body wall by a fold of peritoneum. The ovarian stroma is composed of spindle-shaped cells and intercellular substance with the stroma forming a tough capsule that encloses the ovary except at the ovulation fossa.

The **immature ovary** contains many thousands of primordial follicles, each containing a primordial germ cell (oogonium). Some of the oogonia develop into primary oocytes that undergo the first stage of meiosis, but they do not complete meiosis until after puberty when the follicle is mature. Most of the primary follicles degenerate and only a small percentage will reach maturity and release their ova.

Follicle development involves a change of the epithelial cells surrounding the oocyte from flat to stratified columnar, an increase in the size of the oocyte, and the accumulation of fluid in a cavity lined by the follicular cells. The stroma around the follicle also becomes organized into a membrane (theca). The mature follicle bursts at the ovulation fossa and discharges its contents toward the **Fallopian tube**. Hemorrhage occurs in the center of the collapsed follicle, and the clot is invaded with follicular or granulosa cells, which, together with the thecal cells, form the **corpus luteum**.

Some 75–80% of mares demonstrate **seasonal polyestrous behavior**, whereas 20–25% demonstrate estrous cycles all year round. The distinct seasonal effects on the estrous cycle can be categorized as:

1. The ovulatory phase: the period from first ovulation in the spring until the last ovulation in the autumn

2. Anestrus: the period of ovarian inactivity during winter
3. The transitional phase: the period of irregular or prolonged estrus receptivity in early spring or late autumn.

THE ESTROUS CYCLE

Estrus (*q.v.*) is the period of sexual receptivity. Estrus in the mare lasts on average for **5–7 days** with ovulation occurring 24–48 h before the end of estrus. The cycle is, however, highly variable. Growth of the pre-ovulatory follicle is controlled by the pituitary gonadotropins, **follicle-stimulating hormone (FSH)** and **luteinizing hormone (LH)**.

Plasma concentrations of FSH peak twice during the cycle at 10–11 day intervals. FSH secretion is stimulated by increased day length and suppressed by **inhibin** secreted by developing follicles. The second FSH peak, which occurs during mid to late diestrus, stimulates growth and development of the pre-ovulatory follicle. The final growth and maturation of the pre-ovulatory follicle is associated with the increase in plasma concentrations of LH in early estrus. At this time most of the remaining follicles become atretic and regress. It is thought that this process of follicular selection may occur due to the production of inhibin or inhibin-like substances by the dominant follicle, which will decrease pituitary release of FSH. However, in some cases other large follicles that are present at the time of ovulation may ovulate either within 24 h or later in diestrus.

Estrous behavior (*q.v.*) is stimulated by the high circulating concentrations of estradiol-17β from the pre-ovulatory follicle. The **estradiol peak**, which occurs approximately 2 days prior to ovulation, is thought to contribute to the final maturation of the pre-ovulatory follicle by stimulating further LH release. LH reaches its maximum level at, or shortly after, the time of ovulation and concentrations then decrease slowly over the next 5 days. The first peak of FSH also occurs near the end of estrus and coincides with the LH peak.

Development of the **corpus luteum** (*q.v.*) starts immediately after ovulation. Elevated concentrations of **plasma progesterone** are detected within 24 h and estrous behavior ceases. Plasma concentrations of progesterone peak after approximately 6 days and then plateau. Plasma LH levels are low between days 6 and 15 after ovulation because of the negative feedback action of progesterone on the hypothalamus, causing suppression of gonadotropin-releasing hormone (GnRH).

At day 14 or 15 of diestrus the corpus luteum undergoes **luteolysis** in response to release of **prostaglandin (PG) $F_{2\alpha}$** from the endometrium. Luteolysis results in a rapid decline in plasma progesterone concentrations. This decrease in circulating progesterone removes negative feedback on the pituitary and hypothalamus, plasma concentrations of LH increase, and the mare returns to estrus.

SYNCHRONIZATION OF ESTRUS

Prostaglandins

Mares are responsive to the luteolytic effect of $PGF_{2\alpha}$ over only about 30% of the estrous cycle, therefore prostaglandins are **relatively ineffective** at synchronizing estrus in mares. In practice it has been found that two injections of $PGF_{2\alpha}$ at

an interval of 14–15 days are optimal for synchronization in the mare. Approximately 90% of mares will show heat by 6 days after the second injection.

Progestogens

Progestogens (*q.v.*) (e.g. 0.044 mg/kg **altrenogest** daily PO) may be administered to mares for a period of 15 days (i.e. slightly longer than the normal lifespan of the corpus luteum). Estrus will be delayed until after the end of treatment. Most mares demonstrate signs of estrus within 1–5 days following the last treatment. However, progestogens do not suppress FSH secretion and therefore follicular development and even ovulation may occur during treatment. Thus $PGF_{2\alpha}$ should be administered at the end of progestogen therapy to lyse any corpora lutea that may be present.

Improved control over the cycle can be obtained by using **estradiol** together with **progestogens** because estradiol suppresses release of FSH in the mare. It also seems that progestogens plus estrogens cause greater inhibition of LH than progestogens alone. Progesterone and estradiol are usually given for 10 days (e.g. progesterone in oil 150 mg/day IM, and 17-β-estradiol 10 mg/day IM) and $PGF_{2\alpha}$ is administered at the end of treatment. Follicles predictably ovulate 8–10 days later. Administration of **human chorionic gonadotropin** when the pre-ovulatory follicle reaches 35 mm further improves synchronization by inducing ovulation 36–48 h later.

PREGNANCY

In pregnant mares (*q.v.*), the early conceptus inhibits the release of $PGF_{2\alpha}$ from the endometrium and the primary corpus luteum persists. Numerous follicles develop on the ovaries during the first 3 mo of pregnancy. It is thought that this follicular activity is a result of the continuation of maternal FSH release at 10 day intervals. Progesterone concentrations reach a peak around Day 25 of pregnancy then decrease until Days 40–50, when progesterone again rises to a peak between Days 80 and 90.

The rise in progesterone between Day 40 and Day 90 is associated with the formation of **secondary corpora lutea** on the ovaries. These structures form from ovulation or luteinization of follicles as a result of the luteotropic effect of **equine chorionic gonadotropin** (eCG) produced by the endometrial cups, formed by the invasion of the endometrium by chorionic girdle cells of the trophoblast. Endometrial cup formation begins at Day 25. Detectable concentrations of eCG are present in plasma by Day 40 of gestation. Peak concentrations are reached between Days 55 and 65 and then concentrations decline and are undetectable by Day 150. After regression of the endometrial cups, concentrations of progesterone decrease and remain low between 150 and 300 days of gestation. During the last month of gestation, concentrations of progesterone increase until parturition.

The **placenta** (*q.v.*) starts to secrete progestogens, progesterone and progesterone metabolites around Day 50 and is the sole source of progestogens after the corpora lutea have regressed. Between Days 35 and 40, circulating concentrations of conjugated estrogens increase. A second major increase occurs around Days 70–80 and concentrations finally peak between Days 210 and 240

of gestation. The maternal ovaries appear to be the main source of conjugated estrogens before Day 70. After Day 70, the placenta synthesizes estrogens using steroid precursors provided by the fetal gonads. From Day 200, concentrations of conjugated estrogens decline.

The placenta is also the primary source of **relaxin**. Relaxin is first detected in plasma around Day 70 and increases to initial peak concentrations between 150 and 180 days. After 240 days, relaxin increases progressively until parturition. In the mare, relaxin appears to work with progesterone in maintaining pregnancy and preventing spontaneous uterine contractions. Relaxin levels return to baseline after expulsion of the fetal membranes.

High maternal concentrations of **oxytocin** trigger the rapid increase in concentrations of $PGF_{2\alpha}$ that are present at parturition. These high concentrations of oxytocin and $PGF_{2\alpha}$ may then provide the hormonal stimuli for the powerful uterine contractions that occur during second stage labor.

Hormonal diagnosis of pregnancy

Equine chorionic gonadotropin

Tests are accurate between Days 45 and 100 of pregnancy. A limitation of this test is that eCG is a product of the endometrial cups and therefore is secreted even though fetal death could have occurred.

Estrone sulfate

Slight elevations can be measured after Day 40 but large increases occur after Day 60–70. High circulating concentrations are present only in pregnant mares with normal fetal development.

HORMONAL PROBLEMS OF MARES

Absence of estrus

Four clinical syndromes can result in failure of the mare to manifest estrus: silent estrus, prolonged diestrus, granulosa cell tumors and seasonal anestrus (*q.v.*).

Silent estrus

Mares will occasionally fail to show estrus if there is an unusually short period between luteolysis and ovulation. This can arise if a **large follicle** present at the end of diestrus ovulates shortly after luteolysis.

If $PGF_{2\alpha}$ has been administered to induce luteolysis, ovulation may occur so soon after treatment that the formation of the new corpus luteum masks lysis of the original corpus luteum and can lead to the clinical impression that luteolysis has failed. It is important therefore to **examine follicle development** on the ovaries at the time of $PGF_{2\alpha}$ treatment. Rarely, mares with normal luteal and follicular phases will also fail to show estrus.

Prolonged diestrus

Prolonged diestrus (*q.v.*) can occur in bred and unbred mares and is caused by failure of luteal regression at the normal time in non-pregnant mares. Up to

25% of cycles may be affected and luteal function may persist for 2 mo or more. It is believed that the endometrium of these mares may fail to release $PGF_{2\alpha}$ although in most cases no uterine pathology has been specifically implicated.

In mares with severe **chronic endometrial degeneration** and **pyometra** (*q.v.*), the endometrium is unable to produce adequate concentrations of $PGF_{2\alpha}$ and the corpus luteum persists. However, probably the most common cause of prolonged diestrus is the occurrence of a **diestrus ovulation** on Day 9–14. When $PGF_{2\alpha}$ is released by the endometrium (Day 14 diestrus) the developing corpus luteum is <5 days old and is unresponsive to lysis by $PGF_{2\alpha}$. This newly formed corpus luteum will persist for another 14 days.

Another cause of prolonged diestrus is **early embryonic death** (*q.v.*). The presence of a conceptus within the uterus will inhibit release of $PGF_{2\alpha}$, even if the embryo is lost a few days later, and results in prolongation of the lifespan of the corpus luteum.

Diagnosis is based on history and the stimulatory effect of progesterone on the tone of the uterus and cervix. The condition is treated by IM administration of $PGF_{2\alpha}$. The mare will return to estrus in 3–4 days.

Granulosa cell tumor

Granulosa cell tumor (*q.v.*) is the most common **ovarian neoplasm** in the mare. One of the first palpable changes is an enlarged ovary with loss of the ovulation fossa. Steroid hormones and/or inhibin produced by the tumor have an inhibitory feedback on the hypothalamus and pituitary. The opposite ovary regresses and is typically palpable as hard, small and inactive. One of the behavioral manifestations of a granulosa cell tumor may be **anestrus**. Alternatively, affected mares may exhibit continuous estrus or masculine behavior.

Granulosa cell tumors are diagnosed by history, behavior, rectal palpation, ultrasonography and hormone analysis. Affected mares that show masculine behavior may have elevated plasma testosterone concentrations (>40–100 pg/mL). However, elevated plasma testosterone levels are present in only about 50% of affected mares. Elevated concentrations of inhibin (>1 pg/mL) are commonly present. Mares demonstrating persistent signs of estrus may have elevated concentrations of plasma estrogen.

Granulosa cell tumors (*q.v.*) are usually benign and **surgical removal** of the affected ovary usually allows the other one to resume normal cyclical activity and restores fertility. Rare cases of bilateral granulosa cell tumors have been described.

Seasonal anestrus

It is thought that during the winter there is a **decrease in secretion** of gonadotropin-releasing hormone (GnRH). As day length increases, GnRH release rises, resulting in increased concentrations of circulating FSH and stimulation of follicular development. Final follicular development and ovulation do not occur until estrogen production is high enough to cause feedback on the hypothalamus and pituitary resulting in LH release. This transitional period may last for 2 mo. A number of treatments have been reported to hasten the onset of cyclical activity:

1. **Progestogens** such as **altrenogest** (0.044 mg/kg) administered orally for 10 days will induce ovulation 7–13 days later. This treatment works best when

follicles of at least 20 mm in diameter are present on the ovaries. It is likely that treatment with progestogens primes behavioral centers in the CNS and allows substantial release of LH when they are withdrawn. It is possible that a combination of progesterone and estrogen promotes the onset of cyclicity more efficiently than progestogens alone, because estradiol enhances the FSH response to GnRH in anestrus mares.

2. **Artificial lighting:** 16 h light per day are required to speed up the cycle. The light may be provided by one 200 W incandescent lamp or two 40 W fluorescent tubes per average 3.7 m × 3.7 m loose box. Ovulation is stimulated 8–10 wk after the onset of treatment.
3. **GnRH:** A synthetic GnRH agonist (**deslorelin**) can be administered as a subcutaneous pellet to advance the first ovulation of the year by approximately 18 days. A single implant placed every other day for up to 6–8 doses may be needed.

To aid in diagnosis of the cause of **estrus failure** blood samples can be collected on five occasions at 5-day intervals and assayed for **progesterone concentrations**. During a normal cycle, progesterone concentrations will be low in two of the samples and high in three of the samples. In **persistent diestrus** progesterone concentrations may be high in all five, and during seasonal anestrus progesterone concentrations will be consistently low.

Excessive signs of estrus

Intermittent or **continuous estrus** is most common in mares during the transitional period. It is probably caused by estrogens secreted by successive waves of developing ovarian follicles in the absence of ovulation. After the first ovulation of spring, cyclicity tends to continue normally. Administration of **progesterone** (*q.v.*) tends to hasten the onset of cyclical activity.

Oral or injectable progestogens are also commonly used to suppress estrus in mares during **performance events**. Altrenogest is now permitted by the Fédération Equestre Internationale (FEI) (*q.v.*) under its Veterinary Regulations but can only be given to mares at the manufacturer's recommended dose and on completion of the appropriate form.

A **granulosa cell tumor** (*q.v.*) of the ovary can cause signs of excessive estrus or **nymphomania** due to production of **estradiol** by the tumor. During seasonal anestrus mares may exhibit sexual receptivity. In general, exhibition of estrus behavior in the mare appears to be more dependent on the absence of the suppressive effects of progesterone than on the presence of high concentrations of estrogen.

Male-type behavior

Granulosa cell tumors can present with a history of male-type behavior. In these cases plasma concentrations of **testosterone** (*q.v.*) are generally elevated. Removal of the tumor results in reversion to normal sexual behavior. Approximately 5% of mares exhibit aggressive behavior between 4 and 6 mo of gestation. This behavior is thought to result from the effects of androgens produced by the feto-placental unit.

Progesterone deficiency in pregnant mares

Oral progestogens are now commonly used to support pregnancies in mares that are believed to have **deficient luteal function**. However, it is likely that premature luteolysis is usually the result of premature release of level $PGF_{2\alpha}$ rather than inadequate luteal function. Mares can maintain pregnancy with circulating concentrations of progesterone <2 ng/mL.

It has been reported that **stress** from acute clinical conditions such as colic (*q.v.*) may precipitate abortion in mares with marginal placental production of progestogens and it may be advisable to administer progestogens (11–44 mg **altrenogest** PO s.i.d.) to these mares. However, it should also be considered that mares with marginal progestogen production may also suffer from other signs of abnormal placental function such as poor gas and nutrient exchange. During early pregnancy (≤55 days) endotoxemia (*q.v.*) can cause an immediate release of $PGF_{2\alpha}$, which can lyse ovarian corpora lutea. Pregnancy loss can be avoided by treating these mares with progestogens.

THE TESTIS AND REPRODUCTIVE HORMONES IN THE STALLION

INTRODUCTION

During sexual maturity, the testis (*q.v.*) performs two distinct but related functions: spermatogenesis and androgen production. **Spermatogenesis** takes place in the seminiferous tubules, which are abundantly coiled and constitute 95% of the testis volume. The Leydig (interstitial) cells occur in clumps between the seminiferous tubules and are involved in **androgen production**.

REPRODUCTIVE HORMONES IN THE STALLION

The Leydig cells of the testis produce **testosterone** under the influence of LH from the anterior pituitary gland. The testosterone is delivered to both the local testicular environment and the systemic circulation. High concentrations of testosterone are necessary for maintenance of **spermatogenesis** in the stallion. FSH stimulates Sertoli cells in their role in germ cell development and in production of **inhibin, androgen-binding protein and activin**.

Inhibin and activin feed back negatively on the hypothalamus and pituitary to inhibit and promote, respectively, FSH release. **Androgen-binding protein** binds to both dihydrotestosterone and testosterone, and provides a high concentration of both of these hormones locally around the germ cells.

FSH and LH secretion is stimulated by GnRH (released by the hypothalamus) and is inhibited by estradiol and testosterone. Increasing day length has a positive influence on secretion of gonadotropins. Because of increased circulating gonadotropin concentrations, testosterone concentrations also increase in spring. The stallion testes also secrete high concentrations of estrone sulfate. However, circulating concentrations of estrogen are not influenced by season and are constant throughout the year.

There appears to be little correlation between circulating concentrations of testosterone and **fertility in stallions**. Some stallions with **low libido** (*q.v.*)

have low concentrations of LH in plasma. However, some stallions with vigorous libido and good seminal characteristics may also have low LH concentrations. Preliminary data suggest that GnRH treatment may be beneficial in some cases of infertility in stallions.

CRYPTORCHIDISM

Approximately 50% of supposedly castrated horses presented with male behavior are **cryptorchids** (*q.v.*) and the ability to differentiate between castrates and cryptorchids is therefore important.

In horses <2–3 yr of age, and in donkeys of any age, a **human chorionic gonadotropin (hCG) stimulation test** is recommended for diagnosis. In older horses, a single blood sample for estrone sulfate estimation is adequate. The hCG stimulation test is performed by administering an IV dose of 6000–10 000 IU hCG to the animal; concentrations of testosterone are measured in paired serum samples collected before and 60 min after administration of hCG. In cryptorchids, basal testosterone concentrations are usually >100 pg/mL and the level will increase up to 3- or 4-fold, but geldings have low basal levels (<40 pg/mL) that do not respond to hCG treatment. It has been reported that doubtful results are recorded in 11% of cases.

Estrone sulfate determination is helpful in horses >2–3 yr of age. Cryptorchids have concentrations >400 pg/mL, compared with <100 pg/mL in geldings. This assay has been reported to produce doubtful results in only 2% of cases when performed in horses that are at least 3 yr old. In younger animals, the hCG stimulation test should be used.

THE THYROID GLAND

INTRODUCTION

The thyroid gland is found on the ventral aspect of the neck, loosely attached to the anterior trachea. It consists of a pair of lobes situated on each side of the trachea adjacent to the larynx. These lobes are connected by an isthmus running over the ventral surface of the trachea. The isthmus is a narrow structure and may only be represented by a fibrous band.

The major function of the thyroid gland is the production of **thyroid hormones**. Thyroid hormone secretion is dependent on adequate blood concentrations of **thyroid-stimulating hormone (TSH)** (thyrotropin) and **iodine**. Follicular cells take up iodide from the circulation for incorporation into **thyroglobulin**. This is subsequently broken down by lysosomal enzymes to **tri-iodothyronine (T3)** and **thyroxine (T4)**, which are stored in the colloid of the follicles prior to release into the circulation. The majority of circulating thyroid hormone is bound to blood constituents including thyroid hormone-binding protein and albumin. Unbound ("free") hormone is biologically active.

Thyroid hormones exert effects on almost all body tissues so that manifestations of thyroid dysfunction are **extremely varied**. Central nervous tissues, including the hypothalamus, monitor blood concentrations of thyroid

hormones, particularly T4. Low thyroid hormone concentration elicits a rise in thyrotropin releasing hormone (TRH) secretion by the hypothalamus. This stimulates release of TSH from the adenohypophysis.

Thyroid disease in the horse is rare but may be divided into a number of conditions.

GOITER

Dietary iodine is essential for the production and release of thyroid hormones. In conditions of too much or too little dietary iodine, retention of thyroxine leads to **gross enlargement** of the thyroid gland (goiter). Clinically, goiter due to **excess iodine** is more common and is usually associated with the use of **iodine-rich feed supplements** (especially seaweed-derived preparations). It is easily corrected by reducing the dietary intake. **Neonatal goiter** has been associated with feeding of **seaweed supplements** to the pregnant mare.

Goiter caused by lack of iodine is rare due to the widespread use of iodized salt in commercial feeds and feed supplements. It may occur with the ingestion of goitrogenic substances, especially *Brassica* (*q.v.*).

Goiter in either form is most commonly seen in neonates and has been associated with stillbirth, the birth of weak foals, and foals with forelimb contracture.

HYPOTHYROIDISM

Hypothyroidism has only been recently recognized in the horse with the availability of thyroid hormone assays and the use of thyroid function tests. Clinical signs are varied since thyroid hormones exert widespread effects on body tissues. Old and young horses are most commonly affected. Clinical syndromes in the foal include prematurity, poorly ossified or malformed carpal and tarsal bones, forelimb contracture, ruptured common digital extensor tendons, mandibular prognathism and angular limb deformities (*q.v.*). In the adult horse clinical signs may include dullness, bradycardia, myxedema, agalactia, exercise intolerance and variable appetite. Other reported signs include myopathy in racing animals, and cutaneous signs, particularly alopecia.

Hypothyroidism may be defined as primary, secondary or tertiary. **Primary hypothyroidism** refers to a disease of the thyroid gland itself. **Secondary hypothyroidism** results from reduced secretion of TSH from the adenohypophysis. **Tertiary hypothyroidism** results from inadequate TRH release from the hypothalamus.

Although there are no documented cases of primary hypothyroidism resulting from iodine deficiency in adult horses, this could potentially cause goiter and hypothyroidism. Likewise, immune-mediated thyroiditis has not been definitively diagnosed in the horse. Most cases of primary hypothyroidism are idiopathic. These cases are rare.

Diagnosis of hypothyroidism is based on **dynamic function tests**. Thyroid hormone assays should be performed at a **specialized endocrine laboratory** and the patient needs to be maintained free of all medication for at least 10 days prior to the test. Baseline levels of serum T3 and T4 are measured and then repeated following the administration of **TSH**. A protocol for the TSH

Table 11.2 Expected responses to TSH stimulation test using IV bovine TSH administered IM in normal horses

Time	T3	T4
Baseline	See laboratory normals (0.09 ± 0.02 μg/100 mL)	See laboratory normal (1.8 ± 0.8 μg/100 mL)
3 h	3–5 × baseline	1–2 × baseline
6 h	1–3 × baseline	2 × baseline

stimulation test, together with expected normal responses, is shown in Table 11.2. In primary hypothyroidism a reduced response of T3 and T4 is expected.

If persistently low resting levels of T3 and T4 are found despite a normal TSH stimulation test result, then a **TRH stimulation test** may be used to confirm a state of secondary hypothyroidism, i.e. due to underlying pituitary dysfunction. Where exogenous (bovine) TSH is not commercially available, the routine diagnosis of hypothyroidism will depend on measurement of serum T3 and T4 levels, and the TRH stimulation test. The TRH stimulation test is performed by administering IV 1 mg TRH and collecting blood samples after 2 and 4 h. In normal healthy horses, T3 and T4 concentrations are twice that of baseline after 2 and 4 h respectively. The test can be used to demonstrate hypothyroidism due to abnormal hypothalamus–pituitary–thyroid axis function.

Treatment for primary hypothyroidism involves replacement therapy with oral **levothyroxine sodium** at 10–20 mg/day or iodinated casein at 5 g/day. T4 levels should be monitored 1 wk after treatment commences and the dose adjusted to maintain the T4 level within the normal range.

Low thyroid hormone levels can also occur as a result of suppression of TSH formation and/or TRH-induced TSH release. Causes include **phenylbutazone therapy**, high energy diets, high protein diets, glucocorticoid administration, etc. Phenylbutazone (*q.v.*) is highly protein bound, and it displaces thyroid hormone from carrier proteins. The increased amount of free hormone exerts a negative effect on the thyroid hormone feedback pathway and inhibits the hypothalamus–pituitary–thyroid axis.

SICK EUTHYROID SYNDROME

Sick euthyroid syndrome is recognized in other species, and probably also occurs in the horse. It is characterized by low thyroid hormone levels associated with severe non-thyroid disease. It is believed to be a protective function to preserve calories in catabolic states.

HYPERTHYROIDISM

There are very few well-documented reports of equine hyperthyroidism. Clinical signs include thyroid gland enlargement, tachycardia and arrhythmias, emaciation despite normal appetite, restlessness and excitement. The **diagnosis** is based on the clinical signs and elevated resting levels of T3 and T4.

Treatment is aimed at limiting thyroid hormone synthesis with "thyrostatics" such as **carbimazole**. However, dosage rates of such drugs for use in

the horse have not been evaluated. Thyroidectomy has been used in the past for the treatment of bizarre behavioral problems thought to be associated with hyperthyroidism, but the results were unreliable and now the technique is widely considered unethical.

NEOPLASIA

Thyroid **adenomas** represent the most common form of thyroid disease in the older horse. Only one lobe of the gland is usually affected and presents as a non-painful, progressive swelling on the ventral aspect of the anterior neck. Typically, the adenoma is **non-functional** so there are no associated clinical signs. Occasionally, bizarre signs have been reported in conjunction with a thyroid adenoma and these have resolved following surgical excision. Removal of the affected lobe may be justified on grounds of a space-occupying lesion or suspicion of a thyroid carcinoma. Percutaneous needle biopsy (*q.v.*) of a thyroid swelling will allow differentiation between a carcinoma and an adenoma.

Thyroid carcinomas are rare. Like adenomas they usually present solely as swellings in the thyroid area although other clinical signs have been reported. Signs of coughing, anorexia and depression have been seen, and thoracic and abdominal metastases may be found at post mortem examination. One case had reduced exercise tolerance, which returned to normal following surgical treatment. Both follicular and medullary carcinomas have been identified histologically.

THE PANCREAS

INTRODUCTION

The pancreas is a compound racemose gland that has important exocrine and endocrine functions. Up to a million islets of Langerhans are present in the organ, but these account for only approximately 2% of its total weight. Two major cell types are present in the islet tissue: α cells are responsible for the secretion of **gastrin** and **glucagon**, and β cells are the source of **insulin**.

Insulin is synthesized in the endoplasmic reticulum of the β cell as a single chain polymer, **pro-insulin**, from which the two-chain structure is split off by a trypsin-like enzyme. The rates of pro-insulin and insulin synthesis are highly dependent on **blood glucose** concentration; other factors that stimulate pancreatic insulin release include amino acids, glucagon, enterohumoral factors, growth hormone, corticotropin and vagal stimulation. The major effect of insulin is to **increase the utilization of glucose** by most body tissues. This is achieved by increasing the transportation of glucose across the cell membrane and stimulating lipogenesis. Fasting insulin concentration is usually between <5 and 20 μIU/mL.

DIABETES MELLITUS

Diabetes mellitus has been considered a rare disorder in the horse. The word diabetes generally is associated with a failure of insulin production and the

resulting abnormalities that develop in the control of carbohydrate, protein and lipid metabolism. Therefore diabetes mellitus for a long time was associated with hypoinsulinemia and hyperglycemia. In fact diabetes mellitus is an **extremely complex syndrome** that consists of a number of different disorders.

The National Diabetes Data Group has classified human diabetes into groups to address both the clinical and subclinical stages of the onset of this disorder. These are:

1. Insulin dependent
2. Non-insulin dependent
3. Secondary diabetes
4. Gestational diabetes
5. Impaired glucose tolerance.

Similar groups have also been identified in horses and ponies, and it is appropriate to adopt a similar classification system here.

Insulin-dependent diabetes

Insulin-dependent diabetes is associated with failure to produce or release insulin. This form of diabetes is very rare in the horse and no cases of juvenile-onset insulin-dependent diabetes have been reported. Adult horses and ponies have been noted to develop insulin-dependent diabetes following destruction of the pancreas. In several of these reports the migration of *Strongylus equinus* and *S. edentatus* parasites (*q.v.*) was the apparent cause of the pancreatitis.

The **clinical signs** noted in insulin-dependent diabetes mellitus include weight loss, depression, polyuria and polydipsia. Clinical pathologic abnormalities include hyperglycemia, glucosuria and hypertriglyceridemia. In addition, horses with migrating parasites may have increased eosinophil counts in the leukogram and be hyperglobulinemic.

The **diagnosis** of insulin-dependent diabetes can be confirmed by performing either an oral or IV **glucose tolerance test** (*q.v.*).

Once significant damage to the pancreas occurs with the destruction of the islets of Langerhans, the only available **treatment** is administration of **parenteral insulin**. The insulin dosage should be established by monitoring the response to small doses initially and then gradually adjusting the dosage. In one report of diabetes associated with pancreatitis in a pony, protamine zinc insulin (0.5–1.0 U/kg) was more effective than regular insulin in decreasing the hyperglycemia.

Secondary diabetes

The most common form of diabetes in the horse is secondary diabetes. Secondary diabetes has been reported following **hyperadrenocorticalism** and in association with **granulosa cell tumors** (*q.v.*). Theoretically, it could also occur in association with growth hormone excess and pheochromocytomas (*q.v.*), but neither association has been cited in the literature.

Hyperadrenocorticalism is a common endocrine disorder of older horses resulting from the excessive production of adrenocorticotropic hormone from a pituitary adenoma (*q.v.*). The increased production of cortisol inhibits the function of insulin, leading to insulin resistance and hyperinsulinemia. This is accompanied by hyperglycemia from increased hepatic glucose production and decreased glucose utilization by the peripheral tissues. The mechanisms for impaired glucose tolerance and hyperinsulinemia have not been determined but may result from direct stimulation of pancreatic β cells or a post-receptor defect involving the insulin target receptors. Hyperadrenocorticalism is most readily diagnosed by performing a **dexamethasone suppression test** (*q.v.*).

Non-insulin-dependent diabetes (see peripheral Cushing's disease *q.v.*)

Recently an additional group of pony diabetics has been identified. These ponies are classified as non-insulin-dependent diabetics and are generally **obese** (Table 11.3). Similar findings have been noted in human patients with non-insulin-dependent diabetes, where 80% are obese. These ponies show no abnormal physical or clinical pathologic changes other than being obese. There appears to be a progressive decline in insulin sensitivity associated with increased body condition. Ponies therefore initially show **impaired glucose tolerance** (Table 11.3, group 2) and then develop hyperinsulinemia and hyperglycemia (group 3).

Affected ponies tend to have **increased fasting insulin concentrations** and following the administration of oral glucose become hyperinsulinemic and hyperglycemic. It has been suggested that affected ponies may be susceptible to the development of laminitis (*q.v.*) and the hyperlipemia syndrome (*q.v.*) but it is not determined what roles the hyperinsulinemia and hyperglycemia play. Human patients suffering from non-insulin-dependent diabetes may

Table 11.3 Classification of pony diabetics based on insulin and glucose data following oral glucose administration

	Group			
	1 NI, NG (n = 7)	2 HI, NG (n = 5)	3 HI, HG (n = 8)	4 NI, HG (n = 3)
Body score	6.4 + 0.5	7.8 + 0.6[1]	8.4 + 0.8[2]	7.8 + 0.8[1]
Back fat (cm)	1.2 + 0.4	1.6 + 0.4	2.0 + 0.4[1]	1.9 + 0.5[3]
BLI (μIU/mL)	7.5 + 2.4	22.8 + 13.6	27.9 + 14.1	16.1 + 0.8
BLG (mmol/L)	4.3 + 0.5	4.9 + 0.8	5.1 + 0.5	4.8 + 0.2
TIS (μIU/mL)	270.9 + 75.1	1310 + 995	2191 + 1390[1]	291.3 + 34.7
TG (mmol/L)	53.0 + 6.8	50.8 + 5.3	66.9 + 4.3[2]	66.0 + 2.8[1]
IPR (μIU/mL)	60.4 + 24.2	305.9 + 232.7	452.3 + 308.8	55.7 + 7.5
GPR (mmol/L)	9.3 + 1.4	9.1 + 1.3	11.7 + 0.8[2]	11.8 + 0.5[1]

Data expressed as means + SD.

BLI, baseline insulin response; BLG, baseline glucose; G, glucose; GPR, glucose peak response; H, high; I, insulin; IPR, insulin peak response; N, normal; TG, total glucose; TIS, total insulin secreted.

[1] $P < 0.01$.

[2] $P < 0.001$.

[3] $P < 0.05$.

develop insulin-dependent diabetes following β cell exhaustion. A similar progression in the severity of this disorder has not been noted in ponies.

Ponies with non-insulin-dependent diabetes will show improved insulin sensitivity on feeding a maintenance diet alone or in association with a mild exercise program.

Gestational diabetes

Pregnancy in the mare is a **diabetogenic stress**. During pregnancy, mares may develop hyperinsulinemia, enhanced β cell sensitivity to endogenous and exogenous glucose, increased degradation of insulin, insulin resistance and exaggerated responses to fasting and feeding. These adaptive glucose and insulin changes during pregnancy aim to protect the rapidly growing foal in the final trimester.

Glucose tolerance tests

If a horse or pony is suspected of suffering from diabetes mellitus then either an oral or an IV glucose tolerance test can be performed. The **oral glucose tolerance test** is performed after withholding feed for 16 h and then administering glucose at a dosage of 1 g/kg as a 20% solution by stomach tube. Blood samples are collected for glucose and insulin determination at times 0, 30, 60, 90, 120, 150, 180 and 210 min. Following oral glucose administration normal ponies will tend to double their glucose concentrations between 90 and 120 min then quickly decrease both the insulin and glucose concentrations.

The **IV glucose tolerance test** is performed by administering 0.5 g/kg of glucose IV as a bolus (e.g. 40%) and collecting samples at times 0, 15, 30, 45, 60, 120, 180 and 240 min for glucose and insulin estimations. Insulin-resistant ponies fail to decrease the glucose concentration even with very high insulin concentrations, while insulin-dependent diabetics will have high glucose concentrations with little increase in insulin concentration.

THE PARATHYROIDS AND CALCIUM METABOLISM

INTRODUCTION

The anatomic position of the parathyroid glands is quite variable. One pair is usually embedded in the thyroid glands, while a second pair may be located from the area of the thyroid gland to 15 cm cranial to the first rib.

Calcium metabolism is under the control of a variety of hormones. The most important of these are **parathyroid hormone (parathormone, PTH)** and **vitamin D**, which act on the intestine, bone and kidney. In this way, serum calcium concentration is maintained within closely defined limits. The major stimulus for PTH secretion is hypocalcemia. PTH acts predominantly on the kidneys to increase calcium resorption in the tubule, although calcium resorption in bone is also increased by PTH. It also acts on the renal tubule to decrease phosphorus resorption.

Cholecalciferol (vitamin D_3) is formed predominantly in the skin and is metabolized in the liver and kidney to form the active metabolite 1,25-hydroxy-vitamin D, which facilitates calcium absorption in the small intestine. It is also essential for bone formation, but when present in excess stimulates bone resorption and causes hypercalcemia.

Calcitonin is produced by the parafollicular C cells of the thyroid gland. Its actions are the opposite of PTH, since it inhibits bone resorption and lowers serum calcium.

Serum calcium is present in three forms: ionized, protein-bound and complexed calcium. **Ionized calcium** is the physiologically active form and accounts for nearly half of the total calcium. **Protein-bound calcium** is complexed predominantly to albumin, and alterations in serum proteins will result in changes in the concentrations of protein-bound calcium. Since most measurements of serum calcium only give an estimate of total serum calcium, these values must always be interpreted in conjunction with simultaneous measurement of serum proteins.

HYPERCALCEMIA

Hypercalcemia has been associated with renal disease, neoplasia, vitamin D toxicity and hyperparathyroidism.

Chronic renal failure

Some horses with chronic renal failure (*q.v.*) develop hypercalcemia and hypophosphatemia. The horse relies on renal excretion to eliminate excessive quantities of calcium absorbed from the intestine; chronic renal disease therefore may result in failure of this mechanism.

Ectopic or pseudo-hyperparathyroidism

Hypercalcemia is a relatively common complication of malignancy in humans, but has been identified only rarely in the horse. The tumors most commonly associated with hypercalcemia in the horse are **lymphosarcoma**, **gastric squamous cell carcinoma** and **mesothelioma** (*q.v.*). The hypercalcemia in these cases is thought to result from the secretion of tumor-derived humoral factors, and the syndrome is referred to clinically as ectopic or pseudo-hyperparathyroidism.

The precise nature of the humoral factors causing hypercalcemia is uncertain, but in most cases it appears that it is not PTH. Prostaglandins and osteoclastic activating factor have been implicated in some cases, but other factors are probably important as well. Soft tissue mineralization (especially of the heart and major blood vessels) and hypercalcemic nephropathy have been identified in some cases.

No attempted treatment of this condition in the horse has been recorded, although in other species surgical removal of the tumor mass has been shown to reverse the hypercalcemia.

Hypervitaminosis D

Iatrogenic hypervitaminosis D may result from **overdoses of vitamin supplements** or ingestion of toxic plants with vitamin D activity. Hypercalcemia, hyperphosphatemia and soft tissue mineralization have been recorded in such cases. Treatment consists of removal of the source of excessive vitamin D.

Primary hyperparathyroidism

Primary hyperparathyroidism is very uncommon in the horse and is a clinical condition produced by the inappropriate overproduction of PTH. The precise cause for the autonomous PTH overproduction is often undetermined, even in humans. Persistent hypercalcemia and hypophosphatemia result, and the diagnosis is achieved by detection of a high PTH concentration. A radioimmunoassay for C-terminal PTH has been validated for use in the horse. The clinical features of primary hyperparathyroidism in the horse appear vague, but include intermittent lameness and recumbency.

Nutritional secondary hyperparathyroidism

Nutritional secondary hyperparathyroidism, also known as "**big head**" and "**miller's disease**" (*q.v.*), occurs in horses fed rations containing an **excess of phosphorus relative to calcium**. The disease is seen most commonly in young horses, or occasionally in pregnant mares.

Shifting-leg lameness is a common initial sign and is caused by focal periosteal avulsion, detached or torn ligaments, or subepiphyseal microfractures. The **laminae durae surrounding the teeth may become resorbed**, resulting in difficult and painful mastication, and bilateral symmetrical facial swellings occur.

The ingestion of excessive phosphorus causes hyperphosphatemia and secondary hypocalcemia. This is the stimulus for PTH secretion, which returns the serum calcium levels back to normal. **Parathyroid gland hypertrophy** may result in long-standing cases. The **diagnosis** is made on the basis of the clinical signs and is supported by feed analysis. Radiographic evidence of loss of the laminae durae is also helpful. Serum calcium levels are usually in the low–normal range. The fractional renal excretion of phosphorus is increased.

Treatment consists of correcting the dietary imbalance and supplementing the diet with calcium (e.g. limestone flour).

Chapter 12

The urinary system

D. C. Knottenbelt (Consultant Editor)

Chapter contents

INTRODUCTION

The upper urinary tract comprises the kidney and the ureters. The kidneys are responsible for the fine-tuning of the water and electrolyte balances, and the amount of water ingested or produced metabolically can have a significant effect on urine production. The ureters conduct the urine to the bladder in a

pulsatile fashion with muscular contractions delivering accumulated urine from the renal pelvis to the bladder up to 6–10 times per minute.

The bladder and urethra make up the lower urinary tract. The bladder stores urine and the urethra conducts it out of the body.

Normal horses produce between 5 and 15 mL urine per kg body weight per day but this varies with **food type** and the extent of loss of water from the gut, the respiratory tract and skin. Even during extreme dehydration urine will be produced at approximately 2.5 mL/kg/day.

Renal disease affects the whole body but the common clinical features of equine urinary tract disease are non-specific. From a clinical perspective urinary tract disease is manifest by:

1. Weight loss
2. Abnormal urination (volume or character)
3. Pigmenturia.

Related non-specific systemic signs include anorexia, depression, ventral edema, oral ulceration and colic.

Normal horses pass urine freely after posturing appropriately, and the ability to **posture correctly** has an important role in the ability and willingness of the horse to urinate. If the horse cannot (for pain or physical reasons) posture correctly an impression of urinary tract disease may be displayed.

For the most part, **weight loss** is an indicator of renal disease while bladder and urethral problems are associated with abnormal urination.

NORMAL MICTURITION

The normal equine bladder can accommodate 4–4.5 L of urine. Horses usually urinate four to six times daily and, depending on size, will produce between 3 and 15 L of urine. The volume and composition of normal urine changes frequently in response to external influences such as water consumption, dietary composition, ambient temperature, exercise and natural diurnal variations.

Box 12.1 Definitions of urologic terms

Polydipsia: Increased water intake/thirst beyond normal volume
Polyuria: Abnormally increased urine production/volume of urination
Strangury: Difficulty with urination (usually with straining and, possibly, pain)
Pollakiuria: Frequent urination (not necessarily associated with increased volume)
Anuria: Absence of urine production
Oliguria: Production of reduced volume of urine
Isosthenuria: Urine that has similar osmolarity to serum
Hyposthenuria: Urine that is more dilute than serum
Azotemia: Pathologically increased blood concentrations of urea nitrogen and creatinine (and other non-protein nitrogen) in blood
Uremia: The complex of clinical and pathologic effects of high concentrations of urea on tissues within the body (azotemia)
Pigmenturia: Abnormal coloration of freshly voided urine
Incontinence: Inability to retain urine in the bladder

Bladder function is governed by sympathetic, parasympathetic and somatic nerves. Throughout filling, afferent (sensory) neurons induce increased sympathetic activity, which inhibits detrusor contraction. Passive outflow of urine from the urinary bladder is prevented by muscular tone in the neck of the bladder and the proximal urethra. Bladder distension triggers micturition by coordinated contraction of the bladder detrusor muscle, which generates intravascular (bladder) pressure, and simultaneous relaxation of the bladder and urethral "sphincters". Higher centers in the motor cortex, midbrain and medulla can both inhibit and facilitate contraction by over-riding the automatic local functions. In this way urination can be consciously delayed.

The diagnosis of urinary tract disease presents a **clinical challenge** because many of the most serious signs are subtle. As a result, cases are often presented with advanced disease. Differentiating between **pre-renal** (decreased renal perfusion), **renal** (renal damage or compromise) and **post-renal** (obstructive lower urinary tract disease or uroperitoneum) disease is a cornerstone of renal medicine.

GENERAL PRINCIPLES OF THE DIAGNOSIS OF URINARY TRACT DISEASE

Urinary tract disease presents with a variety of clinical signs that relate to the etiology, the extent of renal compromise and the organs that are affected secondarily. Thus, difficulty with or **pain during urination** can be a sign of an obstructive or inflammatory condition in the lower urinary tract (usually the bladder or the urethra). Polydipsia or oliguric renal failure results in little pain but there are significant alterations in urine production. The volume and quality of urine produced may be the only outward evidence of severe renal disease. **Advanced renal failure** with azotemia and uremia has profound effects on almost all the body organs. Additionally, central nervous signs, anemia, weight loss, oral and intestinal ulceration, are all possible.

Obvious difficulty with urination (**dysuria**) or **variations in the color and character of urine** are often the signs that owners will notice. In contrast, because the early signs of renal or lower urinary tract compromise are often subtle, owners may not notice any problem until the condition is advanced.

A **thorough clinical investigation** is essential in every case of suspected urinary tract disease; the urinary tract should not be overlooked when investigating a variety of other apparently unrelated clinical signs such as **colic** and **weight loss** (*q.v.*) and must be carefully assessed in every case of suspected urinary tract disease.

The clinical investigation of urinary tract disease relies heavily on **urinalysis** and biochemical tests, but subtle (or sometimes more obvious) clinical indicators of disease do exist; the role of the clinician is to identify these and assess their combined importance.

The limitations to clinical examination mean that there is an increased reliance upon other diagnostic aids. Urinary tract endoscopy (including ureteroscopy) and percutaneous and transrectal ultrasonography, in particular, have significantly improved the prospects of a definitive diagnosis. In adult horses, useful physical examination is limited to **rectal palpation**. The procedure is indicated in all cases of suspected urinary tract disease.

RECTAL PALPATION

The value of rectal palpation for urinary tract disease depends upon the relative sizes of the operator and the horse and operator experience. In the case of foals, rectal examination is not feasible but in some cases the bladder can be palpated abdominally.

It is usually only possible to assess the size, texture and outline of the caudal pole of the **left kidney**. The right kidney is best regarded as non-palpable. The size, wall thickness and texture of the **urinary bladder** can be appreciated and sometimes abnormal content or masses can be felt. The **texture** of the bladder can be a major diagnostic aid. In some cases repeated examinations will need to be made to establish variations in function during the normal cycle of filling and emptying.

Unless they are enlarged or inflamed (or both) the **ureters** are not usually identifiable. It may be more rewarding to palpate the distal regions of the ureters of a mare per vaginam. If the ureters can be felt easily, they can be taken to be abnormal. In any case, the **trigone of the bladder** should always be palpated. In mares it may be possible to palpate the vesicoureteral opening directly via the urethra and then it may be feasible to pass a catheter directly into the ureters.

ENDOSCOPY

Cystoscopy is a simple procedure in mares, although it is sometimes difficult to maintain insufflation. Male horses require a longer thinner endoscope (<1 cm diameter, >1 m long). **Videoendoscopy** is very helpful but suction apparatus is essential.

Saline distension of the bladder during endoscopy in both male and female is recommended because, in contrast with air insufflation, there is little or no iatrogenic superficial inflammation. Urine samples should be taken **before insufflation** or distension to avoid artifactual results.

Ureteroscopy and visualization of the renal pelvis is possible with a suitably sized instrument. It is then possible to **sample urine** from each kidney independently. This procedure does, however, carry risks of introducing infection from the lower tract.

Endoscopic biopsy of pathologic lesions is possible but the biopsy instruments are usually too small to obtain meaningful specimens.

ULTRASONOGRAPHY

Ultrasonography is feasible even in large horses, with a suitably configured high power machine (2.5–5.0 MHz). A sector array is required because of the relatively narrow window between the ribs. The right kidney is located behind the dorsal aspects of ribs 12–14, intimately related to the liver, while the left is more caudal and may be visualized from the last rib space or even from the most anterior dorsal aspect of the sublumbar fossa close to the top of the spleen. The size and shape of the kidneys can be estimated reasonably accurately.

Color-flow Doppler can be used to measure blood flow in the renal arteries and veins and in some cases within the substance of the kidney.

Ultrasonography is an essential aid to safe **percutaneous renal biopsy** (*q.v.*).

RENAL BIOPSY

Renal biopsy is a useful technique and can provide a definitive diagnosis in many cases, especially in diffuse renal disease. However, the procedure carries **significant risks** including **perirenal hematoma** and heavy (possibly fatal) **hemorrhage**, and is only justified if histopathology is likely to have a significant influence on subsequent therapy. Biopsy specimens examined by light microscopy may appear normal despite clinicopathologic evidence of severe dysfunction and so the value of biopsy is not always worth the risks. Experience is invaluable in minimizing the problems and meticulous procedural technique will limit the number of biopsies required and the associated risks.

Ultrasound guidance is essential and enables a specific site to be biopsied safely. Biopsy of the right kidney via the 17th intercostal space is the preferred procedure and is diagnostically useful provided that a **diffuse bilateral condition such as chronic active glomerulonephritis is present**. The left kidney is less simple and usually can only be sampled by crossing the spleen first. In some cases the biopsy instrument can be guided past the spleen directly into the left kidney.

Automatic or spring-loaded biopsy instruments and adequate restraint (stocks and sedation) are important considerations. The clinician must ensure familiarity with the specific biopsy instruments to be used.

The procedure is best performed under standing sedation using a suitable chute or stocks and an IV combination of an α_2-adrenoreceptor agonist drug (such as romifidine 0.07 mg/kg, or detomidine 0.03 mg/kg) with an opioid such as butorphanol (0.05–0.1 mg/kg). The procedure should be performed after aseptic preparation of the skin at the chosen site and immediately prior to biopsy an ultrasound check should be made. In some circumstances it may be possible to guide the biopsy instrument using simultaneous ultrasound examination. In all cases biopsy must avoid the renal hilus. Preferred sites are at the caudal pole of the kidney although the location of focal lesions will have a significant influence on the technique and direction of biopsy.

Two biopsies should be obtained: one fixed in 10% formalin solution for histopathology and a frozen one for bacteriology, immunofluorescence testing and electron microscopy.

RADIOGRAPHY

Radiography has limited diagnostic value in examining the urinary system of adult horses, even when contrast studies are used, but in foals the procedure can be helpful. Diagnosis of bladder and ureteral problems in foals can sometimes be confirmed directly but single or double contrast studies can give added information. Inflation of the foal's bladder with 200–250 mL air provides a negative contrast that will possibly identify some pathologic changes in the bladder wall (such as defects in the wall). Positive contrast materials based on iodine (such as **iohexol**) can be infused directly into the bladder via a urethral catheter but can also be infused IV to provide a positive contrast excretory urogram. Positive contrast IV excretory pyelography is performed by injecting an appropriate volume (1 mL/kg iohexol) IV. All these techniques are usually performed in the standing foal.

IV pyelography/excretory urograms can be performed in adult horses and are used mainly to identify ectopic ureters. Suitable contrast medium (e.g.

iohexol) is administered by slow IV injection (at a rate of 1 mL/kg body weight) via a jugular catheter. The first radiographs are taken at 3 min and then sequential views are taken at 2 min intervals thereafter for 6–10 min. By this stage the contrast should be clearly visible in the renal pelvis and passing down the ureters. An ectopic ureter will be seen to discharge into an abnormal site (e.g. the anterior vagina) whereas in the normal ureter(s) the contrast will accumulate in the bladder and be clearly visible. The technique has limitations of size and facilities to take diagnostic lateral radiographs. Combinations of positive and negative contrast can be helpful also but these can be logistically more difficult.

SCINTIGRAPHY

Soft tissue phase gamma scintigraphy and urinary clearance of a radionuclide provide a new and exciting diagnostic mode in some specialized centers. The IV administration of **technetium 99m** results in rapid delivery of the radiopharmaceutical into the urine, and imaging with a high-resolution gamma camera can identify the individual kidneys and ureters within minutes of injection. Delivery to the bladder (or ectopic location of a ureter) can be detected. Similarly a poorly perfused kidney may have little gamma activity when compared to the contralateral normal kidney or when compared with normal kidneys in the event of a bilateral vascular problem. Tumors and sites of inflammation may be detected by prolonged retention of radionuclide in an affected kidney. During orthopedic scintigraphy the delivery of the radionuclide to the bladder can be a significant complication.

HEMATOLOGY AND BIOCHEMISTRY

The hemogram provides non-specific information in cases of **renal failure**. Increases in hematocrit indicate **dehydration**, and in chronic disease a **non-regenerative anemia** is expected. **Leukocytosis** may accompany inflammation of the upper urinary tract and an elevated **plasma fibrinogen** concentration is usually indicative of **septic inflammation**.

Serum creatinine is widely used as an indicator of renal disease while **blood urea** is somewhat less useful. **In combination** these two metabolites can provide significant information but the concentrations of any blood metabolite must be considered along with the **hydration status** of the patient.

Creatinine is a metabolite derived from muscle function that is selectively excreted by the renal tubules after being freely filtered into the urine and is then concentrated in the urine. Dietary protein has no material effect on the production of creatinine. Creatinine is estimated directly from serum or urine and the ratio of blood creatinine to urinary creatinine is usually taken as a measure of renal perfusion or more specifically glomerular filtration rate (GFR, *q.v.*).

Urea excretion is completely passive and the high urinary concentration is achieved directly as a result of medullary hypertonicity in the loop of Henle. Therefore, although high dietary protein results in a corresponding increase in urea excretion, low protein diets do not reduce the "work" of the kidney. Urea is measured from serum or plasma and is a routine laboratory procedure.

Azotemia is a laboratory-derived term used when there are increased blood concentrations of urea and creatinine (and other non-protein nitrogen)

in blood. The term **uremia** (uremic syndrome) is used to describe the widespread effects of high concentrations of urea (azotemia) on body tissues. There is a poor correlation between the severity of uremia and the laboratory-derived concentrations of urea and creatinine. The extent of azotemia is usually highest with renal and post-renal azotemia but the best approach is probably achieved by comparing the blood and urinary creatinine and urea concentrations:

1. A urine to blood creatinine ratio >50:1 (reflecting concentrated urine) would be expected in **pre-renal azotemia**.
2. Urine to blood creatinine ratios <37:1 probably indicate **renal disease**.
3. A high urinary specific gravity (>1.035) is usually present in pre-renal azotemia.
4. Dilute urine in the face of dehydration is consistent with a diagnosis of renal disease.

Repeat estimation of urea and creatinine at 24–72 h intervals over the initial period of treatment is probably the most useful practical indicator of the nature and prognosis of the condition.

Dietary intake and gastrointestinal function, hydration, acid-base balance, GFR, urinary volumes and the type of renal lesion govern plasma electrolyte concentrations. It is seldom possible to define a state that is invariably consistent with renal failure.

Since the kidneys are the main sites of **potassium excretion**, anuria or oliguria is likely to be associated with **hyperkalemia**, but progressive tubular damage may then lead to hypokalemia.

Oliguria and anuria may cause increased plasma concentrations of sodium and chloride, but progressive tubular damage will be associated with their loss and plasma concentrations may reflect this. If tubular damage is associated with polyuria, then plasma concentrations of sodium and chloride may be within reference ranges (*q.v.*) as a result of dehydration. Renal dysfunction may be associated with hypercalcemia and hypophosphatemia.

Renal failure also causes a shift in the **acid-base balance**. Failure of alkali reserve regulation by tubular cells leads to a state of **metabolic acidosis** (*q.v.*); this may cause an increase in respiratory rate and depth (**Kussmaul's respiratory pattern**).

Indirect biochemical indicators of renal disease include anemia (*q.v.*), hypoalbuminemia and hypercalcemia.

Anemia is a common secondary sign of advanced renal failure, arising from the combination of failure of renal erythropoietin production (reduced production of erythrocytes) and direct bone marrow suppression arising from uremia.

Hypoalbuminemia arises from protein loss in the urine.

Pathologic failure of the normally dominant calcium excretion of the equine kidney results in a clear urine (free of the normal calcium carbonate crystals) with calcium retention. Calcium excretion in horses is the dominant feature but the extent depends largely on **dietary calcium** content. Complete absence of calcium carbonate crystals in normal alkaline urine can therefore be physiologic or pathologic. Hypercalcemia can be a helpful diagnostic feature of advanced renal failure, but there are other conditions, including paraneoplastic pseudoparathyroidism (*q.v.*), that result in a similar finding.

URINALYSIS

Visual inspection

Urine should be visually inspected as soon as it is collected; normal horse urine may change color to red or brown after standing due to the presence of an oxidizing agent known as pyrocatechin. Owners observing discolored urine collected on concrete floors or in snow sometimes mistake this as abnormal.

Tables 12.1 and 12.2 list the chemical and sedimentary characteristics of normal urine and the changes associated with disease. It is important to make the distinction between physiologic and pathologic changes in color. **Normal horse urine** varies from pale yellow to almost colorless. The yellow coloration is due to a normal pigment (urochrome) and its intensity can vary in proportion to the specific gravity. Water deprivation results in the excretion of concentrated urine with a higher specific gravity and more intense color. Physiologic dilution of urine can occur with **psychogenic polydipsia** (*q.v.*) and with **excessive fluid therapy**.

Table 12.1 Chemical characteristics of normal equine urine and changes associated with disease

Parameter	Normal range	Disease
pH	7.0–9.0	Acidity associated with metabolic acidosis (e.g. renal failure)
Protein	Usually <100 mg%	Severe proteinuria associated with glomerular lesions. Raised in inflammatory lesions of urinary tract
Glucose	None	Present when hyperglycemia exceeds threshold (Cushing's disease, diabetes mellitus, stress). Presence without hyperglycemia indicates tubular dysfunction
Ketones	None	Ketosis rare—suggests nutritional stress/protein catabolism
Bilirubin	None	Present in hemolysis or obstructive jaundice
Hemoglobinuria	None	Present in intravascular hemolysis (serum appears hemolyzed)
Myoglobinuria	None	Present in rhabdomyolysis (serum appears clear)

Table 12.2 Sedimentary characteristics of normal equine urine and changes associated with disease

Parameter	Normal content	Disease
Hematuria	None	Hematuria reflects inflammation, trauma, neoplasia or coagulopathy in urinary tract. Trace associated with catheterization
Leukocytes	None	Large numbers associated with inflammation of tract (pyuria)
Transitional	Few	Large numbers reflect inflammation, trauma, neoplasia
Bacteria	None	Moderate to heavy Gram smears/cultures reflect pyelonephritis or cystitis
Crystals	Usually calcium carbonate; occasional triple phosphate; occasional calcium oxalate	Large numbers of triple phosphate indicate infection of tract. Large numbers of calcium oxalate are abnormal, but of uncertain significance
Casts	No cellular casts. Occasional hyaline (mucoprotein) casts	Cellular casts reflect tubular damage in association with protein exudation or leakage

The three most common alterations of urine color from the normal pale yellow color are listed in Box 12.2.

Pathologic red to brown discoloration of urine (pigmenturia) may be a result of one of the following:

1. Hematuria (whole blood in urine)
2. Hemoglobinuria (hemoglobin in urine)
3. Myoglobinuria
4. Certain drugs (e.g. phenothiazine, rifampicin and the diagnostic compound bromsulfophthalein).

Red discoloration is usually due to either hematuria or hemoglobinuria (*q.v.*). Brown discoloration of urine is generally due to myoglobinuria (*q.v.*).

Clinical distinction between myoglobinuria and hemoglobinuria can be difficult and usually relies upon electrophoretic or spectrophotometric analysis. Hemoglobin usually derives from **plasma** and so a comparison to plasma can sometimes be helpful. Myoglobin has a lower molecular weight and lower capacity to bind to protein than hemoglobin and so is usually cleared rapidly by the kidney without any discoloration of the plasma.

Alterations in appearance

Apart from foals, normal horses seldom void water-clear urine. Normal urine is characteristically **turbid and mucinous** for two reasons:

1. Mucous glands within the ureters and renal pelvis result in the characteristic **appearance and texture** of equine urine. Mucus secretion is thought to be an evolutionary adaptation to the presence of the rough/irritant calcium carbonate crystals in the urine.

Box 12.2 Common alterations of urine color

Colorless urine
Diseases that result in polydipsia and polyuria (*q.v.*) frequently result in the production of dilute urine that may be water clear. The principal causes and laboratory features of polydipsia/polyuria are summarized in Table 12.4.

Dark yellow urine
Concentrated urine is produced in the face of dehydration (either a result of pathologic or physiologic relative water loss) or in acute oliguric renal failure (*q.v.*). The most common cause of oliguria in the horse is dehydration associated with such conditions as diarrhea and colic (*q.v.*) in which concentrated urine with a deep amber color and high specific gravity may be produced.

Red to brown urine
Urine does not normally contain erythrocytes and it should not have any red discoloration. Samples collected by catheter may have a few erythrocytes; some of these may lyse and so the sample may be red and have an erythrocyte button after centrifugation. Prolonged storage or exposure to air often gives urine a red-brown color (*q.v.*).

2. On normal diets, urine is often saturated with **calcium carbonate**, which precipitates spontaneously and gravitates to the floor while urine is held within the bladder. A sample obtained at the onset of urination may be much less turbid than one passed at the end of the stream. Therefore, naturally voided urine and urine collected by catheter frequently appears to vary in its turbidity depending on the part of the bladder being drained at the time. Thick sediment is obtained from the floor while the supernatant is almost clear. Sediment will usually be noted if the container is left undisturbed for a short time.

Normal horse urine will **foam on agitation** due to the natural protein content.

Routine urinalysis

Routine urinalysis includes the measurement of specific gravity, pH, protein, glucose, bilirubin, urobilinogen and ketones. Usually these are all performed with a single dipstick and results as a rule are clinically reliable. Microscopic examination of urine sediment after centrifugation is a very useful technique but is often complicated by large amounts of calcium carbonate.

Specific gravity

Urine specific gravity (SG) (or, more correctly, its **osmolarity**) is the only indicator of renal **function** in the urinalysis. Urinary specific gravity reflects the ability of the kidney to concentrate urine and is therefore a useful indicator of renal function.

1. The specific gravity of normal equine urine varies between 1.020 and 1.050.
2. Dehydration results in a more concentrated urine (SG over 1.035–1.055).
3. Pre-renal azotemia would be indicated by a high SG and elevated urea/creatinine concentrations.
4. The presence of dilute urine (SG of 1.005–1.020) in an azotemic (elevated creatinine and urea concentrations) or dehydrated horse is indicative of renal azotemia (tubular dysfunction).
5. Fluid therapy in a dehydrated pre-renal azotemia case would result in restoration of the normal concentrations of these metabolites. By contrast, a renal azotemia case would simply produce more urine of an equally dilute nature without normalization of the creatinine and urea concentrations. In acute renal failure, fluid therapy would not normally induce urination within 6 h of the initiation of fluid therapy.

On rare occasions, dilute urine may be found in a hydrated, non-azotemic horse as, for example, in diabetes insipidus (*q.v.*), psychogenic polydipsia (*q.v.*) or diseases that antagonize the action of antidiuretic hormone.

A **24 h water deprivation test** (Box 12.3, *q.v.*) may be necessary to assess renal concentrating ability. However, it is imperative that the horse is carefully monitored during the test to avoid dangerous dehydration. Where dehydration is a real or potential hazard, urine-concentrating ability can be measured following the administration of exogenous antidiuretic hormone.

It should be noted that **renal medullary washout** is due to excessive drinking in the absence of pathology and follows the loss of osmotic gradient

Box 12.3 Water deprivation test

Water deprivation tests are used to identify renal failure and to differentiate psychogenic polydipsia from neurologic (central) and nephrogenic (renal) diabetes insipidus.

These tests **must not** be performed in horses that are azotemic (*q.v.*) or show evidence of any dehydration. It is essential therefore that an **accurate body weight** is taken before embarking on the test, and accurate weighing should be available during the test procedure.

The procedure for a water deprivation test is as follows:

1. Take a routine blood sample and submit for routine hematology, total protein and albumin and urea and creatinine.
2. Weigh the horse accurately.
3. Remove water from the stable in the evening (so that the test can be performed the following morning). Sometimes feed is removed but this is not likely to affect the test materially. Concentrate and salty foods must not be given.
4. Empty the bladder by catheterization and determine urine specific gravity.
5. Weigh the horse and obtain urine and blood samples at 4–8 h intervals.
6. The test should be stopped if the horse shows an ability to concentrate urine (SG rising > 1.025) or if weight loss reaches 5% or if any overt evidence of azotemia or dehydration develops.

Interpretation of the test can be summarized as follows:

1. Normal horses show rapid urine concentration with SG rising >1.025.
2. Horses with psychogenic polydipsia also show normal concentration ability.
3. A low or suboptimal SG suggests diabetes insipidus or renal medullary washout (see text).
4. If urine does not concentrate at 24 h to SG >1.025, an extended modified (partial water deprivation test is advisable) (see text).

within the renal tubules. In this case it is possibly better to perform a **partial water deprivation test**. The partial water deprivation test is performed by restricting water intake to 40–45 mL/kg/day for several days; water should be offered in small volumes frequently through the day. This will usually restore the gradient, the urine SG will rise to >1.025 and the associated polydipsia will usually resolve. An increase in SG >1.025 suggests **psychogenic polydipsia** (*q.v.*) while failure to concentrate >1.025 suggests diabetes insipidus (*q.v.*).

pH

Horse urine is usually **alkaline** (pH 7.0–9.0). Attempts to acidify urine (to assist dissolution of calculi or treat bacterial infections of the lower urinary tract) traditionally relied upon dietary administration of ammonium chloride or sodium acid phosphate (sodium dihydrogen phosphate). **Neither method is well tolerated and neither is effective**.

Acidic urine can be established by alteration of the acid-base balance of the diet (**dietary cation–anion balance/DCAB**). It is calculated using the equation:

DCAB (mEq/kg dry matter) = [Na + K] − [Cl]

Acidification results because of the ion exchange that takes place in the kidney and gastrointestinal tract. A diet with a high DCAB value (300+) increases body pH, while one with a low DCAB (<100) reduces body pH. **A low DCAB diet** is generally high in Cl^- ions. High Cl^- causes a release of bicarbonate ions into the gastrointestinal tract and urine. This leads to a drop in body pH. On the other hand, **a high DCAB diet** is high in Na^+ and particular K^+ ions. High cation intakes increase intestinal loss of H^+ and increase absorption of Na^+ and K^+ leading to an increase in body pH. Low dietary DCAB, i.e. diets that are anionic or acidic, cause a **metabolic acidosis** (*q.v.*), which in turn reduces the pH of blood and urine. If the horse is producing acidic urine, the normal sediment of calcium carbonate crystals may not form. Low DCAB rations also increase urinary mineral loss, particularly calcium, and so the urine could become cloudier, if the urine pH did not become acidic.

Protein

Urine protein concentration in normal horses is usually <1.00 g/L and the protein to creatinine ratio should be <1:1. Although proteinuria (and more specifically **albuminuria**) is frequently used to support a diagnosis of **renal failure** (*q.v.*) or insufficiency, traces of protein are commonly detected in normal horses. This is probably due to the non-specific reaction on "dipstick" tests to alkaline urine. Furthermore, the normal protein content can be misleading.

Abnormal loss of albumin is a result of **glomerular failure** (*q.v.*). The molecules should be retained effectively and, with the exception of the normal proteinuria of young foals (*q.v.*), albuminuria is always significant.

Hemoglobin

Normal horse urine contains neither blood nor hemoglobin. Erythrocytes, free hemoglobin and myoglobin are the most common abnormal pigments in horse urine and they can often be detected visually. **Ortho-toluidine test strips** can identify invisible amounts of blood (**microhematuria**) or hemoglobin and can also differentiate between free hemoglobin (hemoglobinuria) and intact erythrocytes (hematuria) (*q.v.*).

Red cells in the urine (**hematuria**) usually derive from renal or post-renal **hemorrhage**; the latter are more common but the former are usually more profuse (*q.v.*). The red color will fall to the bottom of the sample when centrifuged or allowed to sediment if hemorrhage is present.

Free hemoglobin (**hemoglobinuria)** usually derives from **intravascular hemolysis**. Centrifugation of a truly hemoglobinuric urine specimen will result in no detectable "button" of red cells at the bottom of the tube and a **uniform redness to the spun sample**.

Combined hematuria and hemoglobinuria may be found on some occasions, such as if erythrocytes lyse in hyposthenuric urine, and so both intact cells and free hemoglobin may be detected.

Box 12.4 The Blondheim test for myoglobinuria

Stage 1

1. Add of 1 mL urine to 3 mL of 3% sulfosalicylic acid.
2. Mix and filter or centrifuge.

If the pigment is precipitated it is a protein and therefore *may* be **myoglobin** or **hemoglobin**. If, however, the pigment is not precipitated then the pigment is not a protein and alternative explanations for pigmenturia must be sought.

Stage 2

3. To 5 mL of urine add 2.8 g ammonium sulfate and dissolve by mixing. This brings the urine to 80% saturation.
4. Filter or centrifuge the mixture.

If the filtrate displays an abnormal color, myoglobin is present. If only the normal urine color is present in the supernatant then the precipitated pigment is hemoglobin.

It is important to realize that erythrocytes may hemolyze if the urine sample is either stood for any length of time or if the sample is agitated roughly. Careful collection, prompt cooling of the sample and timely analysis are, therefore, recommended. Collection of free-flow samples during micturition can give a misleading result and so it is sometimes helpful to obtain the **whole urine production** or **sequential samples** so that analysis can provide useful information. Catheterization of the bladder of mares or geldings is practical but again the sample so obtained may be misleading. In general it is wise to collect several samples unless a diagnosis can be established definitively from a single one.

A positive "hemoglobin" test may also arise if myoglobin is present, but it cannot identify myoglobin specifically. Differentiation between myoglobin and hemoglobin can be made using spectrophotometric methods and/or the **ammonium sulfate precipitation test** (Blondheim test*, Box 12.4) (*q.v.*). Unfortunately this test has largely been ignored but it is a simple and practical way of separating out the two major causes of pigmenturia.

The Blondheim test is applicable to freshly voided urine or to properly preserved urine. Urine can be preserved for the test by adjusting the pH to 7.0–7.5 (this actually approximates to normal urine but not necessarily to urine from horses with acidosis) and then refrigerated at 4°C. Urine preserved in this way can be tested for up to 2 mo or more despite a moderate degree of bacterial contamination.

Glucose

Urine glucose tests are extremely sensitive and care must be taken when collecting urine into non-medical receptacles in case there is residual sugar in the container or its cap. **No glucose is present in normal urine**.

* Blondheim, S.H., Margoliash, E., Shafir, E. (1958) A simple test for myohemoglobinuria (myoglobinuria), *Journal of the American Medical Association* 167: 453–454.

A positive glucose test reflects either a **reduction in tubular resorption** (often termed "a reduction in renal threshold") or an **abnormal blood glucose** concentration (often expressed as "exceeding the renal threshold"). **Diabetes mellitus** (*q.v.*) is extremely rare in horses but **glycosuria** is a common feature of **equine Cushing's disease** (*q.v.*); lesser concentrations may simply reflect **renal failure.**

Urine sediment

Microscopic examination of the **centrifuged sediment** in the laboratory is rewarding. Normal sediment usually has a large amount of calcium carbonate crystals. Abnormal crystals include calcium oxalate and calcium phosphate. Urine sediment from normal horses may occasionally contain **hyaline casts that appear as slightly refractile tubular structures**, especially if the horse is undertaking strenuous work, but granular/protein, erythrocytic and fatty tubular casts are abnormal. These are denser and have a better defined form than the rather amorphous hyaline casts. A small number of leukocytes and bacteria may be observed in normal horses, especially in naturally voided samples from mares.

Delays in examination, especially at room temperature, usually cause artifactual degeneration in cells and allow bacterial proliferation. Usually, however, specific cell types can be identified. Samples should be collected fresh so far as is possible and should be collected into a sterile container. The sample should be stored in a refrigerator at 4°C until analysis can be performed. Urinary infection is usually indicated by high numbers of neutrophil leukocytes in urine but this does not indicate specifically if the origin is renal, ureteral or the bladder. It can be difficult to differentiate contaminant (incidental) bacteria from pathogens in samples that have been stored for more than 12 h even if they have been refrigerated. Where cytology only is required, a drop or two of 10% formalin solution can be added to the urine to maintain cell structure. This, however, will clearly completely negate any attempt at culture.

Erythrocytes and ghost cells will be seen in cases of hematuria (*q.v.*) even if a degree of hemolysis has occurred in the urinary tract or after collection of the sample. Grossly abnormal cells, including neoplastic and extensive sheets of transitional or cuboidal epithelial cells, indicate severe abnormality.

URINARY ENZYMES

Gamma glutamyltransferase (GGT) is found in the liver, pancreas and luminal brush border of the proximal tubular cells. This enzyme is not excreted by glomerular filtration, so when it is detected in **urine** it is strongly indicative of **tubular damage**. Because it appears before azotemia develops, it is a sensitive indicator of early (acute) renal tubular disease such as **acute tubular necrosis** (*q.v.*).

Urinary GGT concentrations are conventionally expressed as a ratio to urinary creatinine concentrations to compensate for variations in urine flow rate at the time of sampling:

$$\frac{\text{GGT (IU/L)}}{\text{UCr (}\mu\text{mol/L)}}$$

Horses with **renal compromise** have values ⩾25 but urinary GGT values fall once the acute insult has ceased, despite persistent tubular dysfunction. The value of this assay in progressive or chronic renal failure is therefore doubtful.

GLOMERULAR FILTRATION RATE

In health the **glomerular filtration rate (GFR)** remains remarkably constant due to the intrarenal regulatory mechanisms; the net urinary excretion of an electrolyte is governed by GFR and the efficiency of tubular resorption. GFR can be measured by several methods including clearances of endogenous creatinine or exogenous inulin, or radionuclide (^{99m}Tc-DTPA) or plasma disappearance of sodium sulfanilate, phenolsulfonphthalein or radiolabeled compounds. Certain drugs such as the **potentiated sulfonamides** reduce tubular secretion of creatinine and so may induce a rise in serum creatinine and a fall in measured clearance.

Creatinine is excreted by filtration alone and its rate of excretion therefore provides a good indicator of the GFR, even during renal dysfunction. The only practical method of measuring (estimating) the GFR in horses with normal or near normal renal function is through measurement of the creatinine clearance. Urea is not a useful parameter to use to calculate GFR.

The normal GFR of horses is between 1.6 and 2.0 mL/min/kg and this must be reduced by 60–75% to result in a detectable increase in serum urea and creatinine concentrations. Measurement of the circulating concentrations of creatine and urea are relatively insensitive indicators of renal function because they change relatively slowly with time.

A pathologic reduction in intrarenal blood flow, glomerular damage or loss, or obstruction to the free flow of ultrafiltrate along the renal tubular system causes the GFR to fall, and with it the ability of the kidney to eliminate waste material and to regulate the volume and composition of body fluid will decline. This is manifest as a rise in blood urea and creatinine concentrations and a reduction in the measured GFR.

There is no convenient method of collecting total urine voided by ambulatory foals or mares, but urine output can be collected in male horses by placing a urine collection device around the abdomen. When monitoring urine output in critically ill foals and mares is desired, it can be accomplished by use of an indwelling **Foley catheter** and **urine collection bag** (closed system). The risk of ascending infection can be reduced by placing a one-way valve (such as the cut off finger of a surgical glove) over the end of the catheter to prevent aspiration of air and bacteria.

FRACTIONAL ELECTROLYTE EXCRETION

Creatinine clearance is a useful standard against which the clearance of an electrolyte may be compared in health or disease. The **fractional excretion (FE) of an electrolyte** is defined as the per cent ratio of its clearance to the clearance of endogenous creatinine. In normal homeostatic balance, FE values vary with dietary and water intake variations, but usually fall within a

Table 12.3 Fractional excretion ratios of the major electrolytes as calculated from the serum and urinary creatinine

Electrolyte	Sodium	Potassium	Calcium	Inorganic phosphate	Chloride
FE ratio (%)	0.01–1.00	15–75	2.0–3.0	0.04–1.19	<4

definable range. With a loss of tubular resorption the excretion of an electrolyte is often increased and its FE rises above the normal range. The FE is derived as follows:

$$\frac{\text{urinary concentration of electrolyte (uE)}}{\text{plasma concentration of electrolyte (pE)}} \times \text{urine flow rate/min} \times 100\%$$

divided by

$$\frac{\text{urinary concentration of creatinine (uCr)}}{\text{plasma concentration of creatinine (pCr)}} \times \text{urine flow rate/min}$$

which can be simplified to:

$$\text{FE} = \frac{\text{uE}}{\text{pE}} \times \frac{\text{pCr}}{\text{uCr}} \times 100\%$$

The FE of an electrolyte is therefore calculated from urinary and plasma concentrations of the electrolyte and creatinine. The FE ranges for healthy horses are shown in Table 12.3.

In general terms, a persistent increase in the FE of one or more electrolytes (frequently sodium and phosphorus) is suggestive of **tubular dysfunction** but there are a number of caveats to the interpretation of results of FE calculations:

1. Clearance is influenced by dietary, hydration and endocrine factors.
2. In health, urinary concentrations of electrolytes and their rates of excretion vary between horses and within the same individual through the day.
3. Measurements in horses receiving IV fluids will be spurious, and electrolytes trapped in urinary crystals (calcium and occasionally phosphorus) are not measurable.

DISORDERS OF THE EQUINE URINARY TRACT

URINARY FUNCTION IN NEONATAL FOALS

Special considerations of renal function in the foal

The fetal urinary tract is immature and has limited control of fluid and electrolyte balance and removal of nitrogenous waste products; the fetus relies heavily (but not exclusively) on the placenta.

Normal colt foals will void a normal stream of urine within 4 h of birth while the first urination of filly foals is often delayed up to 6 h. This has implications

for the detection of **patency of the urinary tract** (*q.v.*). Mature renal function is not achieved for several weeks after birth. Foals often have a **transient proteinuria** for the first 2–3 days as a result of filtration of small molecular weight proteins absorbed with colostral protein. The high dietary fluid intake results in **acidic urine** of **low specific gravity** (1.001–1.004), low osmolarity and high volume (148 mL/kg/day, i.e. up to 6–7 L/day). A few epithelial cells and calcium oxalate crystals may be present in normal foal urine. However, the presence of erythrocytes, leukocytes, casts, hemoglobin or myoglobin in foal urine is **always abnormal**.

Serum creatinine elevations in neonatal foals

In the first 1–3 days, creatinine concentrations are often in the range 141–194 μmol/L. This gradually falls to 88–106 μmol/L over the first 2–3 wk as renal function matures. The likely cause is an inability of creatinine to equilibrate across placental membranes. A mildly elevated creatinine concentration in an otherwise healthy foal (that has urinated normally) is therefore probably of little concern. However, if the concentration does not decline over 3–4 days or remains >200 μmol/L on day 3, then **peritoneal or retroperitoneal accumulation** of urine, **renal hypoplasia** or other causes of renal failure should be considered (*q.v.*).

Unlike creatinine, blood urea concentrations in foals are typically low (<5 μmol/L) after day 2 and remain low for the first several months of life. This finding can be attributed to the anabolic state of the growing foal.

The trend in creatinine and urea concentrations in azotemic foals should be closely monitored; a continued increase would suggest renal dysfunction and demands additional evaluation.

Urinalysis in foals

Urinalysis in normal neonatal foals is significantly different from adult horses:

1. Normal foals frequently show a marked proteinuria for 1–2 days after birth.
2. By nature of their milk diet, foals have a **high water intake** (approximately 250 mL/kg/day compared with the adult water intake of 50 mL/kg/day). After day 2, urine is hyposthenuric (specific gravity 1.002–1.006) and remains so for several months.
3. Urine pH is neutral to acidic.
4. Urinary enzyme activity and sodium and chloride clearances may be greater than adult values.

CONGENITAL ABNORMALITIES

Congenital defects in the foal are rare apart from **patent urachus** (*q.v.*) and failure of the **normal fusion** of the urinary bladder (*q.v.*). Reported defects include renal agenesis, polycystic kidneys, renal glomerular hypoplasia and ectopic ureters (*q.v.*). Various dysplastic conditions (where the renal structure has a chaotic or disorganized nature) also occur.

The age of onset of relevant clinical signs is dependent on the degree of renal pathology and the extent of loss of function. In some cases the conditions are fully compatible with life and are only detected incidentally at post mortem examination at a later age; in others clinical signs are delayed until 6–18 mo although some evidence can usually be found before that.

Renal agenesis or hypoplasia/dysplasia

Agenesis of both kidneys is not compatible with life. Foals with renal agenesis will develop renal failure shortly after birth.

Renal glomerular hypoplasia is more common and cases tend to be asymptomatic with stunted growth and chronic renal failure developing as yearlings (*q.v.*). Hypoplasia is diagnosed when one or both kidneys are smaller than 50% of normal or, in the case of unilateral hypoplasia, when the kidney is smaller than a normal kidney. The diagnosis can also be made when the renal mass is reduced by more than one half. However, these parameters may not be easily measured in the live horse and in any case **unilateral hypoplasia** may pass unnoticed. **Bilateral hypoplasia** usually leads to chronic renal failure at an early age.

Renal cysts

Cysts are more common in the cortex than medulla and vary in size from microscopic to large cysts that involve the whole kidney (either singly or in multiple forms). They are usually found incidentally at post mortem or ultrasound examination. They may have no material clinical consequence. It is important to differentiate congenital cysts from acquired cysts: congenital cysts have no scarring while acquired ones invariably have extensive scarring.

Polycystic kidneys

Numerous small, often loculated and variably sized cysts distributed through the cortex in particular are described. The kidneys can be massively enlarged and the expansion of the cysts causes pressure necrosis of the adjacent normal tissue. The condition is difficult to diagnose at an early age but ultrasonography of the kidneys is probably warranted in any young horse that fails to grow normally and particularly when there is evidence of micro- or macro-hematuria or renal failure (or both). The condition is untreatable. **Chronic renal failure** usually develops before 2–3 yr of age but a few cases have survived for longer.

Ureteral defects

Ureteral defects have been reported in both fillies and colts. This rare disorder can easily be confused with traumatic rupture of one or both ureters (*q.v.*). The clinical signs are dependent on the location of the ureteral defect and may range from **urinary incontinence** to **uroperitoneum** (*q.v.*). In some cases, leakage from the ureter fills the retroperitoneal space. In fillies this may cause bulging of the vagina and can then be mistaken for an **intact hymen**. If the retroperitoneal membrane ruptures, then the clinical signs and clinical pathologic changes are identical to those of a ruptured bladder.

Ectopic ureter

Ectopic ureter is the most commonly reported congenital anomaly of the equine urinary tract. Most of the reported cases occur in females but this may in part reflect that incontinence from birth is easier to recognize in females. The condition may develop when:

1. The ureteric bud (metanephric duct) fails to be incorporated into the urogenital sinus or fails to migrate into the bladder neck. In these cases the ureter opens into the vagina near the urethral papilla (or in males into the pelvic urethra near the seminal vesicles).
2. The mesonephric ducts fail to regress. The ureter opens anywhere along the vagina, cervix or uterus. This type does not occur in males.

Clinical signs

Cases are presented when **urine scalding** of the hindlegs is noticed; sometimes this occurs at a later age. The persistent dribbling is easily mistaken for a neurologic problem with the bladder (*q.v.*) but the two conditions affect different ages of horse. **Urine pooling in the vagina** can lead to infertility. Renal function is usually normal but the affected ureter may be grossly dilated and is often infected.

Diagnosis

The precise location of the opening can be visualized in some cases using vaginoscopy, but a contrast excretory urogram may be helpful. Cystoscopy will usually confirm the side of the missing ureter.

Treatment

Treatment usually involves **ipsilateral nephrectomy**. It goes without saying that it is imperative that the correct kidney is removed. Nephrectomy in the horse is a highly specialized procedure that is performed under lateral recumbency general anesthesia. The approach to the left and right kidneys is somewhat different but the surgeon will require to remove the 17th and possibly the 18th rib on the left side and the 16th or 17th on the right side before the kidney can be approached. Once the kidney is identified it can be freed retroperitoneally and the major vessels and ureter can be identified and ligated using an aneurysm hook. The procedure is well tolerated but complications during surgery from blood loss are often catastrophic. **Absolute asepsis** is essential.

Surgical **ureteral relocation** has been reported. This is technically even more difficult than nephrectomy and in any case the abnormal ureter may not function normally. In cases of ectopic ureter the sensible approach is to perform the relatively simpler nephrectomy.

Patent urachus

The urachus is the structure through which fetal urine passes into the allantoic cavity. Normally the urachus closes at birth but **incomplete closure** is a common abnormality of the equine urinary tract. It occurs more commonly in foals with **longer umbilical cords** or with partial torsion of the cord.

Clinical signs

A patent urachus may be present immediately following birth when **persistent dribbling of urine** from the umbilicus may be noticed. More usually, however, the navel is wet and inflamed as a result of the leakage of urine onto the umbilical remnants and surrounding skin. The umbilicus may appear normal during the first days of life but may subsequently become patent.

Urine leakage through the umbilicus may or may not be accompanied by leakage into the **abdominal cavity** or subcutaneous tissues of the abdominal wall. Sometimes the umbilicus remains normal and all urine leakage occurs into the abdominal cavity, presenting signs indistinguishable from **patent bladder syndrome** (*q.v.*).

Sometimes the urachus ruptures more distally than usual, allowing urine to pass into the abdominal musculature or the peritoneal cavity (or both). This is a possible complication of **dystocia** (*q.v.*) or cord tension at delivery (such as might occur during a standing delivery). The swelling may be differentiated clinically from a **hematoma** or **umbilical infection** because it may enlarge quickly and often becomes cold. Subcutaneous accumulation of urine, ventral abdominal swelling, stranguria, signs of colic, and distress are seen and then surgical intervention is essential. Where the condition is suspected, early surgery may be justified because urine is intensely toxic to the local tissues and extensive necrosis can make treatment impossible (or at least extremely difficult).

Patent urachus is also a common feature in older sick and debilitated foals and it is important to differentiate a congenitally patent urachus from an **acquired infected umbilicus** (*q.v.*). A simple patent urachus is not life threatening but a **septic umbilicus** may develop into or be part of a serious **neonatal sepsis syndrome** that can easily result in death.

Affected foals are often septicemic or hospitalized for treatment of prematurity, hypoxic–ischemic encephalopathy, or botulism (*q.v.*) and uroperitoneum is recognized later (e.g. after 5–10 days of treatment). Prolonged recumbency and bladder distension are likely risk factors. Again, urine may be seen to drip continuously from the navel and there may be some more obvious "squirting" during micturition. The inflamed and infected site represents a potential site for bacterial entry to the urinary tract and subsequent development of a local **omphalophlebitis** (*q.v.*) or ascending urinary tract infection, both of which may result in septicemia. Inappropriate weight gain (e.g. >2 kg in 24 h) is another common finding in hospitalized neonates that develop **uroperitoneum**.

Diagnosis

Detailed ultrasonographic examination of the umbilical structures should always be performed because it is sometimes very difficult to differentiate the various conditions on clinical appearance and palpable characteristics alone. Local aspiration of fluid and measurement of its creatinine concentration (two-fold or greater than in serum) may help to confirm the diagnosis.

Treatment

The care of a foal with a patent urachus is dependent on clinical preferences. When it is associated with septicemia and or umbilical stump infection or urachal rupture, a much higher clinician input is required. Underlying primary septicemia should be managed first.

For acquired patency (associated with sepsis) antibiotics are compulsory; if this alone fails to control the leakage within 5–7 days, surgery is probably indicated. A combination of Gram-negative and Gram-positive bacteria are usually implicated in sepsis, and a combination of **gentamicin** (6.0 mg/kg q 24 h) and **crystalline penicillin** (15 000–20 000 IU/kg q 6 h) is usually used by the IV route. Other effective antibiotics include **ticarcillin** (50 mg/kg q 12 h) and **amikacin** (6 mg/kg q 8 h). Third generation cephalosporins including **ceftiofur** (5 mg/kg q 12 h IV) or potentiated sulfonamides (35 mg/kg total substance q 12–24 h) can also be used but selection must depend on specific culture and sensitivity results. A few cases respond to local and systemic antibiotics alone and others respond to **local cautery** using swabs soaked in phenol, 7% iodine solution or silver nitrate styptic pencils (using silver nitrate or phenol swabs) and nursing of the umbilicus.

Provided the foal is not septicemic, **surgical removal** of the entire umbilical remnant is the best approach. Delays simply provide opportunity for deterioration and complication. Surgery removes all infected structures and frees the apex of the bladder from the urachal remnant. The surgical procedure is simple and is described in standard surgical texts.

Ruptured/patent bladder syndrome

Patent bladder affects approximately 1% of Thoroughbred foals; the prevalence in other breeds is not known but all may be affected. The perception that colt foals are more often affected has been challenged. Two distinct types of patency are recognized:

1. **Congenitally patent bladder** where the margins of the bladder defect are smooth and show no evidence of an inflammatory/traumatic origin. Such cases may result from failure of embryologic bladder fusion in the dorsal fold during development. There may be one or more small defects but they can also be extensive.
2. **Traumatic rupture:** Here the defect is hemorrhagic and gives every impression of being a traumatic tear; however it occurs also in the dorsal wall of the bladder, implying that this area may be weaker than other regions.

Because the signs are identical, the clinical syndrome should also include **ureteral rupture**. This syndrome usually occurs as a result of **rib fracture**, often assumed to be a result of abdominal pressure on a distended bladder during parturition or, more likely, trauma in the immediate post birth period. In some of these cases the accumulation of urine can be retroperitoneal and so there may be few easily detectable early indications of the problem.

It is generally assumed that most traumatic ruptures occur during parturition and clinical signs then develop progressively over 36–96 h, but older foals may also have spontaneous ruptures of the bladder or umbilical vessels as a result of local necrosis of these structures, occurring secondary to ascending umbilical infection or cystitis (*q.v.*).

Uroperitoneum may also develop in foals with urachal infection or ischemia (*q.v.*). Disruption of the urachus at the level of the abdominal wall will lead to subcutaneous fluid accumulation and gross local swelling, usually without the severe metabolic/systemic signs associated with a patent bladder.

For practical purposes the etiology is irrelevant as the clinical and pathophysiologic problems are identical. The treatment may, however, vary somewhat.

Clinical signs

Affected foals are usually normal at birth and have a normal post partum adaptive period. They usually feed well and show no problems until 36–96 h of age. The **absence of urine** is highly significant but, remarkably, is easily missed except on higher quality breeding farms. The passage of a normal stream of urine does not necessarily eliminate the possibility of a ruptured bladder because the defect may be small.

The first signs are non-specific and are easily overlooked. The foal shows progressive reluctance to feed properly (**decreased nursing time**), lethargy, depression and increased time spent in recumbency. The foal may exhibit dysuria or pollakiuria with repeated straining and posturing as if to urinate (hindlegs stretched out and the back concave). The other major cause of abdominal straining is **meconium retention/impaction** (*q.v.*) but this usually affects foals within 24 h of birth and they strain with back arched. They also show more overt colic signs.

Abdominal distension may be obvious but if the defect is small this may not be a major feature. **Respiratory distress** secondary to diaphragmatic compression may also be noted. Fluid within the abdomen can usually be identified by ballottement, paracentesis, ultrasonography and standing lateral radiographs.

In the later stages the foal will be reluctant to stand and then unable to stand. Seizures and cardiac arrhythmia may develop secondary to the azotemia and electrolyte imbalances. Cardiac dysrhythmia is usually detectable when plasma K^+ concentration >6.5 mmol/L.

Diagnosis

Ultrasonography can confirm the volume of fluid and even the site and extent of the defect. This technique is totally safe and is recommended in all suspected cases. It may be possible to identify retroperitoneal fluid accumulation. Hyponatremia, hypochloremia and hyperkalemia are highly suggestive of a ruptured bladder. Foals are also azotemic and acidotic but both erythrocyte and leukocyte profiles are usually normal in early, uncomplicated cases. Guided **paracentesis** and standing lateral radiographs are helpful. Comparing the creatinine concentration of abdominal fluid with that in plasma can confirm ruptured bladder. If the peritoneal fluid to plasma creatinine ratio is $>2:1$ then uroperitoneum is present. Additional diagnostic procedures such as injection of dyes into the bladder and retrieval via abdominocentesis and single/double contrast cystography are generally not required.

Treatment

All foals with a ruptured bladder require **surgical correction**. It is neither safe nor wise to rely upon indwelling urinary catheters. Affected foals should, however, be stabilized prior to anesthesia by removal of accumulated urine and restoration of **normal electrolyte status** by infusion of normal saline and possibly bicarbonate solutions IV to normalize the acid-base status. Infusions should be adjusted carefully to address identified deficits by regular electrolyte

and blood gas analysis. Slow draining of abdominal fluid by placement of a **peritoneal cannula** during the preliminary stabilization stage also removes nitrogenous products that can lead to a chemical peritonitis and decreases diaphragmatic compression.

IV fluid therapy with normal saline (0.9%) is essential. Saline replaces Na^+ and Cl^- deficits while supporting and expanding the circulating volume. Sodium bicarbonate may be administered if the foal is acidotic*; dextrose (5%) will help to stabilize the potassium distribution. **There is no possible indication for fluids containing potassium**. If cardiac arrhythmia (*q.v.*) secondary to the hyperkalemia (flattened P waves, widened QRS complexes and spiky T waves on electrocardiography) is present, calcium may be helpful. Diazepam (5–20 mg to effect) can be used IV to control seizures.

Once the patient is stabilized, surgical repair of the bladder defect can be performed. The surgical procedure is performed through a paramedian incision in dorsal recumbency. The procedure is described in standard texts. When the leakage site involves the abdominal umbilical vessels, routine removal of the umbilical remnants (see below) will resolve this problem. Foals that fail to respond adequately to bladder surgery may need further tests to evaluate the ureters for tears (*q.v.*) or for failure of the bladder closure and so careful postoperative monitoring for 7 days is essential.

RENAL DISORDERS

INTRODUCTION

The perceived incidence of renal disease in the horse is low compared with other domesticated species. For practical purposes renal disease is divided into **acute or chronic renal failure.** The clinical circumstances that predispose to renal failure are common, although failure usually remains undetected until some 75% of the functional reserve is lost. At this stage both **uremia** and **azotemia** are detectable.

Over 95% of the filtered water is reabsorbed by the renal tubules and so even small decreases in the absorptive capacity of the tubules will have a disproportionately large effect on urine volume; often even a slight reduction in water absorption by the tubules will result in doubling of the urine output. Renal failure is the term used to describe the state in which renal function cannot maintain normal homeostasis.

The ability of the kidney to concentrate urine declines when 75% of the functioning nephrons have been destroyed. The main clinical feature will be water loss (and consequent **polydipsia**). Renal failure is characterized by a fall in the GFR, which leads to an increase in the circulating concentration of nitrogenous waste products (azotemia).

Two major types of renal failure are recognized clinically:

1. **Acute renal failure:** Acute renal failure means abrupt failure of renal excretory function owing to depression of the glomerular filtration.

* The volume (mL) of molar (8.4%) bicarbonate required can be calculated from the equation: Base excess × 0.3 × body weight (kg).

2. **Chronic renal failure:** The distinction between acute and chronic renal failure is not always clear from either the clinical or biochemical investigations. It is entirely possible that an acute episode can be superimposed on the chronic state, and progression to chronic renal failure is a common sequel to profound or long-standing acute renal failure or where treatment for acute renal failure is inappropriate or inadequate.

A raised serum urea concentration (azotemia) may arise from:

1. Pre-renal problems
2. Renal disease
3. Post-renal problems (obstruction).

More than one of these may be present at the same time in an individual patient. Azotemia is often the **first indicator** of renal dysfunction in the horse since earlier clinical signs may be non-specific.

The diagnosis of renal disease centers on detection of **failure of function**. Failure to clear waste products is identified by a fall in the GFR and/or the presence of azotemia (*q.v.*). Loss of water and electrolyte homeostasis is identified by abnormal changes in the urinary specific gravity, tubular function tests and plasma electrolyte concentrations. In addition, evidence of kidney damage may be revealed by abnormal inclusions in the urine (proteinuria, glycosuria, cells and casts), while anatomic changes may be appreciated by palpation, ultrasonography and, if appropriate, biopsy (*q.v.*).

Collectively, this information provides an objective measure of the extent of dysfunction and even possibly the etiology. However, the specificity and sensitivity of many of the tests currently used is questionable.

ACUTE RENAL FAILURE

Acute renal failure (ARF) in adults and foals is a clinical syndrome associated with **abrupt reduction of glomerular filtration** and is usually a consequence of:

1. Pre-renal factors, which reduce vascular perfusion.
2. Renal (intrinsic) factors, e.g. hypoperfusion or ischemia. Ischemic (vasomotor nephropathy) or toxic damage to tubules, tubular obstruction, acute glomerular nephritis leading to primary reduction in filtration capacity of the glomeruli and interstitial inflammation and edema are primary causes of intrinsic renal failure.
3. Post-renal urinary obstruction.

Examples of the factors responsible for its development are listed in Box 12.5.

Etiology

Renal tubular epithelial cell degeneration or (tubular) necrosis may follow prolonged renal ischemia from any of the pre-renal vascular disturbances but **nephrotoxic chemicals** and drugs, particularly the **aminoglycoside antibiotics**, are most commonly implicated.

The etiology in foals is often subtly different from adult horses but the principles of diagnosis and management are similar. In foals there is perhaps an

Box 12.5 Examples of factors associated with the development of acute renal failure in the horse

Pre-renal factors
- Dehydration
- Endotoxemia
- Hemorrhage
- Cardiovascular insufficiency

Intrinsic factors
- Prolonged pre-renal disturbance
- Nephrotoxins
  - Drugs
  - Toxic plants
  - Mycotoxins
  - Heavy metals
  - Hemoglobinuria
  - Myoglobinuria
- Intrinsic diseases
- Glomerulonephritis
  - Pyelonephritis
  - Renal lithiasis
  - Hydronephrosis
  - Neoplasia

Post-renal factors
- Urolithiasis (ureter/bladder/urethra)
- Bladder rupture
- Urethral trauma
- Obstructive neoplasia

even more pressing need to recognize and counter the condition because of the fragility of the neonatal physiology and lack of renal maturity. Foals that experience dystocia, premature placental separation or placentitis (*q.v.*) may become hypoxic during birth and also develop acute renal failure.

Acute tubular necrosis is the most common pathologic lesion causing ARF in **neonatal foals** arising from hemodynamic or nephrotoxic causes but it is also an important cause in **adult horses**.

Hemodynamic causes of acute tubular necrosis occur most commonly in septicemic foals or in foals with acute diarrhea where severe volume depletion and renal ischemia predispose to renal damage. Many cases are identified during or after episodes of diarrhea and are probably a direct consequence of poor renal perfusion. Surprisingly, diarrhea-related ARF does not always seem to be associated with the severe forms of diarrhea.

In both foals and adult horses, **hydration and electrolyte status** are critical factors in the safe use of potentially nephrotoxic drugs; a well-hydrated patient with normal electrolytes will tolerate the drugs much better than a dehydrated patient with concurrent diarrhea, septicemia or endotoxemia.

Nephrotoxicity from endogenous toxins (e.g. hemoglobin, myoglobin) or exogenous toxins (e.g. aminoglycosides, tetracyclines, non-steroidal anti-inflammatory agents) is another significant cause of ARF. **Aminoglycoside toxicity** is probably the most significant cause of toxigenic acute renal failure in foals and to a lesser extent in adult horses. These antibiotics have a direct toxicity to tubular cells in which they selectively accumulate. Healthy kidney tolerates a single overdose without detectable detriment, and toxicity is much more likely with prolonged high doses in excess of 10 days.

Gentamicin (6 mg/kg q 24 h) or **amikacin** (6.0 mg/kg q 12 h) may be safely administered for >10 days if the patient is adequately hydrated, appropriate trough concentrations in the plasma are measured and normal creatinine concentrations are maintained. Single daily doses of gentamicin are microbiologically effective but significantly reduce nephrotoxicity. Sick neonates are often critically ill and/or dehydrated and are at much greater risk. Regardless of which aminoglycoside antibiotic is selected, monitoring **trough concentrations** (<2 μg/mL for gentamicin and <4 μg/mL for amikacin) will limit the risks.

Premature foals appear to be at even greater risk of nephrotoxicity. Carefully planned fluid therapy to correct dehydration and maintain blood pressure will reduce the risks considerably.

Multifocal renal abscesses and/or septic embolism as a complication of neonatal septicemia can lead directly to ARF. Infection is caused by a mixed population of both Gram-positive and Gram-negative bacteria. *Actinobacillus equuli* (*q.v.*) is the most common pathogen causing renal abscesses. It has a predilection for renal tissue and may infect foals in utero or within the first 48 h of life, producing septicemia. Affected foals usually die acutely from septic shock before clinical signs of ARF develop or, if they survive long enough, may develop purulent glomerulonephritis.

Inflammatory parenchymal diseases are rarely reported in adult horses. Some inflammatory conditions are unilateral; because of compensatory activity by the healthy kidney there will be no overt or biochemical evidence of renal failure.

Pre-renal factors are probably the most common cause of ARF. Sustained, marked hypotension and hemodynamic disturbances that impair renal perfusion such as acute diarrhea, endotoxemia or toxic forms of colic (*q.v.*) have the potential to cause ARF because they are associated with **hypovolemia** and **circulatory insufficiency**. Hemorrhagic shock, severe intravascular volume deficit (as with **enterocolitis**), septic shock and coagulopathy (*q.v.*) are important risk factors for vasomotor acute renal failure. In these cases the primary condition may be the major concern but the renal effects are important.

Vasomotor nephropathy results from renal vascular constriction as a result of endogenous pressor agents. The predominant lesion in vasomotor nephropathy is acute tubular necrosis, although diffuse renal cortical or renal medullary necrosis may occur in some cases.

Non-steroidal anti-inflammatory drugs (NSAIDs) can cause **medullary crest necrosis**, detectable as gross or micro-hematuria but, unless this is severe, clinical signs and creatinine elevations are unlikely; indeed, creatine concentrations may actually fall. Most horses show no obvious adverse effects to NSAIDs (*q.v.*) so long as the dose, frequency and courses are correct and they are **not dehydrated**. Excessive doses, over-frequent administration, dehydration, gastrointestinal disease (ulceration) and protein-losing enteropathy and other concurrent

nephrotoxic drugs may precipitate an **acute renal failure crisis**. A single overdose or prolonged low-dose course of NSAIDs in normally hydrated healthy horses is unlikely to cause significant damage. The use of NSAIDs in dehydrated or hypovolemic patients increases the risk of acute renal failure. **Chronic interstitial nephritis** and **nephrolithiasis** (*q.v.*) have been reported in some horses receiving high doses of NSAIDs over long courses (months to years).

Organic or inorganic mercury, cadmium, zinc, arsenic and lead salts (*q.v.*) are nephrotoxic and accidental ingestion may result in acute tubular necrosis and ARF. The clinical effects are widespread and renal failure (either acute or chronic) is unlikely to be the main or only clinical sign. If ingestion is suspected then a **full forensic analysis** is warranted.

Pigment nephropathy (*q.v.*) may arise from either hemoglobinuria or myoglobinuria. Although many texts describe the development of acute tubular necrosis and ARF secondary to rhabdomyolysis (*q.v.*), this is in fact uncommon unless the condition is severe and prolonged. Hemolysis is an even less common cause of pigment nephropathy than myopathy. However, cases with severe hemolysis or those with hemolysis accompanied by disseminated intravascular coagulopathy are at significantly greater risk.

Subclinical glomerular damage also accompanies a number of other diseases, especially immune-mediated disorders such as purpura hemorrhagica (*q.v.*), but ARF is rarely significant unless any of the factors listed in Box 12.5 are present.

ARF can also be caused by infection with *Leptospira interrogans* serovar *pomona* but this is poorly documented in horses. **Leptospirosis** (*q.v.*) should be included in the list of possible causes of ARF when an underlying primary disease leading to vasomotor nephropathy is not apparent and there has been no exposure to nephrotoxins.

Clinical signs

Acute renal failure may be transient (subclinical) if hypotension or vasomotor constriction to the kidneys is corrected quickly and there are no other complicating factors. Also, it is **usually reversible** over a period of days or weeks depending upon the severity of the causative insult and the effects of treatment and elimination of causative factors. If a state of ARF is sustained for any significant time **azotemia** (*q.v.*) will develop.

Depression and subcutaneous and pulmonary **edema** are early signs in foals. **Oliguria** or even **anuria** can develop 12–24 h before significant depression or azotemia is recognized. Urine output should be carefully monitored in all sick foals. **Fluid retention** during incipient ARF can be detected from inappropriate weight gain (e.g. >2 kg in 24 h).

Because of the range of clinical disorders that can provoke pre-renal failure, the presenting signs may simply reflect the primary disease. For example, acute diarrhea, colic, laminitis or hemolytic anemia (*q.v.*) may predispose to renal failure yet mask its clinical expression. In other cases, azotemia may be associated with moderate to profound **depression**.

The volume of urine passed may vary from low (oliguria) to excessive (polyuria). **Oliguria** is typical in early stages as the GFR falls and the resulting urine is usually concentrated (high SG). As tubular damage progresses the urine becomes progressively more dilute. **Urine color** may therefore vary

between normal (concentrated), pale (dilute), or discolored (e.g. hematuria). There are concurrent disturbances of fluid, electrolyte and acid-base balance and these can be life threatening.

Although the clinical signs of the primary condition vary and may mask evidence of ARF, a **disproportionate depression** and anorexia with or without signs of mild colic are suggestive of ARF. Nephrotoxic ARF should be considered when horses being treated with aminoglycosides become inexplicably depressed and inappetant within 2–3 days of the start of treatment.

Polyuria may be detected before the onset of depression and anorexia or, if the patient becomes oliguric, mild **stranguria** and repeated posturing to urinate may be observed. Ataxic or manifest neurologic signs similar to **hepatoencephalopathy** (*q.v.*) may be seen in severe ARF.

Although grossly discolored **pigmenturia** is not a prerequisite for the development of renal failure in cases of azoturia or intravascular hemolysis, ARF should be suspected in horses that become anorectic and depressed within 7 days of an episode of tying-up (*q.v.*) or a hemolytic crisis.

Infectious acute renal failure is characterized by fever, partial anorexia, depression and gross hematuria. Rapid development of azotemia and low urine specific gravity (<1.020) without bacteriuria may be encountered.

Post-renal obstructions leading to renal failure present with overt discomfort, anuria and/or dysuria.

Rectal palpation may reveal enlarged, painful kidneys in some cases of ARF and any enlargement can be confirmed by renal ultrasonography. **Renal ultrasonography** may also reveal perirenal edema, loss of corticomedullary distinction and/or renal pelvis dilatation. Obstructions of the lower urinary tract are easily recognized per rectum unless the bladder has ruptured.

Diagnosis

A diagnosis is confirmed from history, potential exposure to nephrotoxins, clinical signs and laboratory findings. ARF should be suspected in patients showing **more marked depression** and anorexia than would be expected with the primary disease process and in patients that fail to produce urine within 6–12 h of initiating fluid therapy. A tentative diagnosis of nephrotoxicity can be based on a history of **aminoglycoside use** (*q.v.*) and azotemia plus enzymuria with the presence of casts in the urine. The increase in **creatinine** (*q.v.*) is much greater than increases in blood urea, often resulting in a urea–creatinine ratio <10:1. Hyponatremia, hypochloremia and hypocalcemia are usually present and, in more severe cases, hyperkalemia, hyperphosphatemia and metabolic acidosis may also be detected.

Seroconversion or high serum titers and positive fluorescent antibody test results for *Leptospira* spp. (*q.v.*) confirm exposure to the bacteria.

Urinalysis should be performed on all horses in which ARF is suspected:

1. A **low urine specific gravity** (1.020 or less) in the face of dehydration and gross or microscopic hematuria are common findings with ARF.
2. Proximal tubular damage results in **increased urinary gamma glutamyltransferase** (GGT) activity and/or glycosuria.
3. Significant **proteinuria** (urine protein to creatinine ratio >2:1) supports a diagnosis of glomerular disease.

4. Urine **sediment** may reveal casts and increased numbers of erythrocytes and leukocytes while subjectively the amount of urine calcium carbonate crystals may be decreased.
5. Increased **fractional clearances** of sodium and phosphorus are also common. However, administration of IV fluids to healthy horses will also result in increased fractional clearances of sodium, chloride and phosphorus and so electrolyte clearances should be determined using the initial urine sample voided after admission or a sample collected via catheterization before urine could be altered by fluid therapy.

The most accurate assessment of renal function involves measurement of **glomerular filtration rate (GFR)** but this is seldom pursued in practice. Changes in GFR can be more practically assessed by **daily creatinine estimation**.

Glomerular injury can be confirmed by renal biopsy (*q.v.*) but this is rarely indicated in cases of ARF because the diagnosis is usually obvious and there are significant dangers of life-threatening hemorrhage with the procedure. Renal biopsy is mostly indicated in the evaluation of horses with ARF for which no clinical or historical cause can be established.

Response to fluid therapy is an important consideration, especially in oliguric acute renal failure. Oliguria that fails to resolve in spite of fluid therapy is an early indicator of vasomotor acute renal failure. Production of dilute urine (specific gravity <1.020) that may be discolored through hematuria and/or hemoglobinuria may be observed once urination is re-established. Even if urine is "clear", micro-hematuria is usually present; this will be detectable with a **urine dipstick**. Proximal tubular damage may also impair tubular resorption of glucose and so **glycosuria** (*q.v.*) will be present (also detectable on dipstick).

Serum creatine kinase and aspartate aminotransferase are invariably elevated during any (even a mild) episode of rhabdomyolysis (*q.v.*). Since there is little preformed creatinine in muscle, rhabdomyolysis alone does not produce an increase in creatinine and so any elevations are likely the result of ARF.

Management

Treatment of ARF in all ages of horse centers on correction of the primary problem. Restoration and maintenance of the hydration status through twice daily measurement of body weight and repeated blood analysis are important.

Infection control

Control of infection with appropriate antimicrobial therapy is essential, especially in foals, but unless this is carefully planned it may simply shift the problem to toxic nephropathy. Ideally, all **nephrotoxic agents** should be discontinued; this is usually impossible in septic foals because the **aminoglycosides** are by far the best approach to many neonatal infections. If septic embolism/septicemia is suspected, IV therapy with combination of **penicillin and gentamicin** (*q.v.*) for a prolonged period is recommended. Careful planning, determination of plasma aminoglycoside concentrations and adjustment of the dosage will limit renal tubular damage.

Urine output measurement

Urine output must be monitored in all septic and diarrheic foals; if oliguria or anuria develop IV fluid therapy is essential:

1. Physiologic (0.9%) saline or a 5% dextrose solution is the ideal fluid. Hydration is maintained so as to restore deficits and ensure a suitable maintenance flow. A 50 kg foal that is 5% dehydrated will need a volume of 1 liter of fluid and then maintenance at 5–10 mL/kg/h.
2. Fluids with potassium must be avoided since hyperkalemia is a complication with potentially fatal consequences.
3. Fluids must be carefully monitored in conjunction with urine output; excess fluid can cause volume overload and pulmonary edema, which will cause a progressive increase in the foal's respiration rate.

If the foal fails to urinate in response to fluids, then low-dose **dopamine** (2–5 μg/kg/min IV) should be administered. Higher concentrations should not be administered as renal artery vasoconstriction will occur and complicate the problem. The diuretic **furosemide** (0.5–1 mg/kg IM or IV) can also be administered, as it is **synergistic** with dopamine in inducing urine production. If the foal still fails to urinate, IV **mannitol** or **dialysis** may be considered.

Dialysis

Dialysis is usually restricted to transperitoneal separation in foals only. Arterial dialysis has been described but it is an almost impossible technique in practice. Peritoneal dialysis is a mechanism for temporary reduction of nitrogenous and other waste materials that will diffuse across the peritoneal lining into an electrolyte introduced into the peritoneal cavity. Usually a volume of **Hartman's solution (Ringer lactate)** or **saline** (up to 3–5 L) is introduced into the peritoneal cavity and this is left in situ for up to 230 min before draining via a dependent egress port. In the foal a continuous flow mechanism can be used whereby fluid is run into the peritoneal cavity and simultaneously drained from a dependent point through a one-way valve system. Progress is monitored by repeated estimations of urea and creatinine. Complications include peritonitis (*q.v.*) and repeated blocking of the egress drain. If sedation or analgesia (or both) is necessary, **xylazine** (1 mg/kg IV) or **detomidine** (0.03 mg/kg IV) can be administered provided intravascular volume and blood pressure are not overly compromised. Peripheral vasodilators and hypotensive agents (e.g. acepromazine) should not be used.

General principles of fluid therapy

Because ARF is usually (but not always) treatable, the essential principles in treating uncomplicated cases are to identify and remove the underlying cause while correcting fluid, electrolyte and acid-base imbalances. The extent of azotemia and serum concentrations of sodium, chloride, potassium and bicarbonate must be closely monitored, at least once daily.

The causes of ARF may be more obvious to the clinician than the state of renal insufficiency they produce. Hemodynamic disturbances such as acute diarrhea, hemorrhage, congestive heart failure and bacterial toxemia should

be treated appropriately. Potential **iatrogenic causes** of tubular necrosis (nephrotoxic drugs) should be withdrawn.

After correction of volume deficits and electrolyte and acid-base abnormalities, an attempt should be made to determine whether the animal is oliguric or non-oliguric (polyuric); the prognosis for recovery is more favorable with **non-oliguric acute renal failure**.

In all cases, initial treatment is centered on **rational fluid therapy**. Sodium and chloride replacement can be accomplished by using 0.9% NaCl IV and/or oral replacement therapy until hydration and electrolyte status are normalized. Serum potassium concentrations should not be required unless there is a post-renal obstruction or rupture of the urinary tract. Correction of the mild hypocalcemia should not be needed.

Large volumes of fluid may be given by **nasogastric tube** providing there is no concurrent gastric reflux. Up to 8 L warm water or isotonic electrolyte solution may be given to a 500 kg horse and repeated every hour providing reflux is checked before administration. In critical cases, sterile fluids can be given rapidly IV at 10 L/h if two veins are catheterized simultaneously.

In **non-oliguric cases**, once volume deficits have been replaced IV saline is maintained by infusion until a marked fall in serum creatinine concentration is achieved. Fluid volume replacement is then reduced until a steady state is obtained. During infusion the **conjunctivae** should be examined periodically for evidence of edema (chemosis) indicative of **over-hydration**. Diuretics are usually unnecessary in non-oliguric cases. Non-oliguric horses pass moderate volumes of dilute urine during the initial 6–12 h of treatment.

With **pre-renal azotemia**, creatinine should decrease by at least 30–50% within the initial 24 h of fluid therapy. In intrinsic ARF creatinine remains unchanged or may even increase during the fluid therapy. Some horses may remain hypotensive (systolic pressure <80 mmHg) despite administration of large volumes of IV fluids because fluid accumulates extravascularly as edema or is sequestered into the abdomen, chest or lungs. If systemic blood pressure remains low, hypertonic saline, dobutamine and/or or other pressor agents may be needed to restore blood pressure and glomerular filtration.

The position is significantly different in **oliguric ARF**. Oliguric horses fail to produce expected amounts of urine in the initial 12–24 h of IV fluid therapy and the bedding remains dry. Edema (fluid overload) can develop rapidly in horses with oliguric acute renal failure. Fluid and electrolyte replacement should be followed by diuretic treatment. Parenteral furosemide stimulates urination within 30–60 min and so requires repeated dosage (1 mg/kg q 2 h). Continued fluid administration should be restricted to maintenance requirements (20–50 mL/kg/day) and overhydration (indicated by chemosis) avoided. Fluid and sodium replacement and normal systemic blood pressure must be monitored closely because excessive fluid will result in **generalized edema**, which may initially be seen as chemosis (conjunctival edema).

If oliguria persists after 12–24 h of appropriate fluid and electrolyte replacement and restoration of systemic blood pressure, **furosemide** (1 mg/kg IV q 2 h) should be administered. However, this is often ineffective in increasing renal blood flow, GFR and tubular flow in horses with acute renal failure. If urine is not voided after the second dose, administration of **mannitol**

(1 mg/kg as a 10–20% solution) and/or a **dopamine** infusion (3–7 μg/kg/min IV) can be instituted.

If over 24–72 h this approach converts oliguria to polyuria, treatment can be discontinued; however, continued close monitoring is required over the next few days.

Fortunately, the majority of horses with ARF resulting from **acute tubular necrosis** (ATN) are non-oliguric rather than oliguric, and administration of furosemide, mannitol or dopamine is not needed in most of cases of non-oliguric acute renal failure. As long as the horse is eating and drinking well, IV fluids can be discontinued.

Monitoring therapy

Repeated **monitoring of vital signs** (body temperature, heart and respiratory rate, capillary refill time and body weight), hematocrit and total plasma protein concentration must be undertaken. Twice daily body weight measurement may be the only indicator of fluid retention (patients should not gain weight after rehydration); this is particularly obvious in foals (see above). Careful recording of fluid intake (oral consumption plus fluid therapy volume) and urinary output is helpful.

If treatment for oliguria is unsuccessful for >72 h, the prognosis becomes grave and **dialysis** (*q.v.*) is indicated. However, peritoneal dialysis (or hemodialysis) is a specialized procedure (*q.v.*) and the complications are probably a strong deterrent.

After volume deficits have been restored and polyuria has been achieved, fluid therapy (0.9% NaCl or another balanced electrolyte solution, 40–80 mL/kg/day) is maintained to promote a continued decrease in creatinine. **Fluid therapy** may need to be continued (20–40 mL/kg/day) for several days until creatinine returns to reference values and the horse is eating and drinking adequate amounts. **Oral salt** (25–50 g twice daily) will encourage drinking and diuresis. **Potassium chloride supplementation** (25 g twice daily) helps to balance urinary losses. If the patient remains anorexic, 50–100 g of dextrose per liter of fluids is helpful but if anorexia persists for several days caloric intake may need to be provided by nasogastric tube feeding or total parenteral nutrition.

Creatinine should be measured within 3–5 days of cessation of therapy to ensure that it has not increased. Occasionally, creatinine may not decrease to below 2–3 mg/dL despite continued fluid therapy. In some horses a normal creatinine will only be achieved after some months but continued measurements should establish a "beneficial" trend. Some cases have a persistently elevated creatinine indicative of a permanent loss of renal function and a shift to chronic renal failure (*q.v.*).

Obstructive causes of renal failure usually require **surgical treatment** together with correction of fluid, electrolyte and acid-base balance.

If an **infectious cause** is suspected antibiotics are indicated but care should be taken in the selection to ensure maximal tubular distribution without toxicity. Successful treatment has been accomplished with IV fluids and penicillin (15 000–25 000 IU/kg q 12 h) using either IM **procaine benzylpenicillin** or IV **sodium benzylpenicillin**. The treatment course often needs to be at least 5 days.

Prognosis

The prognosis for ARF depends on the duration and severity of the problem as well as the ability to eliminate the primary problem. It would seem reasonable to assume that foals that have suffered from ARF will have an increased risk of developing chronic renal failure in later life but this is not yet established.

Non-oliguric to polyuric acute renal failure generally has a favorable outcome as long as the duration of ARF is limited, the underlying disease processes can be corrected, and there are no complications that cannot be removed or treated, such as concurrent treatment with other **nephrotoxic drugs** such as non-steroidal anti-inflammatory drugs (phenylbutazone in particular).

The prognosis for oliguric cases is much poorer and there is a higher tendency to progression to **chronic renal failure**. However, prompt diagnosis and rational treatment improves the outlook. The well-being of the patient is often a good index of the effects of treatment. Progressive dullness and inappetance indicates that the problem is not being controlled effectively. If this state persists, **acute tubular necrosis** (*q.v.*) will develop and the prognosis is correspondingly worse.

CHRONIC RENAL FAILURE

Chronic renal failure (CRF) is an **irreversible state**, caused by a progressive intrinsic disease of both kidneys and characterized by a progressive decline in GFR, in which there is an **absolute loss** of functional nephrons. CRF may be divided by clinical and pathologic findings into two broad primary categories:

1. Glomerular disease
2. Tubulointerstitial disease.

Pathology in one portion of the nephron usually leads to altered function and eventual pathology in the entire nephron. Primary lesions are rare but include **progressive tubular necrosis** (unresolved acute tubular necrosis), **pyelonephritis** (possibly in association with urolithiasis), **glomerulonephritis** (usually immune mediated), **amyloidosis** and **neoplasia**.

Etiopathogenesis

Primary glomerular diseases that can lead to CRF in horses include:

1. Glomerulonephritis
2. Non-specific glomerulopathy
3. Renal glomerular hypoplasia
4. Amyloidosis.

Glomerulonephritis is the most common glomerular disease causing CRF. Most cases are **immune mediated**, resulting from immune complexes being deposited along the glomerular capillaries or in situ formation on the glomerular basement membrane (suggesting a type III hypersensitivity). **Streptococcal antigens** (*q.v.*) have been suggested as an important trigger for development of proliferative glomerulonephritis. However, immune complex deposition is far more frequent than CRF so a more complex pathogenesis is likely.

Tubulointerstitial diseases causing CRF (also called chronic interstitial nephritis) include:

1. Incomplete recovery from acute tubular necrosis
2. Pyelonephritis
3. Nephrolithiasis
4. Hydronephrosis
5. Renal dysplasia.

Chronic interstitial nephritis (CIN) and fibrosis may be the most common cause of CRF in horses. Interstitial nephritis (tubulointerstitial disease) usually develops as a sequel to acute tubular necrosis (*q.v.*) consequent to exposure to **nephrotoxins** or **vasomotor nephropathy** (*q.v.*). Other causes include drug-induced interstitial nephritis, urinary obstruction, pyelonephritis, renal hypoplasia/dysplasia, and papillary necrosis (a feature of non-steroidal drug use).

Although the majority of horses that develop ARF attributable to these causes recover with apparently normal renal function (they remain non-azotemic), a few may survive with significant loss of renal functional mass and subsequently (**often years later**) develop signs of CRF attributable to chronic interstitial nephritis.

In horses <5 yr of age that develop CRF that cannot be attributed to other causes, anomalies of development including renal hypoplasia, dysplasia, or polycystic kidney disease (*q.v.*) should be strongly suspected.

Bilateral septic pyelonephritis is a result of an ascending infection, but is a very rare cause of CRF. It is often accompanied by nephrolithiasis and/or ureterolithiasis (*q.v.*). Possible instigating or predisposing conditions include dystocia, bladder paralysis and bladder neoplasia (*q.v.*). Gram-negative organisms appear to be the most common causative agents, although *Staphylococcus* spp., *Streptococcus* spp. or *Corynebacterium* spp. may be isolated, and mixed bacterial infections are not uncommon.

Rarer causes of CRF in horses include renal (or generalized) amyloidosis, neoplasia, focal glomerulosclerosis-like disease, and chronic oxalate nephrosis; the latter is most probably a consequence, rather than a cause, of CRF.

Unfortunately, because renal disease is invariably advanced on first presentation, the inciting cause is difficult to establish, and **end-stage kidney disease (ESKD)** may be the only realistic pathologic diagnosis. Possible causes may be deduced from the history rather than clinical findings at presentation, especially for primary tubulointerstitial diseases. Supportive laboratory assessment, renal ultrasonography and renal biopsy seldom confirm the primary condition.

Clinical signs

Chronic (progressive) weight loss is the most common clinical sign of CRF. A small **plaque of edema** between the forelimbs occurs commonly but large plaques of ventral edema and filling of the limbs are less common. Patients are frequently oliguric; moderate polyuria and polydipsia (PU/PD) (*q.v.*) are usually present but may not be noticed by the owner. Lethargy and weakness and anemia (hematocrit 20–30%) from decreased renal erythropoietin production are fairly constant but non-specific findings. Dysuria is not reported unless there is underlying pyelonephritis, bladder paralysis, lithiasis (in ureter or bladder),

lower urinary tract infection or neoplasia (*q.v.*). Significant alterations in urine composition may help to support the diagnosis in some of these cases. Hematuria (gross or microscopic) or pyuria may be present with pyelonephritis, urinary calculi or neoplasia. Although abdominal pain would be expected, colic signs are seldom reported in horses with obstructive nephroliths or ureteroliths.

The loss of calcium excretory function and renal mucus production, and the consequent polyuria result in a **characteristic water-clear high volume urine output**. Accumulation of **dental tartar**, especially on the incisors and canine teeth, **melena** and **oral ulcers** are other occasional findings.

Growth and performance may be reduced in horses with renal hypoplasia, dysplasia or polycystic kidney disease (*q.v.*).

Diagnosis

A diagnosis of CRF is most commonly made in horses presented with weight loss and/or decreased performance with azotemia and isosthenuria[1]. A horse may be azotemic for a considerable period without showing obvious clinical signs. It can therefore be difficult to differentiate between acute and chronic failure since acute onset of signs may occur in both situations. A definitive diagnosis of renal failure relies on **combinations of biochemical tests**.

Moderate to severe azotemia (creatinine concentration >200 μmol/L) is usual. The urea to creatinine ratio may vary according to protein intake, muscle mass, hydration and degree of azotemia but is usually 10:1 or greater. Mild hyperkalemia, hyponatremia and hypochloremia are commonly found. Hypercalcemia, with serum concentrations sometimes exceeding 9–12 mol/L, is sometimes **but not always** found; actual concentrations vary according to diet and extent of azotemia. Serum inorganic phosphate concentration is usually normal to decreased. Metabolic acidosis is a common finding with ESKD.

Hypoproteinemia (mainly hypoalbuminemia) is associated with protein losing nephropathy and intestinal ulceration. Hyperglobulinemia may be detected in horses with immune-mediated diseases or chronic pyelonephritis (*q.v.*).

Urine is transparent and typically **isosthenuric** (SG 1.008–1.014), although heavy proteinuria may increase this to 1.020. Quantification of proteinuria requires biochemical tests rather than a dipstick test. The urine protein–creatinine ratio is usually >2:1. In the earlier stages of glomerulonephritis excessive urine protein is primarily albumin, but with progression of glomerular pathology an increasing amount of globulin is also lost in the urine. Horses with CIN usually do not have significant proteinuria.

Pyuria (>5 leukocytes/high-power field) and significant bacteriuria on sediment examination may be detected in cases with pyelonephritis or lower tract infections. Usually, >10 000 colony-forming units/mL suggest infection but lower numbers can reflect significant pathology.

Rectal examination and ultrasonography may be helpful if the kidneys are small or distorted. Palpably enlarged ureters or ureteric calculi are always significant. Horses with significant renal parenchymal damage and fibrosis may show ultrasonographic evidence of calculi and a loss of corticomedullary distinction. The echogenicity of renal tissue may be similar to or even greater than

[1] Isothenuria – a condition in which the kidneys produce urine with a specific gravity of protein-free blood plasma.

that of the spleen. IV pyelography provides little information in adult horses and its use is generally limited to foals <50 kg. When hematuria or dysuria accompanies CRF, cystoscopic examination can be helpful in determining the side (e.g. right vs. left) from which renal hematuria is originating and allows assessment of urine flow from each kidney.

Measurement of GFR provides the most accurate assessment of renal function and repeated measurements at monthly or longer intervals can be a useful index of progression of CRF. It is also a useful measure of renal function in horses that are thought to be suffering from early CRF before significant azotemia has developed.

Renal biopsy (*q.v.*) is rarely justifiable since treatment of CRF (and in particular ESKD) is supportive and long-term prognosis poor.

Treatment

Treatment in horses presented with end-stage kidney disease (ESKD) is only supportive/palliative. The condition is usually so advanced that any treatment is unlikely to be successful. In CRF the causative condition is seldom identifiable and may no longer be present. The primary objective is to provide sufficient fluids and electrolytes to stabilize patients with polyuria and so prolong their lifespan and improve their well-being. In most cases there is a need for sodium and chloride replacement: at its simplest this can be provided by ad libitum **water** and free choice **salt**. However, **if edema develops, as in glomerular disease, sodium should not be supplied**.

Plasma transfusions to replace albumin are of limited benefit, but **diuretics** such as IV **furosemide** (1–3 mg/kg q 12 h) may help if hydration is satisfactory. The survival time with glomerular disease is shorter than in the case of tubulointerstitial disease and no useful rationale has emerged for treating the underlying disorder. Nutrition in cases of CRF should aim at supplying readily digestible carbohydrate. Reduction in dietary protein is usually suggested but protein deprivation does not in fact reduce the "work" of the kidney.

Some improvement may be expected where there is an acute, reversible component such as exposure to nephrotoxins or vasomotor nephropathy secondary to diseases producing hypovolemia (e.g. diarrhea or sepsis causing volume depletion) exacerbating the condition. Ascending urinary tract infection and/or obstruction can also exacerbate CRF. If an acute component is detected, it should be corrected rapidly. Treatment of CRF consequent to glomerular nephritis is even less rewarding than that caused by **tubulointerstitial disease** (CIN) (*q.v.*).

Management changes in cases with relatively stable CRF should be kept to a minimum and made gradually. Treatment consists of **supportive care**, providing sufficient fluids, electrolytes and nutritional support. Water should be available at all times, and salt (60–120 g added to the feed) can be provided as long as edema or hypertension is absent. If edema develops, salt should be restricted, even if hyponatremia is present. If **metabolic acidosis** is detected (e.g. blood pH is <7.35 or serum bicarbonate concentration is <20 mEq/L) and the patient is not edematous, sodium bicarbonate powder (100–200 g/day) or a mix of sodium bicarbonate and salt should be added to the diet to maintain serum electrolyte concentrations and acid-base balance within reference ranges.

Progression of disease should be monitored with the full range of tests at regular intervals (usually 2–3 mo maximum). The effect of electrolyte

supplementation on progression of CRF is unclear as high salt diets may actually hasten the decline in GFR and exacerbate proteinuria in human patients with CRF. Decreasing calcium intake (e.g. replacing alfalfa or other legume hays with grass hay) may result in a restoration of normal serum calcium concentration. Regular administration of vitamin B complex and **anabolic steroids** may be helpful to stimulate appetite. If appetite remains good, anabolic steroids may further limit muscle wasting and may increase packed cell volume.

NSAIDs and corticosteroids are best avoided or, if considered essential for other reasons, should be used very carefully.

Diuretics may temporarily reduce edema, and plasma transfusions may be of temporary benefit to horses with edema and hypoalbuminemia. IV **furosemide** may be given at 1–3 mg/kg q 12 h).

Nutritional management (*q.v.*) is probably the most important aspect of supportive care. Cases of CRF are often inappetant and so a **highly palatable diet** is essential. Frequent small appetizing meals, feeding smaller meals more frequently, and varying the diet (e.g. offering various types of concentrate feeds as appetite may vary from day to day) are helpful methods to increase food intake. Increasing carbohydrate (grain) intake and up to 0.5 L of corn oil per day are recommended. Omega-3 fatty acids (available in linseed oil or flaxseed oil) may retard progression of the disease. Restriction of dietary protein intake is not helpful; a greater benefit is gained from provision of adequate amounts of dietary protein and energy to meet, or slightly exceed, predicted requirements while maintaining a neutral nitrogen balance. Adequacy of dietary protein intake can be assessed by the **urea to creatinine ratio** (*q.v.*): values >15:1 suggest excessive protein intake while <10:1 may indicate protein–calorie deficit.

Currently, dialysis systems (*q.v.*) involving either peritoneal dialysis or full arterial dialysis are probably both impractical and unhelpful.

Prognosis

The rate of decline in GFR varies between affected horses: the short-term (i.e. months to a couple of years) prognosis is guarded to favorable while the long-term prognosis remains poor.

Although progressive loss of nephron function makes long-term treatment impossible, many horses with early CRF may remain active and useful for some months to a few years. Provided that creatinine remains <200 μmol/L, and the urea to creatinine ratio <15:1, affected horses seem to maintain a reasonably good attitude, appetite and body condition. Once creatinine exceeds 200 μmol/L, the rate of progression of CRF appears to accelerate and signs of **uremia** (e.g. anorexia, poor haircoat and loss of body condition) become much more apparent. Deterioration is usually rapid. Although threshold values for creatinine are prognostically useful at first, progression of CRF is highly variable. Ultimately all cases will require humane euthanasia.

PIGMENTURIA

Until the true nature and source of any grossly red to brown discoloration of urine is established, the condition is best termed *pigmenturia*. There are many causes of pigmenturia in horses although the prevalence of each of these is low. From a urinary tract perspective by far the most common cause is **hematuria**.

The specificity of the ortho-toluidine dipstick test is low and a positive result can be shown with:

1. Hematuria (blood) (Box 12.6)
2. Hemoglobinuria (free hemoglobin), which can arise from a number of causes of hemolytic disease (*q.v.*) (Box 12.7)

Box 12.6 Causes of hematuria

- Urinary tract infection
  - Pyelonephritis
  - Renal abscess
  - Cystitis
  - Urethritis
- Urolithiasis
  - Renal calculi
  - Cystic calculi
- Urinary tract neoplasia
  - Renal carcinoma
  - Bladder neoplasia
- Renal infarction
  - Strongyle damage to renal vessels
  - Endocarditis
- Coagulopathy
  - Warfarin toxicity
  - Disseminated intravascular coagulation
  - Thrombocytopenia
  - Late hepatic failure
  - Hemophilia
- Urinary tract trauma
- Endometrial and vaginal diseases
- Preputial and penile diseases

Box 12.7 Causes of hemoglobinuria

- Infectious causes
  - Equine infectious anemia
  - Equine babesiosis (piroplasmosis)
  - Equine ehrlichiosis
- Toxic agents
  - Wilted red maple leaves
  - Onions
  - Phenothiazine
- Immune-mediated hemolysis
  - Isoimmune hemolytic anemia
  - Autoimmune hemolytic anemia
  - Incompatible blood transfusion

3. Myoglobinuria (muscle pigment myoglobin), the main causes of which are exertional rhabdomyolysis (azoturia) (*q.v.*) and post-anesthetic and nutritional myopathy (*q.v.*).

The nature of the condition responsible has a significant bearing on the management of the problem from a renal perspective.

Hematuria of any description always has **urinary tract implications**. By contrast, free hemoglobin and myoglobin usually have a pre-renal origin without any underlying renal disease. However, it is important to recognize that they may have **long-term effects** on renal function and may under some conditions cause both acute and chronic renal failure (*q.v.*).

Rhabdomyolysis and hemolysis are generally accompanied by other clinical signs while hematuria throughout urination may be the presenting complaint for urinary tract infection (cystitis or pyelonephritis), urolithiasis, urinary tract neoplasia, idiopathic renal hematuria or drug toxicity (NSAIDs, particularly phenylbutazone) (*q.v.*).

Gross pigmenturia throughout urination is consistent with rhabdomyolysis, hemolysis or hemorrhage from the kidneys, ureters or bladder (*q.v.*) while **pigmenturia (usually hematuria) at the beginning or end of urination** may be associated with lesions in the distal or proximal urethra, respectively. **Pigmenturia that is variable through urination** usually indicates a hemorrhagic focus in the bladder or urethra.

Differentiation between hemoglobinuria and myoglobinuria can be made using an **ammonium sulfate precipitation test** (**Blondheim test**, see Box 12.4, *q.v.*).

Diagnosing the cause of hematuria depends on a thorough clinical examination of the horse, followed, where applicable, by more detailed examination of the urinary tract. There are several possible causes of persistent or recurrent hematuria (see Box 12.6) including:

1. **Cystic or ureteral calculi** (*q.v.*).
2. **Chronic cystitis.** This is rare in horses as a primary event, although their short urethra renders mares more susceptible.
3. **Coagulopathy.** Urinary tract bleeding can be a feature of hemorrhagic disorders (*q.v.*) but usually there are concurrent signs such as epistaxis and oral/mucosal bleeding.
4. **Idiopathic renal hemorrhage**, which results from spontaneous (unexplained) often massive (life-threatening) intermittent hemorrhage from one or both kidneys in the absence of any other identifiable cause of hemorrhage. All diagnostic procedures are very unrewarding; in spite of the large clots of blood and profuse hemorrhage, a primary disease process cannot often be found even at post mortem examination. Endoscopically, blood clots may be seen exiting one or both ureteral orifices. The condition is seen in both males and females of all breeds although Arabians are over-represented. Usually renal function is normal.

   Treatment of idiopathic renal hemorrhage consists of support for acute blood loss, including blood transfusions (*q.v.*). Systemic coagulant therapy with vitamin K, α-amino-caproic acid or IV formalin is of no value. If a unilateral hemorrhage is consistently identified, ipsilateral nephrectomy is

indicated but there remains a risk of occurrence in the remaining kidney, especially in the Arabian breed.

5. **Urethral hemorrhage.** A defect or tear in the proximal urethra at the level of the ischial arch that results in obvious (often quite profuse) bleeding at the end of urination is a condition that occurs predominantly in **Standardbred geldings**. The etiology is likely a "blow-out" of the corpus spongiosum penis during strong urethral contractions at the end of urination (or during ejaculation in stallions). Cases void normal urine without any discomfort, and urethral contractions at the end of urination result in squirts of bright red (sometimes clotted) blood. Endoscopically, a lesion is typically seen along the dorsocaudal aspect of the urethra at the level of the ischial arch but even with a videoendoscope it may be difficult to identify. There is no related renal or other urinary tract disease.

   Urinalysis is normal although a sample collected at the end of urination may be positive for blood. The diagnosis is made via **endoscopic examination** of the urethra. External palpation of the urethra in this area is usually unremarkable but can assist in localizing the lesion because external digital palpation can be seen via the endoscope. With hematuria of several weeks' duration, there is little evidence of inflammation; rather, the lesion appears as a fistula communicating with the vasculature of the corpus spongiosum penis.

   A few cases resolve spontaneously but many are persistent. A temporary sub-ischial "incomplete" urethrotomy may be successful in treatment. The surgery is performed after sedation and epidural or local anesthesia. A catheter is placed in the urethra and a vertical incision made into the corpus spongiosum penis but not into the urethral lumen. The surgical wound is left to close by second intention and hematuria should resolve within a week following this procedure. In effect, the surgery is simply preventing continued pressure disruption of the defect until it has healed fully.

6. **Renal or bladder neoplasia** (see below).

POLYURIA–POLYDIPSIA

INTRODUCTION

Urine production and water consumption vary with age, diet, workload, environmental temperature and gastrointestinal water absorption. A "pathologic" state of **polyuria–polydipsia (PU/PD)** (*q.v.*) is taken to be when urine production >50 mL/kg/day and/or water consumption >100 mL/kg/day. For a 500 kg horse this equates to 25 L of urine and a water intake of 50 L per day.

The major causes of PU/PD in horses include (Table 12.4):

1. Chronic renal failure (*q.v.*)
2. Equine Cushing's disease (hypothalamic degenerative disorder/pituitary adenoma) (*q.v.*)
3. Primary or "psychogenic" polydipsia (*q.v.*)
4. Diabetes insipidus (*q.v.*).

Table 12.4 Causes and laboratory features of polyuria

Disease	Causes	Possible hematology and serum biochemistry changes	Possible urinalysis changes
Chronic renal failure	Glomerulonephritis Interstitial nephritis Pyelonephritis Amyloidosis Oxalate nephropathy	Elevated serum urea Elevated creatinine Hypercalcemia Hypophosphatemia Hypochloremia Hyponatremia Hyperkalemia Hypoalbuminemia Anemia Leukocytosis	Reduced SG Acidic pH Proteinuria Glucosuria Granular casts
Cushing's syndrome	Pituitary adenoma of the pars intermedia	Neutrophilia Lymphopenia Hyperglycemia Hyperlipemia	Glucosuria
Diabetes mellitus	Chronic pancreatitis Pancreatic neoplasia	Hyperglycemia Hyperlipemia	Glucosuria Ketonuria
Addison's disease	Adrenal insufficiency	Hyponatremia Mild hypokalemia	Reduced SG
Diabetes insipidus	Central diabetes insipidus (e.g. with pituitary tumor) Nephrogenic diabetes insipidus	Nil	Reduced SG
Psychogenic water drinking		Nil	Reduced SG

Less common causes include excessive salt consumption, central and nephrogenic diabetes insipidus, diabetes mellitus, sepsis and/or endotoxemia and iatrogenic causes (e.g. sedation with α_2-agonists, corticosteroid therapy or diuretic use).

EQUINE CUSHING'S DISEASE

Equine Cushing's disease (ECD) (*q.v.*) is a common disorder of the **geriatric horse** resulting in hyperadrenocorticalism and hypercortisolemia. PU/PD is a prominent sign of the condition, occurring in >70% of cases. It is likely that owners do not always recognize PU/PD in these cases because the water intake is only around twice normal and therefore less than would be seen with psychogenic polydipsia (*q.v.*) or diabetes insipidus (around five times normal). Furthermore, old horses are often left to their own devices and abnormally high water intake and urine production may not be reported at all.

ECD causes PU/PD through several mechanisms; it is likely that the PU/PD is a result of variable combinations of several physiologic mechanisms that are not related to abnormal renal function. The suggested mechanisms include:

1. **Osmotic diuresis** as a result of hyperglycemia and glycosuria. The renal threshold for glucose in horses is 7.5–8.0 mmol/L; when plasma glucose

concentration exceeds this, glycosuria occurs. This is a **primary polyuria that results in polydipsia**.

2. An antagonistic effect by cortisol on the action of antidiuretic hormone (ADH) on the collecting ducts. The major effect is on urine production and so the polydipsia is secondary.
3. Decreased ADH production and release as a result of direct pressure on the neurohypophysis would result in central diabetes insipidus. Again, polydipsia in this case is secondary to polyuria.
4. Central stimulation of thirst by **hypercortisolemia**, i.e. this is a primary polydipsia that results in polyuria.

PSYCHOGENIC POLYDIPSIA

Primary or "psychogenic" polydipsia is probably the most common cause of complaint for PU/PD in adult horses. This is not a renal disease—renal function simply has to cope with a vast increase in water intake. Horses with this problem are generally in **good body condition** and are not azotemic. Further, the magnitude of polyuria is typically dramatic with owners reporting that horses drink two to three times more water than their stable mates and stalls can be flooded with urine. It may become a **stable vice**.

The diagnosis of primary polydipsia is supported when there is no alternative diagnosis such as excessive salt intake, hyperadrenocorticalism/ECD syndrome or renal failure. Diabetes insipidus (*q.v.*) is excluded by demonstrating urinary concentrating ability after water deprivation. Following water deprivation sufficient to cause a 5% body weight loss (usually 12–24 h), urine specific gravity should be >1.025.

Where medullary washout has occurred as a result of prolonged polyuria, the osmotic gradient between the lumen of the collecting tubule and the medullary interstitium may be diminished so that ADH has limited concentrating effects. In this case water deprivation may lead to an increase in urine specific gravity to values >1.020.

In horses with primary polydipsia of several weeks' duration that fail to concentrate their urine after 24 h of water deprivation, a modified water deprivation test (*q.v.*) may be indicated. Water intake is restricted to approximately 40 mL/kg/day for 3–4 days. Urine specific gravity should >1.025 if medullary washout is present. If urine specific gravity remains in the isosthenuric range (1.008–1.014), the polyuric horse should be further evaluated for early chronic renal failure (*q.v.*).

DIABETES INSIPIDUS

Diabetes insipidus (DI) results from failure of production of antidiuretic hormone (ADH), (**neurogenic DI**) or decreased sensitivity to circulating ADH of collecting duct epithelium (**nephrogenic DI**). With both forms of DI, dramatic PU/PD may be reported and affected animals fail to concentrate urine in the face of water deprivation.

Either of these conditions is rare in horses but the diagnoses remain a possibility. After determining that an equine patient with PU/PD is not azotemic,

the initial diagnostic test to differentiate DI from primary polydipsia is a **water deprivation test** (*q.v.*). Particular care should be taken if DI is suspected because the animal has no ability to concentrate urine in the face of deprivation and may become substantially **dehydrated** (10–15%) within 12 h of water deprivation. Because equine ADH cannot be measured, the concentrating ability of the kidney can be tested by measuring **urine SG** before and after administration of synthetic ADH (60 IU, IM or SC, q 6 h).

IATROGENIC POLYURIA

The most common iatrogenic cause of polyuria is excessive fluid therapy. PU/PD is not a common feature of **glucocorticoid therapy** in horses although it has been reported. A **transient diuresis** accompanies sedation with the α_2-agonists **xylazine** and **detomidine**. This is likely to be a result of activation of α_2-adrenoreceptors on collecting duct epithelial cells.

DYSURIA

INTRODUCTION

Dysuria means **difficult and/or painful micturition**, and the sign is invariably related to the bladder or urethra. There are four major causes of dysuria:

1. **Neurogenic dysuria** (incontinence) (dyssynergia and paralysis) (*q.v.*).
2. **Obstructive dysuria**.
3. **Neoplastic dysuria** (*q.v.*).
4. **Inflammatory dysuria** (urinary tract infections). These can be anatomically divided into those affecting the **upper urinary tract** (kidneys and ureters) and those affecting the **lower urinary tract** (bladder and urethra). The former are less common but potentially life-threatening while the latter are usually less serious. Infections involving the whole tract are likely, especially if the primary problem is in the kidney.

URINARY TRACT INFECTIONS

Etiology

The urinary tract is usually almost sterile (although in mares there may be a low level of residual infection in the urethra). Because the sterility of the urinary tract relies heavily upon a **flushing mechanism** (rather than any secretory function), alterations in the normal flow patterns as result of neurologic or physical obstructions commonly result in infection. There is a close relationship between urinary tract infection (UTI) and alterations in function and lithiasis and partial obstructions. The most common risk factors for development of UTI in horses are:

1. **Bladder paralysis.** Horses with bladder paralysis (**detrusor dysfunction**) or decreased urethral sphincter tone (from trauma or neurologic disease)

are clearly at greater risk of UTI than horses with normal detrusor and urethral sphincter function (*q.v.*).

2. **Concurrent urolithiasis.** There is controversy about the primary event in horses with lithiasis (*q.v.*) and infection. In any case both problems have to be dealt with if UTI is to be controlled.
3. **Urethral damage,** e.g. foaling trauma in mares, neoplasia or habronemiasis in males (*q.v.*).

Iatrogenic infection following **bladder catheterization** is an accepted risk because it is virtually impossible to perform this in a sterile fashion. If the bladder is healthy and functioning normally there should be no residual infection. However, when urethral or bladder mucosa has been damaged or when urine stasis (**bladder paralysis**) is present, catheterization has a far greater risk of producing more persistent infection. Significant infection can also develop if an indwelling catheter is in place and the end is not protected by a one-way valve that prevents aspiration of air.

Escherichia coli, *Staphylococcus* spp., *Corynebacterium* spp., *Pseudomonas aeruginosa*, *Proteus mirabilis*, *Klebsiella* spp. and *Enterobacter* spp. are the most common pathogens (*q.v.*).

Clinical signs

Upper tract inflammation produces less specific, more subtle clinical signs and so may be easily overlooked. Horses with upper tract infection often have concurrent signs of **systemic infection** such as fever and weight loss.

Lower tract infection typically shows disturbances in urine flow but seldom any evidence of systemic infection. Dysuria, stranguria, pollakiuria and incontinence may be present. **Chronic infection** may cause perineal urine scalding in mares and sheath and hindleg dermatitis in males. Gross **pyuria** may also be observed as passage of mucopurulent debris in otherwise clear urine.

Diagnosis

The presence of urinary tract infection is based on clinical signs and laboratory analysis of blood and urine samples.

Lower tract inflammation seldom results in any hematologic or biochemical changes while chronic upper tract infection may induce total protein and globulin increases. Azotemia only develops when both kidneys are severely infected. **Bacteriologic culture** of urine obtained from the bladder or specifically from either ureter or kidney may identify specific infections and their antibiotic sensitivity.

Rectal examination may help confirm the diagnosis and the extent of urinary tract involvement or a predisposing cause, e.g. enlarged and atonic bladder, cystic calculi, accumulation of sabulous urine sediment or a bladder mass. **Chronic cystitis** (*q.v.*) also usually leads to bladder wall thickening. **Ultrasonography** may help to focus on abnormal renal size, shape or consistency in horses with upper tract infections in particular.

Endoscopic examination is potentially very useful but before embarking on ureteroscopy the operator must be aware that there is a risk of carrying infection to the renal pelvis from the urethra or bladder. With long-standing cystitis, especially when bladder paralysis is the underlying cause, ureteral orifices may become dilated (and appear wide open) allowing for vesicoureteral reflux and development of ascending pyelonephritis. Collection of a urine sample from each ureter can be helpful.

Treatment

Treatment is focused on the primary cause and the secondary effects of the infection, especially if they are long standing. Antibiotic selection is critical to success but the major mechanism for maintaining urinary tract sterility is **flushing**, and so where there are problems with bladder or urethral function the control of infection may be much more problematic. Important aspects of antibiotic therapy include:

1. Antibiotic sensitivity profiles of the bacteria involved
2. Delivery of the antibiotic to renal tissue and urine
3. Activity of the antibiotic within the urinary tract
4. Compatibility with other drugs
5. Ease of administration (practicality)
6. Toxicity (potential or actual)
7. Expense.

In vitro resistance to a particular antibiotic may not preclude successful treatment with the drug as long as **high concentrations** are achieved in urine. Similarly, in vitro susceptibility does not always guarantee a successful response to treatment.

Potentiated sulfonamides are a mainstay of therapy; trimethoprim–sulfa combinations at 35 mg/kg (total substance) can be administered PO (q 12 h) or IV (q 12 h) and maintained for up to 21 days or more without significant harmful effects in most cases. This combination is useful because both components are excreted into urine in high concentrations in a non-metabolized state. They are also very safe even in very ill or dehydrated horses.

Penicillin administered parenterally (e.g. procaine benzylpenicillin 20 000 IU/kg q 12 h for 5–7 days) is effective for treating upper or lower UTIs caused by susceptible *Corynebacterium* spp., *Streptococcus* spp., and some *Staphylococcus* spp. and *Leptospira* spp.

Gentamicin (6.0 mg/kg q 24 h IV) (*q.v.*) and other aminoglycosides should be reserved for resistant lower tract or acute life-threatening infections caused by Gram-negative organisms. The drugs are however **nephrotoxic** and should certainly not be used when there is renal failure.

Cephalosporins, tetracyclines and chloramphenicol are concentrated in urine and can be useful in treatment.

Enrofloxacin (2.5 mg/kg PO or IV) can be used for resistant infections but it has severe side effects on growth plates in young growing horses.

Prolonged courses of antibiotics are required in all urinary tract infections; courses of 1–6 wk may be indicated. Ideally, a **midstream voided urine** sample should be submitted for bacterial culture 2–4 days after initiation of therapy and again 1–2 wk after treatment has been discontinued. Urine submitted for culture must be cooled as quickly as possible to 4°C and cultured as soon as possible after collection. Prolonged room temperature storage results in significant overgrowth and bacterial contamination.

Urinary acidification can be helpful in controlling bacterial growth and enhancing antibiotic function, but it is not easy to achieve. The horse is singularly resistant to acidification of the urine using ammonium chloride (15 g q 6 h PO) or sodium dihydrogen (acid) phosphate (25 g q 12 h PO). It may be possible to acidify urine using a diet with a **high dietary cation–anion balance (DCAB).** This is a little researched and poorly understood aspect of equine nutrition but it can be useful to establish a mildly acidic urine. The DCAB is a measure of the acid-base balance of the horse as affected by the diet (*q.v.*).

Low DCAB diets (i.e. those that are anionic or acidic) induce metabolic acidosis and this results in acidification of the urine.*

Low DCAB diets have a significant effect on mineral metabolic status. They induce an increased calcium loss in the urine due to the role of the kidney in maintaining acid-base balance. Mineral deficiencies may be masked under these conditions.

Recurrent infections with the same pathogen should alert the clinician to the possibility of a primary focus in the upper tract, e.g. **nephroliths** (*q.v.*) or other parenchymal disease. Cystoscopy and ureteral catheterization can also be pursued. Recurrence with a different pathogen suggests an anatomic or functional cause of abnormal urine flow.

URINARY TRACT CALCULI

Urinary tract obstruction (obstructive dysuria) is a relatively common event in horses and is a considerable therapeutic challenge. Mares seldom have bladder or urethral obstructions.

Calculi may develop within the kidney, the ureters or the bladder. Obstructive urinary disease may occur in these organs depending on the exact location and the extent of the obstruction the calculi cause. The urethra may also be obstructed in male horses.

Urinary tract calculi are most commonly composed of calcium carbonate and/or calcium phosphate. In any site they probably require a **nidus** of some sort, although this is usually not recognized clinically; interstitial inflammation, infection or fibrosis or an area of medullary crest necrosis adjacent to the renal pelvis are examples of nidus formation. **NSAID use** is also a possible risk factor. Anomalies of development (e.g. renal hypoplasia, dysplasia or polycystic disease) or prior exposure to **nephrotoxins** could also provide a nidus for stone formation. Renal pelvic calculi can be identified

* Baker, L.A., Toliff, D.R., Freeman, D.W., Teeter, R.G., Breazile, J.W. (1992) Effects of dietary cation-anion balance on acid base status in horses, *Journal of Equine Veterinary Science* 12: 160–163.

ultrasonographically and sometimes take on the "**staghorn**" shape of the renal pelvis.

Renal and ureteral calculi can produce partial or complete obstruction of one or both sides of the upper urinary tract and can lead to acute renal failure. **Nephroliths** (*q.v.*) usually develop within or adjacent to the renal pelvis and obstruction can lead to hydronephrosis; the more distal the obstruction the more extensive will be the pressure-induced changes. **Ureteral obstructions** therefore cause the most extensive problems. Nevertheless, involvement of a single kidney or limited areas of one or both kidneys may show little or no clinical evidence. When both sides of the upper tract are affected, the condition typically progresses to **chronic renal failure** (*q.v.*).

Most ureteroliths originate as nephroliths (either from the renal pelvis or the renal parenchyma) that pass into the ureter where they become lodged and enlarge over time. Ureteral stones mainly lodge in the distal ureter; they may be palpable per rectum or visible endoscopically at the vesicoureteral opening. They rarely cause colic.

Many cases with renal or ureteral calculi have no clinical symptoms but **weight loss**, unexplained loss of performance and chronic renal failure may be reported. In addition to intermittent signs of mild colic, unilateral nephroliths may occasionally cause intermittent or persistent obvious hematuria. However, gross hematuria is uncommon unless stones have been passed into the bladder or urethra; urinalysis usually reveals pigmenturia and microscopic hematuria.

Cystic calculus is the most common form of urolithiasis in horses. Males are at greater risk than females; this may simply be because small calculi are easier to pass in mares. Bladder calculi are usually single, large spiculated, roughly spherical (but sometimes ovoid and lodging in the neck of the bladder) stones composed of calcium carbonate crystals. Less commonly, multiple stones can be found.

Hematuria after exercise is a common sign of bladder calculus. Pollakiuria, stranguria or incontinence and, in some cases, abdominal pain may also be observed. Less commonly, dysuria may be caused by accumulation of urine sediment in the ventral aspect of the bladder. This condition is termed **sabulous urolithiasis** (*q.v.*). Bladder calculi result in recurrent cystitis and urinary infections (often with different organisms).

Total urethral obstruction causes progressive colic and signs of distress. An enlarged, turgid bladder is detected per rectum. The exact location of the obstruction may be identified by rectal examination and palpation of the ischial urethra. **Bladder rupture** is likely to develop before any evidence of renal failure develops; this may be confirmed by careful clinical investigations supported by elevations of potassium and creatinine/urea. Abdominal ultrasound and paracentesis will confirm the presence of urine in the abdomen. Partial urethral obstruction is usually accompanied by dysuria, incontinence and urine scalding of the hindlimbs.

Prolonged acute obstruction may result in a permanently paralyzed, nonfunctional bladder. Fortunately the effects are reversible if treated early enough and so prompt relief of obstruction is crucial. Calculi, neoplasms, congenital anomalies and preputial edema and inflammation can produce partial or complete urethral obstruction.

Diagnosis

Diagnosis of nephrolithiasis or ureteral calculus is very difficult because clinical signs are mild (**recurrent colic**) or non-existent and azotemia is usually absent. Often the calculi are found incidentally during routine examination or at necropsy. Small calculi passing into the bladder may obstruct the urethra and so the **entire urinary tract** should be evaluated carefully in cases that have recurrent urethral obstruction. This is the more important because multiple small calculi are rarely associated with the bladder. Furthermore, upper tract calculus should be suspected in horses with **recurrent urinary tract infections** with the **same organism**. Concurrent azotemia (*q.v.*) may be a direct result of bilateral calculus formation but can simply be a component of a more extensive renal pathology.

Transabdominal ultrasonography is a valuable tool for detection of nephroliths, dilatation of the renal pelvis (or complete hydronephrosis) and renal fibrosis (increased echogenicity). Small nephroliths (<1 cm in diameter) can be missed despite a complete ultrasonographic examination. Transrectal ultrasonography is also useful for detection of ureteral dilatation and lithiasis.

Bladder calculi are usually identifiable by **rectal palpation**; most can be felt with only the hand and wrist in the rectum. The bladder is usually small and cystic calculi can be missed if the examiner passes quickly beyond the calculus during the rectal examination. Ultrasonographic diagnosis is not useful unless there are several stones present. Endoscopic examination is the method of choice; the number, size and location of the stones can be identified.

Diagnosis of urethral obstruction is based on clinical signs, rectal examination findings, external examination of the penis and prepuce, and passage of a catheter or endoscope.

Treatment

If upper urinary tract obstruction is diagnosed before development of more severe azotemia, nephrotomy and/or ureterotomy may be required. **Electrohydraulic lithotripsy**[1] is possible in specialist hospitals and is the preferred technique for removal of ureteral stones. However, both procedures are very difficult and nephrectomy may be a slightly simpler solution to a unilateral problem.

Bladder calculi are best removed via **laparotomy**. The rarer condition in mares is amenable to manual removal via gentle manual **urethral dilatation** (with a small hand), with or without **urethral sphincterotomy**. A calculus removed from the bladder should be examined carefully for smooth facets that might indicate the presence of other stones.

Urethral calculi can either be removed via a **sub-ischial urethrotomy** over the site of obstruction or by hydropulsion through the urethrotomy incision; excessive tissue trauma may increase the risk of urethral stricture and recurrent urolithiasis.

In theory, urinary acidification with **ammonium chloride** (50–200 mg/kg/day PO) or **ammonium sulfate** (200–300 mg/kg/day PO) should help but this is not easily achieved. Similarly, **reducing dietary calcium** (e.g. by removing alfalfa from the diet) is theoretically of help. A more practical

[1] A procedure to break up stones in the urinary tract using shock waves.

recommendation may be to administer **25–50 g of salt** in the feed daily to increase water consumption and urine flow.

Prognosis

The prognosis for renal or ureteral calculus is very guarded simply because the cause is unknown and therefore prevention is not usually feasible. Furthermore, it is impossible to remove every calculus.

Following removal of bladder calculi the chances of recurrence are low.

URINARY INCONTINENCE

INTRODUCTION

Urinary incontinence is a relatively common problem in horses and is a considerable **diagnostic challenge**. Urinary incontinence develops when intravesicular pressure generated by the detrusor exceeds outflow resistance generated by the urethral sphincter and results in involuntary passage of urine. This may occur with both neurologic and non-neurologic disorders.

The main problems with the clinical investigation relate to the late presentation of cases and the extent of secondary changes including **perineal scalding** in mares and **hindlimb dermatitis** and **penile paralysis** in males (*q.v.*). As is typical of any neurologic disorder, the opportunities for treatment are limited and even the retardation of progression is sometimes impossible.

Horses with detrusor dysfunction typically develop **sabulous urolithiasis** (*q.v.*), an accumulation of a large amount of urine sediment in the ventral aspect of the bladder that exacerbates bladder distension and contributes to further loss of detrusor function and eventual complete bladder paralysis (*q.v.*).

Urinary incontinence in the horse can result from:

1. **Congenital defects** of the urinary tract, e.g. ectopic ureter (*q.v.*).
2. **Urolithiasis** (*q.v.*).
3. Secondary incontinence from long-standing **lumbosacral or lower back** problems that make it difficult for horses to posture to urinate, resulting in incomplete bladder emptying. Calcium carbonate crystals accumulate in the ventral aspect of the bladder and as this becomes heavy and, in some cases, quite firm it further prevents complete bladder emptying. This condition, which has been termed **sabulous urolithiasis** (*q.v.*), can accompany bladder paralysis of any cause but may also be able to produce secondary bladder dysfunction without underlying neurologic problems.
4. **Neurologic diseases** (*q.v.*) accompanied by bladder dysfunction.
5. **Trauma.** Trauma-induced incontinence may develop after physical disruption of the urethral sphincter in mares as a breeding or dystocia injury (*q.v.*) or in both sexes following sacral or spinal injury.
6. **Neoplasia** (*q.v.*). Horses with neoplasia of the lower urinary tract can also present with incontinence but other complaints (e.g. stranguria or hematuria) are usually reported as well.

NEUROGENIC INCONTINENCE

Neurologic disorders (*q.v.*) that commonly result in bladder paralysis and incontinence include:

1. Spinal or pelvic trauma
2. Equine herpesvirus myelitis
3. Cauda equina neuritis (polyneuritis equi)
4. Sorghum ("Milo grass") toxicosis
5. Equine protozoal myelitis
6. Rabies.

Categories

For the most part, **neurogenic dysuria** can be divided into three categories, each of which has a distinctive general clinical character (Box 12.8).

Although the classical separation of lower from upper motor neuron bladder dysfunction may be useful for neuroanatomic localization of spinal cord disease, it is important to recognize that the separation is not absolute.

Involuntary urine passage that is limited to exercise may indicate decreased sphincter tone, rather than detrusor dysfunction, as the cause of incontinence. Similarly, horses that posture to urinate are assumed to have intact sensation of

Box 12.8 Categories of neurogenic dysuria

1. Upper motor neuron dysfunction/interruption
Upper motor neurons in the lumbar or higher portions of the spinal cord are damaged; this causes increased urethral resistance, leading to increased intravesicular pressure before voiding can occur. A tense, moderately enlarged bladder is identified by rectal examination.

2. Lower motor neuron dysfunction
The pathology originates in the gray matter of the sacral spinal segments or in the peripheral pathways of the sacral nerves. Lower motor neuron damage leads to loss of detrusor function and overflow incontinence. A large, easily expressed bladder is found on rectal palpation.

3. Dyssynergia (loss of detrusor–urethral sphincter coordination)
Dyssynergia (detrusor areflexia) arises from injury to the spinal cord above the sacral segments. It results in detrusor hyperreflexia and detrusor–external sphincter dyssynergia, a lack of coordination between detrusor and urethral sphincter activity. This causes an imbalance between the detrusor and urethral muscles (dyssynergia) resulting in short bursts of urine under high pressure but with painful and abrupt cessation. **Rectal examination** may reveal a turgid bladder that is small, normal or large in size. Incomplete bladder emptying may occur and so sabulous urolithiasis can develop and culminate in detrusor paralysis.

bladder fullness while those that never posture have likely lost bladder sensation as well as motor function.

Despite a large number of possible causes, the prognosis for recovery from incontinence due to **bladder paralysis** is generally poor because **sabulous concretions** and **urinary tract infection (UTI)** quickly complicate the problem.

Upper motor neuron signs of bladder dysfunction may be missed in horses until **overflow incontinence** develops as a result of accumulation of urine sediment (sabulous urolithiasis) and progressive loss of detrusor function. For these reasons bladder paralysis and overflow incontinence, consistent with lower motor neuron disease, may occasionally be found in horses with neurologic diseases that typically do not affect the gray matter of the sacral segments (e.g. **cervical stenotic myelopathy** or **equine degenerative myelopathy**) (*q.v.*).

Diagnosis

Diagnosis of neurogenic incontinence is directed to defining a cause if possible or at least establishing the extent, location and possible nature of the problem as well as any secondary conditions, e.g. infection, calculus or sabulous urolithiasis, that will affect the prognosis. Nevertheless in many cases a definitive etiology cannot be reached and then an anatomic description is used.

The history is essential because the initiating cause may have occurred months to years before incontinence actually became a problem and there may be historical facts that help considerably with a diagnosis, e.g. **ingestion of sorghum**, contact with **rabies** (*q.v.*) and previous contact with **respiratory tract infections** or a **traumatic episode**.

Direct observation of any attempts made by the animal to urinate is important. Inevitably a full neurologic examination (*q.v.*) is essential to establish if the dysuria has a neurologic basis and to identify the likely location for this. Although upper motor neuron signs are initially different from those of lower motor neuron disease, incontinence is usually not recognized until **overflow incontinence** develops as a result of sabulous urolithiasis (*q.v.*) and progressive loss of detrusor function. This explains why bladder paralysis and incontinence may occasionally be found in horses with other neurologic diseases including vertebral stenosis/instability (wobbler) (*q.v.*) cases, equine degenerative myelopathy (*q.v.*), and even viral encephalomyelitis, including equine herpesvirus (*q.v.*), rabies (*q.v.*) and the viral encephalitides (*q.v.*). Concurrent signs of lower motor neuron dysfunction such as loss of anal or tail tone or upper motor neuron dysfunction (e.g. ataxia) may help to differentiate the conditions and focus on a possible site for the pathology.

Rectal palpation will usually discriminate between accumulation of urine sediment (which can be indented with firm digital pressure) and a bladder calculus. Further, the latter problem does not present with overflow incontinence during palpation of the bladder.

Endoscopy and ultrasonography are used to establish the presence of complicating factors such as lithiasis, tumors and inflammation (*q.v.*). With longstanding incontinence and detrusor dysfunction, the ureteral openings may become dilated due to chronic distension and a loss of bladder compliance. Endoscopic visualization of open ureteral orifices would imply occurrence of vesicoureteral reflux and increased risk of upper tract infection.

Laboratory analyses of blood and urine, including a **quantitative urine culture**, should be performed in all horses with incontinence because infection is an almost invariable consequence of incontinence.

Treatment

Treatment is always directed toward correction of underlying causes but treatment of **neurogenic dysuria** is frequently unrewarding. Excessive amounts of calcium carbonate sludge can be washed out of the bladder using a urinary catheter. This gives temporary relief in a few cases but overt signs soon recur and secondary infections often develop to complicate the condition. Neurogenic dysuria/incontinence caused by equine herpesvirus myelitis (*q.v.*) and equine protozoal myelitis (*q.v.*) offers some hope of resolution.

Removal of sabulous crystalloid material and placement of a **temporary indwelling bladder catheter** in recent onset bladder paresis may be helpful because the intravesicular pressure is eliminated and so permanent detrusor atony is minimized. Antimicrobial treatment, ideally based on urine culture results, is also indicated in all cases of bladder paralysis.

The parasympathomimetic drug **bethanechol** has been recommended (0.25–0.75 mg/kg SC or PO) for improving detrusor tone and strength of contraction in horses with bladder paralysis. Bethanechol also increases ureteral peristalsis and relaxes the bladder neck and external urethral sphincter. The drug should never be given IV or IM. The response can be disappointing in long-standing cases. **Phenoxybenzamine** (0.7 mg/kg PO, q 6 h), an α-adrenergic blocker, decreases urethral sphincter tone and can be used with bethanechol in cases with upper motor neuron bladder dysfunction. In horses with evidence of urethral sphincter hypotonia, the sympathomimetic agent **phenylpropanolamine** (1 mg/kg PO, q 8–12 h) can be attempted but results are again likely to be disappointing.

It is not uncommon for geldings with incontinence and sabulous urolithiasis to be presented for suspected **cystolithiasis**. These patients should be carefully evaluated before an unnecessary cystotomy is performed because thick urine sediment can generally be removed by **bladder lavage** (via a urethral catheter) and rectal manipulation of the bladder.

Horses recovering from anesthesia or those that have not been comfortable with the circumstances of urination (such as transport or long distance riding) may develop a **spontaneous urethral spasm**. This condition is easily relieved by **catheterization** and is a major indicator for **prophylactic catheterization during anesthesia**. It seems that the overdistended bladder is less able to empty normally, and excessive straining may be seen with a fine dribble of urine or no urine at all. **Decompression of the bladder** with an indwelling urinary catheter is also the treatment of choice for horses with acute onset of bladder paresis and incontinence attributable to neurologic disease such as herpes myeloencephalitis or equine protozoal myelitis (*q.v.*).

Post partum mares may develop **urine retention** associated with bladder and/or urethral trauma. Early recognition of this complication and temporary placement of an indwelling balloon catheter to decompress the bladder is the treatment of choice. Despite aggressive post partum management, some affected mares may never fully recover bladder or urethral sphincter function.

If the condition is not immediately recognized, complete bladder paresis and incontinence may develop months to years later.

Indwelling urinary catheters should always be fitted with a **one-way valve** (made from a cut-off condom or surgical glove finger) to prevent aspiration of air and development of infection.

Ascending urinary tract infection is a major complication of incontinence and so full urinalysis is essential. **Prophylactic antibiotics** should probably always be used.

Prognosis

Horses with subtle neurologic deficits accompanied by incontinence or with idiopathic incontinence are often not presented until months or years after the onset. **Irreversible detrusor dysfunction** regardless of the initiating cause is usually untreatable and the best that can be expected is to manage the condition and its secondary effects. The long-term prognosis for recovery is usually very poor. Most causes of **neurogenic dysuria** are untreatable even if a definitive cause can be established. Almost invariably, the long-term prognosis is hopeless; in almost every case, the progression of the disease results in euthanasia.

Equine herpesvirus myelitis and equine protozoal myelitis (*q.v.*) are probably the only conditions that carry any chance of resolution, but even this may be difficult and incomplete.

NEOPLASIA

ETIOPATHOGENESIS

Urinary tract neoplasia is rare and the large majority of tumors are secondary. Primary tumors occur in the kidney (nephroblastoma and renal carcinoma) and the bladder (squamous cell carcinoma and more rarely transitional cell carcinoma).

Renal cell carcinoma (or adenocarcinoma) occurs more frequently in older horses but nephroblastomas may be detected in young horses. Nephroblastoma usually remains limited to the kidney but renal cell carcinomas (*q.v.*) commonly metastasize to the liver and lungs.

Fibromatous polyps may also occur in younger horses while **bladder tumors** usually develop in middle-aged to older horses.

The most common secondary tumors tend to affect the kidney and include lymphosarcoma, hemangiosarcoma and melanoma (*q.v.*).

CLINICAL SIGNS

Clinical signs of all tumor types include various combinations of hematuria, pollakiuria and stranguria, weight loss and recurrent colic. Sudden death may occur if the neoplasm hemorrhages into the abdomen or thorax.

Bladder tumors may be palpable per rectum but should not be confused with a **cystolith** or **sabulous accumulation**. Azotemia is not commonly present

but mild anemia may be detected when gross hematuria is observed. Neoplastic cells may be found in urine but this is unusual and they may be masked by inflammatory cells and hemorrhage.

Renal tumors may result in marked enlargement of the kidneys such that both the left and right kidneys may be found on rectal palpation. In other cases tumors may be small, circumscribed lesions within a kidney that cannot be felt during rectal palpation. Small tumors may also be difficult to visualize on ultrasonographic examination. Thoracic radiographs are helpful in detecting pulmonary metastases.

DIAGNOSIS

The diagnosis of bladder neoplasia may be confirmed by cystoscopic examination and biopsy. Renal biopsy may be performed under ultrasonographic guidance and a pinch biopsy can be obtained endoscopically from the bladder or the urethra.

TREATMENT

In theory, unilateral renal neoplasia can be treated by nephrectomy but most renal cell carcinomas have **metastases** by the time the diagnosis is made. Surgical intervention is of little benefit to horses with disseminated disease.

Treatment of bladder tumors includes surgical excision and/or topical chemotherapy (via endoscopic delivery) (*q.v.*) using either **5-fluorouracil** or **piroxicam**. Doses and courses of treatment have not yet been established for any of these compounds and there are currently too few reports to make conclusive recommendations.

Chapter 13

The stallion and mare reproductive system

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Chapter contents

INTRODUCTION

It has often been suggested that the equine species inherently achieves comparatively low fertility figures and that domestication makes matters worse. With good management, this is not the case. Analysis of the annual *Returns for Mares*, published by Weatherbys, keepers of the UK and Irish Thoroughbred Stud Book, shows that some well-managed Thoroughbred stallions, with mares indirectly selected for good fertility by fees, regularly achieve conception rates of 90–100% and live foal rates of approximately 80–90%. Even for the total Thoroughbred population of UK and Ireland, there is evidence that conception and live foal rates have increased and that barren mare rates have decreased over the last 20 years, suggesting improvements in management. Data from the same source demonstrate a linear decline in the fertility potential of mares with age. The live foal rate of 4-year-old mares is approximately 75%, whereas that of 20-year-old mares is approximately 50%. Although directly comparable data do not appear to be available from other countries, there is no reason to believe that the results of similarly managed equine populations are significantly different.

An infertile mare is incapable of conceiving when mated by a fertile stallion and is thus, by true definition, a sterile mare. The latter is uncommon, in contrast to the temporary breeding failures that are relatively common, and these mares are more correctly termed **subfertile**. A **barren mare** is one that is not pregnant at end of the breeding season, for whatever reason.

Reproductive success is measured in terms of the birth of a healthy foal and failure may thus involve problems that may occur at any stage of the events which lead to that end, i.e. the stallion (libido, ejaculatory or seminal abnormalities), the non-pregnant mare (failure of conception), the pregnant mare (early fetal death, abortion or periparturient fetal death) and/or the management of all these events. The veterinarian must consider all "links" of the reproductive "chain" when aiding management or investigating problems.

THE STALLION

CONGENITAL ABNORMALITIES

Gonadal dysgenesis

Chromosomal abnormalities, definable by karyotype, have been reported in infertile and subfertile stallions.

Hermaphroditism

This rare condition can be differentiated into true hermaphroditism, male pseudohermaphroditism (testes plus female external genitalia) and female pseudohermaphroditism (ovaries plus rudimentary tubular reproductive tract plus external genitalia resembling those of the male). These horses are sterile and unsuitable for breeding purposes. **Reconstructive surgery** can make them resemble one or the other sex.

Testicular aplasia/hypoplasia

Aplasia is the rare failure of development of one or both testes. In **hypoplasia**, which is not uncommon in some native pony breeds and other horses, one or both testicles are smaller than expected for age and breed of stallion and may vary in consistency from hard to soft. Diagnosis is made subjectively by **palpation** or more objectively by measuring the length, width and height of the fully descended testicle though the scrotum with calipers or ultrasonographic imaging. The condition has been associated with cryptorchidism, hermaphroditism and chromosomal abnormalities, e.g. XXY (**Klinefelter's syndrome**). Normal fertility (cryptorchidism), reduced fertility or infertility is observed. Collected ejaculates can range from totally aspermic to within normal in vitro parameters. The condition must be differentiated from testicular atrophy.

Monorchidism

Complete absence, through failure of development, of one testicle is rare in the stallion but such cases may be normally fertile.

Cryptorchidism

Stallions with cryptorchidism are colloquially called **rigs**. Cryptorchidism is the failure of one (unilateral cryptorchidism) or both (bilateral cryptorchidism) testes to descend, with their tunics, though the inguinal canal into the scrotum. **Inguinal cryptorchidism** (the retained testis is in the inguinal canal) may be temporary or permanent. **Abdominal cryptorchidism** (the retained testis is in the abdomen) is permanent. In unilateral cryptorchidism, which is most common, sperm production is not necessarily affected and such stallions are often normally fertile. Bilateral, especially abdominal, cryptorchids are infertile. A **genetic predisposition** is suspected for the condition and therefore many breed societies do not register cryptorchids to be used for breeding.

Diagnosis is made clinically by careful visual inspection and palpation of the scrotum, if necessary after tranquilization. Both the visual and palpable absence of one or both testicles and the absence of castration scars on the scrotum are indicative of the condition. Serum estrone sulfate levels (>0.2 ng/mL) in horses over 3 years old suggest cryptorchidism. The **hCG (6000 IU) stimulation test** provokes a rise in serum testosterone level (>100 pg/mL) as measured prior to and 30–120 min after IV injection in cryptorchids and this test should be used in horses younger than 3 yr old, in donkeys and in others where estrone sulfate levels are equivocal. Clinicians are advised to consult the laboratories to which

they refer samples for endocrinologic analyses for their reference ranges and interpretations as assays may differ significantly between laboratories. Ultrasonographic examinations may be used to identify a testicle located in the inguinal canal. Laparoscopic examination may be useful to confirm the presence or absence of abdominal testicles in those horses where a reliable history of a previously attempted castration is not known.

Treatment of choice is the localization of the ectopic testis or testes followed by **bilateral castration**. Abdominally and sometimes inguinally retained testes are now often removed by laparoscopic surgical techniques.

Congenital testicular rotation

A 180° rotation of one or both testes can be diagnosed by palpation, where the tail of the epididymis is found to be directed cranially. This condition is caused by malpositioning during testicular descent and is rarely associated with complications. Transient testicular rotation can occur.

Acute testicular torsion

Testicular rotation must be differentiated from acquired **testicular torsion**, which is characterized by rotation of the testicle and spermatic cord by greater than 180° and which is accompanied by signs of acute colic and swelling of the testicle and scrotum. Acute testicular torsion requires urgent surgical correction.

Inguinal/scrotal hernia

The colt foal presents with a unilateral or bilateral swelling, associated with intestines, alongside the testes, in the scrotum. This may be confirmed by **ultrasound imaging**. If intestinal **strangulation** occurs, there are signs of acute colic. To prevent this possibility it is usually prudent to castrate the foal and close the enlarged inguinal ring or rings. As the condition is believed to be heritable, it is considered wise to seek permission from the owner to perform bilateral castration.

INJURIES TO THE GENITAL ORGANS

Penis and prepuce

Traumatic injuries may result from kicks at mating, the use of stallion rings and brushes, injury by vulvar sutures at mating, incorrectly prepared or used artificial vaginas, and accidents involving gates, fences or sticks. There may be open skin wounds in addition to hemorrhage and edema.

First aid treatment with local applications of **cold water and/or crushed ice** is recommended. Systemic non-steroidal anti-inflammatory drugs (NSAIDs) and antibiotic therapy are indicated to reduce swelling and to control secondary infection. Dependent edema and swelling may be controlled by the provision of mechanical support with a custom-made sling using women's tights or similar materials. The stallion should be kept quiet and sexual stimulation avoided; tranquilizers, which cause penile relaxation, are contraindicated.

Complications include **lateral or ventral deviation** of the penis associated with fibrosis and adhesion formation, damage to the closed vascular system of the corpus cavernosum penis and reduced libido or abnormal mating behavior associated with pain or apprehension.

Urethra

Urethral injury may follow penile trauma, the passage of urethral calculi (*q.v.*), repeated catheterization, endoscopic examinations, or the use of tight stallion rings or irritant chemicals. **Hemospermia** and secondary infection with *Pseudomonas aeruginosa* (*q.v.*) are recognized sequelae that can result in subfertility. Diagnosis is by urethral endoscopic, contrast radiographic and bacteriologic examinations. Treatment with repeated **urethral flushing** with 1% silver nitrate solution has been helpful in some cases.

Testes

Testicular injuries may be caused by kicks received at mating or by accidental injuries involving fences, gates, poles and harness lines. Scrotal edema, hemorrhage, hematomas, lacerations and orchitis may occur and result in transient or permanent disturbance of spermatogenesis, depending on severity. More rarely, anti-sperm antibody production and epididymal obstruction may follow.

Immediate first aid treatment with local applications of cold water and/or crushed ice is recommended. Systemic NSAID and antibiotic therapy is indicated to reduce swelling and to control secondary infection. Ultrasound imaging may monitor the extent of damage, during the acute and healing phases. Where damage to one testis is severe, unilateral castration may be indicated in order to avoid anti-sperm antibody production.

Epididymis

Epididymal injury may result in obstruction, which is characterized by a **sperm-free ejaculate** and distended ampullae. Diagnosis is made by external palpation and ultrasound scan. Rectal palpation and ultrasound imaging of the ampullae reveal distension. Treatment consists of massaging the ampullae **per rectum** and inducing extreme sexual excitement, followed by ejaculation until sperm-rich ejaculates are obtained. It has been reported that the administration of 10–20 IU oxytocin per 450 kg body weight, IV, after ejaculation in conjunction with massage of the ampullae and repeated ejaculation until normal sperm is obtained has been successful in some cases. **Oxytocin** may help by increasing the contractility of epididymal smooth muscle.

Ampullae

Ampullary blockage can occur apparently spontaneously in breeding stallions for reasons that are not understood. Diagnosis is made, following a period of infertility and azoospermia, by palpation and ultrasound imaging of the ampullae per rectum, revealing distension. Treatment consists of massaging the

ampullae per rectum and inducing extreme sexual excitement, followed by ejaculation until sperm-rich ejaculates are obtained. Oxytocin therapy, as described above, may help by increasing the contractility of ampullary smooth muscle.

BEHAVIORAL ABNORMALITIES AND EJACULATORY DYSFUNCTION

The events leading to normal mating are regulated by a complex pattern of reflexes that are under hormonal and autonomic nervous control (*q.v.*). The phenomenon of sexual excitement and enthusiasm before and at mating is called **libido**. Sexual arousal results in penile erection, teasing, mounting, intromission, thrusting, ejaculation, resting, withdrawal and dismount.

Ejaculation can be divided into emission and ejection. **Emission** consists of those events leading to the emptying of the contents of the caudae epididymis, ductus deferentia, ampullae, prostate gland and seminal vesicles into the penile urethra. This is accompanied by closure of the neck of the urinary bladder. These events are controlled by the sympathetic nervous system (α-adrenergic mediation). The preganglionic sympathetic nerve fibers that leave the lumbosacral segment of the spinal cord, with their principal connections in the caudal mesenteric plexus, constitute the efferent arch of the emission reflex. Sympathetic stimuli mediated by the pudendal nerve and sacral segment of the spinal cord lead to **ejection**, i.e. the voiding of formed semen though the penile urethra. Ejection is principally the result of rhythmic contractions of the ischiocavernosus, bulbospongiosus and urethralis smooth muscles. Rhythmic dorsoventral movements of the tail ("flagging") and contractions of the anal sphincter accompany ejaculation. Five to ten jets of semen, in decreasing volume, sperm concentration and pressure, are produced.

Low libido

This most frequent of behavioral disorders is characterized by diminished or a lack of sexual interest and arousal when the stallion is presented with estrous mares. In sexually active stallions, over-use, change of location and management, abusive handling, accidents in the covering yard, unsuitably constructed phantoms and the incorrect use of artificial vaginas can lead to this disorder. It is often seen in **young or inexperienced stallions** that have been actively discouraged from exhibiting normal sexual behavior during competition careers. The abuse of **anabolic steroids** during a competition career can lead to breeding shyness and is associated with small testicular size and low levels of circulating androgens (*q.v.*).

A detailed examination must be performed in order to detect abnormalities such as the presence of stallion rings, painful lesions of the penis and physical lameness, which must be eliminated before presenting the stallion to an overtly estrous mare. Retraining stallions with reduced libido to assume normal mating behavior requires time and patience from experienced handling staff. Once the novice stallion has experienced his **first ejaculation** he will usually exhibit normal libido and mating behavior. Retraining involves the enhancement of sexual arousal by presenting a variety of estrous mares to the stallion to attain maximum stimulation. Allowing the stallion to run freely

with receptive estrous mares will often achieve success. Digital stimulation of the base of the penis, with or without the application of hot compresses may help stimulate ejaculation. Non-steroidal analgesic agents, such as **phenylbutazone**, can help overcome musculoskeletal sources of pain.

When these methods are not successful, the additional use of pharmacologic agents may be considered. **Human chorionic gonadotropin (hCG)**, 5000 IU administered IV 2 h prior to mating, is often tried first. Shy stallions with low levels of circulating androgens can be treated with gonadotropin-releasing hormone (GnRH). The injection of 50 μg GnRH SC 2 h and again 1 h before mating has been suggested.

Anxiety in breeding stallions can be treated using 0.05 mg/kg (not exceeding 20 mg) **diazepam**, administered slowly IV 5–7 min before mating. Mild transient ataxia may be observed for 3–4 min following injection.

Excessive libido

Stallions that exhibit excessive libido can pose a serious threat to handlers and mares in terms of physical injury. Most cases result from **poor stallion management** and handling, and in these cases treatment consists of retraining both the stallion and his handlers. The truly savage stallion often shows periods of normal behavior followed by episodes of unpredictable aggression and cannot be reliably retrained. Circumstantial evidence suggests that family traits exist.

Ejaculatory failure

Ejaculatory failure is seen in stallions that exhibit normal mounting, intromission and thrusting, yet fail to emit and eject semen. Frustration leads to **aggressive behavior** toward mares and handlers. Ultimately, libido declines and at that stage it may be difficult to differentiate from primary libido failure. Ejaculatory failure may be caused by a variety of conditions including musculoskeletal pain, aorto-iliac thrombosis, pleuritis, orchitis, urethritis and penile injuries (*q.v.*). Poor semen collection technique may produce a negative experience that may lead to partial ejaculation. Retrograde ejaculation into the bladder has been postulated but has yet to be conclusively confirmed in the stallion.

For the treatment of primary ejaculatory failure (including "retrograde ejaculation") the administration of 0.01 mg/kg **norepinephrine** (noradrenaline) IM 15 min prior to mating and 0.015 mg/kg **carazolol** (a β-adrenergic antagonist) IM 10 min prior to mating has been recommended. Reports suggest that 100–600 mg **imipramine** PO b.i.d. for a minimum of 2 wk may improve ejaculatory competence. When given in tranquil surroundings, 0.66 mg/kg xylazine IV can induce ejaculation at rest, i.e. without erection or mating, in approximately 25% of stallions. In cooperative stallions this technique can be used to collect semen into a plastic bag, which is tied over the prepuce with a girth strap.

Urospermia

Urospermia, which appears to happen more frequently in older stallions, can occur intermittently. It leads to the contamination of an ejaculate with urine,

rendering the semen **non-viable**. The postulated cause is incompetence of the neck of the bladder. The ejaculate is discolored, the smell of urine can be detected and indicator strips confirm **high urea** concentrations. No specific pharmacologic therapy, including the use of diuretics, has yet been described and management should be directed toward encouraging the stallion to empty his bladder shortly before mating. Physical exercise often stimulates urination.

Azoospermia and oligospermia

Azoospermia is a rare condition in which the ejaculate is devoid of spermatozoa. It is usually associated with a **bilateral blockage** of the ampullae or ductus deferens. Treatment consists of transrectal manual massage of the ampullae, extreme sexual stimulation and repeated encouragement to ejaculate. If the blockages can be relieved by this method, subsequent ejaculates and fertility return to normal.

Oligospermia, where ejaculates contain smaller than normal numbers of spermatozoa, is most commonly seen in **aging stallions** in association with testicular atrophy. The spermatozoa that are present in the ejaculate are usually morphologically normal and exhibit normal progressive motility. Affected stallions must be managed carefully by limiting the number of matings per day to a minimum, by careful mare management.

VENEREAL AND OTHER INFECTIONS OF THE GENITAL ORGANS

Venereal infections can be caused by bacteria (*Taylorella equigenitalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*) or viruses (equine herpesvirus 3, equine viral arteritis) (*q.v.*) and may be transmitted at natural mating, through artificial insemination or by iatrogenic mechanical transfer. Generalized infectious processes, while they may primarily involve other organ systems, can affect the male reproductive tract. Pyrexia leads to disturbances in spermatogenesis. This results in a **reduction in seminal sperm** concentration and fertility approximately 4–6 wk after the pyrexia. Infections of the internal genitalia (orchitis, epididymitis, seminal vesiculitis, prostatitis), unless secondary to injury, are unusual in stallions but may result in pain, visible swelling and leukocytes in the ejaculate, which may lead to reduced or absent libido, poor sperm motility/viability and depressed fertility.

Bacterial infections

T. equigenitalis, *K. pneumoniae* (capsule types 1, 2 and 5) and *P. aeruginosa* are distinguished from other equine bacterial pathogens (e.g. *Streptococcus* spp., *Staphylococcus* spp., *Escherichia coli*) by their potential to spread venereally and to cause outbreaks of **endometritis** within groups of previously healthy mares. The stallion's external genital skin is normally colonized by a diverse microflora of these non-venereal microorganisms. When *T. equigenitalis*, *K. pneumoniae* or *P. aeruginosa* (*q.v.*) are introduced to and proliferate on the genital skin, the stallion seldom shows clinical signs of illness or abnormal semen quality but may become a mechanical transmitter of infection to mares,

which develop endometritis. Treatment therefore aims to eliminate the organism and to re-establish the normal genital skin microflora.

The Horserace Betting Levy Board (HBLB) of UK has produced a highly successful framework for the control of venereal diseases for the Thoroughbred industry by issuing the *Common Code of Practice for the Control of Equine Bacterial Venereal Diseases (including Contagious Equine Metritis) and Equine Viral Arteritis in France, Germany, Ireland, Italy and the United Kingdom*. This Code is updated on a yearly basis and other breed societies are recommended to follow similar guidelines. Clinicians in other countries are recommended to seek the guidance of their own appropriate industry and veterinary organizations. Semen intended for export must be collected from stallions that fulfill the health requirements of the importing country.

The HBLB *Code of Practice* requires that swabs are taken from the urethra, urethral fossa, prepuce and pre-ejaculatory fluid of all Thoroughbred stallions in France, Germany, Ireland, Italy and UK, on two occasions not less than 7 days apart, after January 1 and before the start of the mating season. Similar sets of swabs are also taken from the stallion during the breeding season if there is clinical evidence to suggest that venereally transmitted endometritis is affecting his mares (successively mated mares returning to estrus, often early, with vulvar discharges or cytologic and bacteriologic evidence of endometritis). The swabs are submitted for bacteriologic examination by quality assured **designated laboratories** that examine specifically for *T. equigenitalis*, *K. pneumoniae* (capsule types 1, 2 or 5) and *P. aeruginosa*, in addition to other potential non-venereal pathogens, and provide official certification. Contagious equine metritis (CEM) (*q.v.*) is a **notifiable disease** in the UK, France and Ireland.

If one of these three bacterial pathogens is isolated from a stallion, the start of mating is delayed or mating is stopped until the significance of the organism, in terms of its potential to produce outbreaks of true venereal disease, is determined.

Two strains of ***T. equigenitalis*** (streptomycin sensitive and resistant) have been identified but both have clinically demonstrated their potential to produce outbreaks of true venereal disease in mares. The stallion is treated daily for 5 days by teasing him to penile erection and then thoroughly washing the penis and prepuce with chlorhexidine surgical scrub (4% weight/volume), rinsing and drying, and then applying 0.2% nitrofurazone soluble ointment (if available), particularly packing the urethral fossa and diverticulum. Following treatment, it is recommended that a **normal genital skin microflora** should be established as soon as possible, and an individually prepared bacterial broth culture of specifically selected common equine genital commensals may be applied.

Many strains of ***K. pneumoniae***, identified by capsule type, have been isolated and only capsule types 1, 2 and 5 have clinically demonstrated their potential to produce outbreaks of true venereal disease in mares. Capsule types 7 and 68 and many others have been isolated from the genitalia of individual stallions and mares but have not clinically demonstrated their potential to cause true venereal disease. They have sometimes been isolated from equine feces, urine and other non-genital sites. Therefore, **further specialized laboratory examination** of the isolate is required before the decision is made to treat the stallion.

If capsule types 1, 2 or 5 are isolated (or another capsule type if it is demonstrated to be causing true venereal disease), the stallion is treated daily for

7 days by teasing him to penile erection and then thoroughly washing the penis and prepuce with non-antiseptic soap and water to remove all the accumulated smegma. Following this, his penis and prepuce are washed with an aqueous solution of 1% hypochlorite solution, rinsing and drying, and then applying soluble gentamicin ointment, particularly packing the urethral fossa and diverticulum. Some stallions may show signs of local sensitivity to this treatment with inflammation and discomfort. In such cases, care must be taken to keep the penile skin supple to prevent cracking. Following treatment, it is recommended that a **normal genital skin microflora** should be established as soon as possible, and an individually prepared bacterial broth culture of specifically selected common equine genital commensals may be applied. *K. pneumoniae* is frequently difficult to treat and **repeated attempts** may be required before success is proven.

Many strains of ***P. aeruginosa*** (*q.v.*), identified by serotype, have been isolated, but no association has been proven with their potential to produce outbreaks of true venereal disease in mares. *P. aeruginosa* has been isolated from individual mares with endometritis and from equine feces, urine and other non-genital sites, but the organism has also been isolated in outbreaks of true venereal disease. The clinician therefore has no alternative but to treat all isolates as potential venereal disease risks, unless a **test-mating program** can be arranged. Even if this shows that the isolate is not being transmitted to the test mares, it is probable that the organism will cause endometritis in mares who are "susceptible" to infection and these may be very difficult to treat.

The stallion is treated daily for 10 days by teasing him to penile erection and then thoroughly washing his penis and prepuce with **non-antiseptic soap** and water to remove all the accumulated smegma. Following thorough drying, his penis and prepuce are thoroughly sprayed with **1% silver nitrate** solution. Following treatment, it is recommended that a normal genital skin microflora should be established as soon as possible, and an individually prepared bacterial broth culture of specifically selected common equine genital commensals may be applied. *P. aeruginosa* is frequently difficult to treat and **repeated attempts** may be required before success is proven. Recently, success has been achieved following local treatment of enrofloxacin-sensitive strains of *P. aeruginosa* with 50 mg/mL enrofloxacin. The 10% (100 mg/mL) injection preparation is diluted 50% with water and massaged liberally and thoroughly into the erect penile and preputial skin, daily for at least 7 days.

After the stallion has been treated for any of these three organisms, **three sets** of urethral, urethral fossa, prepuce and pre-ejaculatory fluid swabs are taken at intervals of not less than 7 days to confirm removal of the organism. The first swab should not be taken until at least 7 days after treatment has been completed. The stallion should then be test mated to **at least three mares** before the normal mating program is started or resumed.

Viral infections

Equine herpesvirus 3 (EHV-3, coital exanthema)

EHV-3 infection (*q.v.*) causes the development of **small vesicles** on the penis and the prepuce up to 10 days after mating a carrier mare. Stallions may exhibit generalized symptoms of lethargy, anorexia and pyrexia, libido is

depressed and they may be unwilling to mate mares. The vesicles form pustules before eroding and then ulcerating and becoming secondarily infected with bacteria resulting in purulent crust formation and discharge from the surface of the penis. This may be confused with excessive **smegma formation**.

Immunity is short-lived but the condition often recurs with less severe clinical signs. The stallion can become a symptomless carrier with periods of **typical herpesvirus recrudescence**.

Diagnosis is made on the basis of typical clinical signs, often following the occurrence of symptoms in mares covered by the stallion. The definitive diagnosis may be confirmed during the acute stage by isolating the virus from swabs and scrapings taken from the edge of erosions. Histologically, typical herpesvirus inclusion bodies can be demonstrated from fresh lesions and herpesvirus particles can be seen with an electron microscope. **Serologic examinations** can be used to confirm exposure to the virus. Complement fixing and neutralizing antibodies reportedly peak 14–21 days after infection. The former decline by 60 days while the latter can be demonstrated for (at least) up to 1 yr.

Mating should be suspended for 10 days, during which time treatment is aimed at controlling secondary bacterial infection. **Topical disinfection** with povidone-iodine surgical scrub, followed by the application of sodium fusidate ointment, is indicated in severe cases. In all but severely affected stallions, lesions have healed by 10 days to 2 wk after infection, and mating may resume. The infection has **no direct effect on the fertility** of either stallions or mares.

Equine viral arteritis (EVA)

EVA (*q.v.*), which is spread via respiratory and venereal infection, is caused by a member of the Togaviridae family. While clinical outbreaks of a disease similar to EVA are described in the veterinary literature of the last century, the virus was first isolated from an outbreak in the USA in 1953. Until 1993, the clinical disease had not been reported in the UK or Ireland and the level of seropositivity seen in these horse populations was $<1\%$.

Epidemiologic evidence obtained from serologic studies performed internationally suggests that the virus is being **spread globally** through increased transport of some populations of horses and semen. Standardbreds, Thoroughbreds and other breeds have been affected by outbreaks in North America and elsewhere. Serologic studies of Warmblood breeds in various European countries have shown significant levels of exposure. The virus is spread **by aerosol** via the respiratory route and **in semen** at mating or insemination.

Typical cases show marked pyrexia, conjunctivitis, serous nasal discharge, head and limb edema, periorbital swelling and skin rashes. Stallions can develop edema of the scrotum and prepuce. Hematologic examinations, performed during the acute phase, reveal leukopenia. The virus may be isolated from peripheral leukocytes, nasopharyngeal swabs and urine during the acute phase. Serologic confirmation can be obtained using serum neutralizing (titers $>1:4$) or complement fixation tests from serum samples taken during the acute and convalescent stages of the disease. Approximately one third of infected stallions become permanent **seminal "shedders"** and therefore persistent carriers of the disease. Infected and symptomless seropositive stallions should be screened by **seminal virus isolation**.

Treatment is symptomatic and supportive and **most horses recover**, with the exception of some pneumonic foals. Prevention is based on identification of acute cases and symptomless carriers, followed by isolation and segregation.

In Kentucky, stallions are examined serologically prior to the start of the breeding season and seropositive stallions are test mated to determine if they are seminal "shedders" of the virus. Shedding stallions can only be mated to seropositive or vaccinated mares. A **safe and effective but live vaccine** is available in North America but is not licensed for use in many other countries, including the UK. It has been shown to be helpful in limiting the spread of the disease in outbreaks. A **formalin-fixed vaccine** is licensed for use in Germany and is available in the UK for use under the terms of a Government Animal Test Certificate (ATC), and under similar arrangements in Ireland and France, and is widely used for breeding stallions. A similarly prepared formalin-fixed vaccine has been shown to protect stallions in Japan from becoming semen shedders.

Artificial insemination using transported EVA-contaminated semen can result in the infection of the recipient mare and transmission to other in-contact horses via respiratory spread. Mare owners importing semen to UK and Ireland should establish the **antibody status of the donor stallion** before importation so that they do not import EVA to these highly susceptible horse populations. (See also the *Common Code of Practice for the Control of Equine Bacterial Venereal Diseases (including Contagious Equine Metritis) and Equine Viral Arteritis in France, Germany, Ireland, Italy and the United Kingdom* and the British Equine Veterinary Association's *Code of Practice for Artificial Insemination*.)

EVA is a **notifiable disease** in the UK and Ireland.

Protozoal infection

Trypanosoma equiperdum

Dourine (*q.v.*) is a venereal disease that was prevalent in western Europe during the earlier part of the 20th century but has not been reported to occur there for many years. It is a **notifiable disease** in many countries. The disease is still seen in horses in Asia, Africa, South America, southern and eastern Europe and Mexico. It is transmitted in semen at natural mating or insemination.

Clinical signs appear from 5 to 6 days to several weeks after infection and include pyrexia, anorexia, edema of the genitalia, discharge from the urethra and characteristic raised urticarial skin plaques (2–10 cm in diameter) that appear on the lower parts of the body and then disappear within hours. If these plaques persist they leave depigmented areas. **Small pustules** develop in waves on the penis and prepuce. They ulcerate and heal slowly leaving slightly elevated unpigmented scars reminiscent of those seen following EHV-3 infection (*q.v.*). Penile and generalized muscular paralysis can develop, leading eventually to emaciation, lameness and death. Differential diagnosis includes EHV-3 and the paralytic form of EHV-1. Diagnosis is confirmed **serologically** with complement fixation test or demonstration of the organism in smears of exudative fluid. Treatment is attempted with **quinapyramine sulfate** (3 mg/kg SC) but it is not known whether recovered stallions are safe for breeding purposes; eradication is therefore the best policy.

NEOPLASTIC DISEASES OF THE GENITAL ORGANS

Tumors situated on the penis, prepuce and scrotum can cause pain, hemospermia and loss of libido. **Squamous cell carcinoma** (*q.v.*) is the most commonly seen penile tumor of horses, often arising from the areas of the urethral process at the tip of the glans, with a predilection for unpigmented skin. The tumor ulcerates and then proliferates and can spread to regional lymph nodes. If removed early in its course the condition may be cured, and surgical debulking followed by laser or cryosurgery has been found to be particularly useful. Where local recurrence occurs, **penile amputation** is indicated. The diagnosis can be confirmed by histologic examination.

Melanomas, fibromas, sarcoids, hemangiomas and fibropapillomas can be encountered on the skin of the penis, prepuce and scrotum, as they can elsewhere on the body (*q.v.*).

Tumors of the testis and epididymis are usually unilateral and benign or of low malignancy. They include seminomas (mainly encountered in older stallions), lipomas, Sertoli and interstitial cell tumors. Dermoid cysts, teratomas and adenocarcinomas have also been reported. Diagnosis is facilitated with the aid of **ultrasound imaging**. Tumors must be differentiated from abscesses or hematomas. Testicular biopsies, not performed without risk, may be indicated to reach a definitive diagnosis. Treatment for **seminoma**, the most commonly seen equine testicular neoplasm, is unilateral castration, i.e. removal of the affected testicle.

SEMINAL CHARACTERISTICS AND MORPHOLOGY

The evaluation of semen samples is required for so-called "breeding soundness" examinations, infertility investigations and evaluation for suitability for preservation using chilling or freezing. Complete ejaculates can be obtained, from most but not all stallions, with artificial vaginas or condoms. Incomplete samples can be obtained from a stallion's penis or a mare's vagina or uterus immediately after dismount. These incomplete samples are of limited value only, but can confirm the presence of live sperm. Ideally, in order to obtain **optimal information**, a stallion should be allowed to ejaculate several times during the fortnight preceding collection. A 2–3 day rest should then be allowed before collecting two ejaculates spaced 1 h apart. When fertility problems occur with popular stallions during the breeding season it is seldom possible to organize 2 days of rest.

Normal ejaculates are gray to opalescent in appearance, odorless and do not contain clots, blood or urine. Total volume varies according to age, time from the preceding ejaculate and degree of sexual excitement. The proportion of gel to gel-free fractions varies between stallions and especially with degree of sexual excitement. The gel is removed and the gel-free volume of semen is measured. Gel-free semen volumes >40 mL can be considered normal in 500–600 kg stallions.

Sperm **concentration** can be measured with a hemocytometer chamber or a spectrophotometer calibrated for stallion semen. Depending on the ejaculation frequency and timing of ejaculations prior to collection, sperm concentrations

can vary between 50 and 700 $\times$ 10^6 spermatozoa per mL. The total number of sperm per ejaculate is then obtained by multiplying the sperm concentration with the gel-free volume.

Initial **motility** of spermatozoa is usually estimated subjectively, within 5 min of collection, on a microscope slide at 37°C. Overall motility should range from 60% to 80% with 40–70% progressive motility. Dilution in semen extender will increase these figures due to decreased viscosity. These estimations are subjective and vary from one observer to another. More objective computerized motility analyzers are available for equine use.

As an estimate of sperm **longevity**, raw sperm kept at 37°C should not show significant decreases in motility over the first 30 min. Motility can be comparatively estimated periodically until <10% sperm are alive, when the semen is maintained in dark and airtight conditions at room temperature (22°C), but precise reference data have not been published. Semen extended in equal volumes of a standard skim milk and glucose extender and kept at 4°C should maintain sperm motility of greater than 40% when warmed to 37°C after 24 h. Correlation between the fertility of fresh raw semen and motility of extended chilled semen at 24 h has not been satisfactorily established. The pH of semen immediately after collection should be 7.2–7.6.

Sperm **morphology** may be examined by viewing unstained fixed slides under phase contrast or differential interference microscopy. Alternatively, spermatozoa can be stained following fixation and examined by conventional light microscopy. The classical nigrosin/eosin and some other stains allow differential staining of those sperm which were considered live and those that were dead at the time of collection. There are special acrosome stains. Hematoxylin and eosin stain permits the examination for leukocytes and primitive spermatogenic cells. **Primary sperm abnormalities** are those acquired during spermatogenesis, **secondary abnormalities** occur during maturation, storage in the epididymis and ejaculation, and **tertiary abnormalities** occur after collection. Sperm are classified, according to morphologic features, as normal sperm, abnormal heads, detached heads, proximal mid-piece droplets, distal mid-piece droplets, abnormal mid-pieces, and abnormal tails. Further morphologic features can be ascertained using electron microscopic examinations. A normal equine ejaculate should contain a minimum of 50–55% morphologically normal sperm. **Sperm chromatin assays** are available at specialized laboratories.

No precise correlation between individual seminal characteristics and fertility exists as mare and managerial factors are at least as important, if not more important, for results obtained in a commercial breeding program. The evaluation of repeated semen samples combined with history, physical examination and behavioral observations must be considered prior to making conclusions and recommendations concerning an individual stallion's fertility. The **total number of normal motile spermatozoa** that a stallion can repeatedly produce is probably the most useful parameter that can be determined by semen analysis, in terms of the prediction of fertility potential. The numbers and fertility potential of the mares that he is expected to mate or inseminate are very important as are the managerial and veterinary supervision of the stallion and his mares.

THE NON-PREGNANT MARE

CONGENITAL ABNORMALITIES

Gonadal dysgenesis

The most common chromosome abnormalities seen in phenotypic females are the 63XO or 64XY genotype, or a variety of combinations of **mosaicism**. The most common clinical presentations are persistent anestrus, non-cyclic estrus or conception failure. Gynecologic examinations reveal persistently small (<1 cm) and echographically non-functional ovaries and a small uterus. Endometrial biopsy reveals marked endometrial hypoplasia. The diagnosis is confirmed by **karyotyping** and affected mares are permanently sterile.

Developmental abnormalities

Vaginal agenesis has been seen in the occasional mare. Gynecologic examinations reveal what appears to be a thick, **imperforate hymen**. Palpation and echographic examinations reveal discontinuity between the uterus and the vagina. Affected mares are unsuitable for breeding purposes.

ESTROUS CYCLE ABNORMALITIES

The **normal mare** is seasonally polyestrous, with transitional periods of varying length before and after winter anestrus. Normal cyclic ovulatory estrous periods occur, varying with individuals, between February/March/April and September/October/December in the northern hemisphere. The normal estrous period is 3–5 days of estrus (sexually receptive, follicular phase), with ovulation occurring at or near its end, followed by 14–16 days of diestrus (sexually non-receptive, luteal or progestational phase).

Prolonged diestrus

Inadequate endogenous endometrial gland prostaglandin ($PGF_{2\alpha}$) secretion causes failure of normal luteolysis, resulting in persistence of the corpus luteum and therefore **prolonged diestrus** (≥21 days) (*q.v.*). Gynecologic examinations reveal a pale, dry, tightly closed cervix and a peripheral progesterone level of ≥2 ng/mL. After careful **echographic confirmation** of non-pregnancy, the administration of exogenous $PGF_{2\alpha}$ usually results in luteolysis followed by normal ovulatory estrus within 3–7 days.

Shortened diestrus

Endometritis (*q.v.*) causes premature endogenous endometrial $PGF_{2\alpha}$ secretion, resulting in premature luteolysis, shortened diestrus (≤12 days) and premature return to estrus. **Gynecologic examinations** reveal an inflamed, moist, relaxed cervix, sometimes but not always with purulent discharge, and a peripheral progesterone level of ≤1 ng/mL. After confirmation of uterine infection with cytologic and bacteriologic examinations, uterine antibiotic

treatment and correction of predisposing factors, e.g. **pneumovagina** (*q.v.*), will usually be followed by normal diestrus length.

Silent estrus

For perhaps psychological reasons, apparently normal cyclic ovarian activity is not associated with sexual receptivity in some mares. Gynecologic examinations reveal a pink, moist, relaxed cervix; palpation and echographic examinations reveal mature ovarian follicular activity and a peripheral progesterone level of ≤1 ng/mL. Treatment is **tranquilization**, the administration of exogenous estradiol benzoate or artificial insemination (if appropriate).

Ovulation and luteinization failure

Little is known of the incidence or pathogenesis of **ovulatory abnormalities**. When echographic examinations are routinely used to monitor ovulation, it is recognized that in some mares typical echographic signs of ovulation, indicating follicular evacuation and collapse, do not always occur although the mare ceases to be sexually receptive and peripheral progestogen levels rise to ≥2 ng/mL. This is assumed to indicate **ovulation failure**. Conversely, typical echographic signs of ovulation (follicular evacuation and collapse) may occur although the mare remains sexually receptive and peripheral progestogen levels remain at ≤1 ng/mL. This is assumed to indicate **failure of luteinization**. In some mares a large, apparently mature follicle fails to ovulate, persists and develops particulate or flocculent fluid, sometimes with fibrinous strands. These are referred to as **anovulatory follicles**. On the basis of gross and histopathologic examinations of one such case only, these may be analogous to the follicular cysts that are well recognized in women.

Ovulation delay

If an otherwise apparently normal ovarian follicle appears to suffer a delay in ovulating, the administration of **human chorionic gonadotropin (hCG)** or synthetic **gonadotropin-releasing hormone (GnRH)** is usually followed by apparently normal ovulation.

PERINEAL CONFORMATION ABNORMALITIES AND INJURIES

The "normal" mare has three functional **genital seals** that form barriers between the external environment and the uterine lumen: the vulva, the vestibule and the cervix. During estrus, the vulva and the cervix relax, leaving the vestibule as the sole remaining seal. When the upper commissure of the vulva is high in relation to the pelvic brim, the vestibular seal is compromised and pneumovagina (*q.v.*) (**"wind-sucking"**) occurs. When the vulva slopes cranially toward a "sunken" anus (increased angle of declination), **pneumovagina** is complicated by fecal material falling into the vestibule. When the vestibule and urethral opening are displaced cranially, **urovagina** (*q.v.*) may occur. Pneumovagina, urovagina and/or vestibular fecal soiling lead to cervicitis and endometritis, which, if left untreated, usually result in conception or early pregnancy failure.

Pneumovagina

Pneumovagina is corrected by Caslick's vulvoplasty and/or Pouret's perineal reconstruction operations.

Caslick's vulvoplasty operation is performed if the pneumovagina is caused by a simple elevation of the upper commissure of the vulva above the pelvic brim, as judged by digital examination. With the mare bridled and restrained as for a routine gynecologic examination, the tail is bandaged and the perineum is washed and prepared. Under **local infiltration anesthesia**, a thin strip of the mucocutaneous junction is removed from either side of the vulva, from the upper commissure to the level of the pelvic brim. The adjacent exposed submucosal tissues are then sutured together to relocate the upper commissure ventrally. Once a mare has been "stitched", an episiotomy operation **must be performed before each subsequent foaling** and repaired again afterwards.

Pouret's perineal resection operation is performed if the angle of declination of the vulva is such that simple Caslick's vulvoplasty is insufficient to correct the pneumovagina. This procedure is best performed under hospital/clinic conditions with the mare sedated and restrained in stocks. **Epidural anesthesia** (*q.v.*) is induced, the tail is bandaged, the rectum is evacuated of feces and the perineum is clipped and prepared for surgery. Local anesthetic solution is infiltrated into the rectovaginal shelf. A horizontal skin incision is made halfway between the anus and the upper commissure of the vulva. The submucosal tissues are dissected and the rectovaginal shelf is split horizontally by sectioning the muscular and ligamentous connections between the anus, vulva, caudal rectum and vagina until the peritoneal reflection is reached. The subcutaneous tissues and then skin are apposed using a T-shaped closure to make maximal use of the horizontal perineal shelf that has been produced. No attempt is made to close the perineal "dead space" and the end result is to allow the upper commissure of the vulva to return to its "normal" caudal position, independent of the cranially displaced anus. Careful aftercare is required to prevent post-surgical abscess development and to deal with any local seromas that may occur.

Urovagina

Some cases of urovagina occur temporarily in association with an **enlarged uterus** (e.g. during the post-parturient period) and these respond to medical treatment for acute endometritis and delayed uterine involution. Others may respond to Pouret's perineal resection operation, which allows the urethral opening in the vestibule to return to a more "normal" caudal position. Intractable cases may require caudal relocation of the urethral opening, for which a number of vestibuloplasty operations have been described.

Vulvar and vaginal injuries

Injuries to the vulva may occur following direct trauma, e.g. a kick. They should always be repaired with care to restore a functional vulvar seal, in order to preserve the mare's future fertility. Rectovaginal injuries rarely occur during mating and more commonly occur at parturition.

CERVICAL INJURIES

Injuries to the cervix may occur at mating or at parturition or abortion.

Cervical lacerations

Full-thickness lacerations always carry a poor prognosis for future fertility because it is frequently difficult to restore adequate function and many suffer late-gestational failures with posterior pole placentitis. Surgical repair is performed under hospital conditions, with the mare sedated and restrained in stocks. **Epidural anesthesia** (*q.v.*) is induced, the tail is bandaged, the rectum is evacuated of feces and the perineum is clipped and prepared for surgery. Stay sutures are placed to open the vulvar lips to the buttocks to provide maximal exposure. Stay sutures are placed in the distal edges of the cervical laceration, which are then retracted as far distal as possible to aid exposure. With long instruments, the edges of the laceration are debrided and are apposed with a three-layer closure, i.e. external mucosa, connective tissue and internal mucosa. **Careful postoperative care**, with repeated digital manipulation with an **antibiotic/hydrocortisone ointment**, is necessary to prevent adhesion formation and to restore a functional cervical canal.

Some mucosal tears and focal adhesions may be repaired by repeated digital manipulation with an antibiotic/hydrocortisone ointment, to restore a functional cervical canal.

Cervical incompetence

Cervical incompetence may follow injury to the cervical musculature at mating or, more commonly, at parturition or abortion. The cervical seal may be disrupted and late-gestational failures may occur with posterior pole placentitis. The defect can be palpated digitally and attempts at repair, where indicated, are best made by converting the defect into a full-thickness cervical laceration and repairing it surgically as described above.

VENEREAL INFECTIONS

Infectious conditions may be acquired by the mare at mating. In France, Germany, Ireland, Italy and the UK, the HBLB's voluntary Code of Practice (*q.v.*) provides a framework for the control of equine venereal diseases in the Thoroughbred horse and some other equine populations. Many other breed societies have adopted similar codes and it is in the interests of the total horse population that these guidelines (or other appropriate codes in other countries) are followed by all. Clinicians in other countries are recommended to seek the guidance of their own appropriate industry and veterinary organizations.

Equine herpesvirus 3 (EHV-3)

Equine coital exanthema (*q.v.*) results in small vesicles forming at the vulvar mucocutaneous junction and sometimes over the adjacent perineal skin,

appearing approximately 7 days after mating. The vesicles may cause irritation but are rarely associated with pyrexia. They soon burst, leaving ulcers that become secondarily infected with external genital bacteria unless treated with local applications of antibiotic or antiseptic ointments. The condition is not associated with subfertility or infertility and mares may become pregnant following the mating at which they were infected. Diagnosis is by clinical appearance and the history of recent mating, but can be confirmed by histologic examination of lesion biopsy or viral serologic tests, if necessary. Healed lesions on the vulva or penis may remain depigmented.

Equine viral arteritis (EVA)

This togavirus causes pyrexia, depression, conjunctivitis, increased respiratory rate, skin lesions, and edema of the limbs, head and trunk. Mares may be infected at natural mating or during artificial insemination with semen from virus-shedding stallions. Mares who are infected during pregnancy, via the respiratory route, may abort.

The incubation period ranges from 3 to 14 days with an average of 7 days. Diagnosis is confirmed by virus isolation from respiratory secretions or urine, or by a greater than four-fold increase in serum neutralizing EAV antibody titer (seroconversion). Immunity following infection or live virus vaccination is life-long and therefore **viral serologic tests may indicate past challenge rather than active infection**. The carrier state has not been identified in mares and so a seropositive mare with no signs of active infection and a static or falling serum neutralizing EAV titer is considered immune and of **no risk for transmission** of infection to other horses.

Equine arteritis (*q.v.*) appears to be endemic in some populations of horses, notably Standardbreds and Warmbloods, throughout the world, as judged by levels of seropositivity. In the UK the incidence of seropositivity in indigenous horses is extremely low and it must be assumed that the UK mare population is very susceptible to the clinical disease. The first small and limited outbreak of EVA occurred in the UK in 1993. Cases were isolated and the outbreak was successfully controlled. Outbreaks of EVA involving stallions have since occurred in France and in Ireland. Measures designed to prevent the recurrence of EVA in France, Germany, Ireland, Italy and the UK are recommended in the HBLB's voluntary Code of Practice (*q.v.*).

Taylorella equigenitalis

Taylorella equigenitalis is a small, slow-growing (3–7 days on specialized hemolyzed blood agar), Gram-negative, microaerophilic, catalase-positive, oxidase-positive but otherwise biochemically unreactive coccobacillus. It is the cause of **contagious equine metritis** (CEM), which was first defined in Newmarket in 1977. It causes **epidemic acute endometritis**, with clinical signs varying from a copious mucoid/gray vaginal discharge, which may be first seen as early as 2 days after mating, to no gross signs of abnormality. The acute endometritis usually causes conception failure, but some mares resolve the acute infection soon enough to allow conception and normal pregnancy to proceed. Mares may become symptomless carriers, the **clitoral fossa and sinuses** being the important sites of persistence. The diagnosis is confirmed

by the growth of the organism from **endometrial (acute infection) and/or clitoral (carrier state) swab samples**.

Acute endometritis can be successfully treated by repeated intrauterine irrigation with penicillin. At the same time the clitoral fossa and sinuses must be thoroughly and repeatedly treated by washing with **chlorhexidine solution** and packing with **nitrofurazone ointment**. Following this external genital "sterilization" it is prudent to treat the clitoral fossa and sinuses with an actively growing bacterial broth purpose-made from **normal equine external genital commensals**, to discourage the overgrowth of *Pseudomonas* spp. or *Klebsiella* spp.

In intractable cases, **clitoral sinusectomy**, performed under local infiltration anesthesia with the mare sedated and restrained in the standing position, may be required.

Contagious equine metritis (CEM) (*q.v.*) is a notifiable disease in several countries including the UK, France and Ireland. In the UK, the isolation of *T. equigenitalis* must be reported by the isolating laboratory.

T. equigenitalis has been successfully eradicated from the Thoroughbred horse population of the UK by the vigorous application of the HBLB's Code of Practice (*q.v.*). It remains endemic in many non-Thoroughbred horse populations in mainland Europe and therefore the potential for reintroduction remains, as demonstrated by transmission of CEM by a Warmblood stallion imported into the UK in 2002 and the isolation of the organism from an imported Warmblood stallion in 2005.

Klebsiella pneumoniae

Some strains (capsule types) of this Gram-negative, lactose-fermenting, aerobic bacillus, which produces luxuriant mucoid pink colonies on MacConkey's agar overnight, can cause venereal disease. Capsule types 1, 2 and 5 have been known to cause epidemics of **acute endometritis**, with a variable cream-colored vaginal discharge that may be first seen as early as 3–4 days after mating. Capsule types 7, 30, 68 and those isolates that do not type with capsule-typing antisera 1, 2, 5, 7, 30 and 68 have not yet been reliably associated with true epidemic venereal disease but may, as any other bacteria may, cause acute endometritis in so-called "susceptible" mares. The acute endometritis usually causes **conception failure**, but some mares resolve the acute infection soon enough to allow conception and pregnancy to proceed, sometimes followed by placentitis, gestational failure or the eventual birth of a septicemic foal, suggesting that the organism can persist. Mares may become **symptomless carriers**, the clitoral fossa and urethra being the most importantly recognized sites of persistence. Diagnosis is confirmed by the growth of the organism from endometrial (acute infection) and/or clitoral/urethral (carrier state) swab samples.

Acute endometritis can be successfully treated by **repeated intrauterine irrigation** with gentamicin, or sometimes neomycin. At the same time the clitoral fossa, sinuses and urethral opening must be thoroughly and repeatedly treated with **gentamicin** ointment. Following this external genital "sterilization", it is prudent to treat the clitoral fossa and sinuses with an actively growing bacterial broth purpose-made from normal equine external genital commensals, to encourage the establishment of a normal external genital microflora. In intractable cases, **clitorectomy**, performed under local infiltration anesthesia

with the mare sedated and restrained in the standing position, may be required to resolve the problem.

The incidence of isolation of *K. pneumoniae* (capsule types 1, 2 and 5) from Thoroughbred mares in the UK has been significantly reduced by the application of the HBLB's Code of Practice (*q.v.*).

Pseudomonas aeruginosa

Some strains of this Gram-negative, lactose-fermenting, aerobic bacillus, which produces luxuriant greenish, foul-smelling colonies on MacConkey's agar overnight, can cause venereal disease, with a variable cream-colored vaginal discharge which may be first seen as early as 3–4 days after mating. Strain typing may be performed but, unfortunately, no reliable association between strain type and the potential to produce true epidemic venereal disease has been found. "Non-venereal" strains, as with any other bacteria, may cause **acute endometritis** in so-called "susceptible" mares. The acute endometritis usually causes conception failure, but some mares resolve the acute infection soon enough to allow conception and pregnancy to proceed, sometimes followed by placentitis, gestational failure or the eventual birth of a septicemic foal, suggesting persistence. Mares may become symptomless carriers, the **clitoral fossa** being the importantly recognized site of persistence. Diagnosis is confirmed by the growth of the organism from endometrial (acute infection) and/or clitoral (carrier state) swab samples.

Acute endometritis can be successfully treated by **repeated intrauterine irrigation** with gentamicin, or ticarcillin and clavulanic acid. At the same time the clitoral fossa and sinuses must be thoroughly and repeatedly treated with gentamicin ointment or repeatedly treated with **1% silver nitrate solution** (for its desiccant effect). Following this external genital "sterilization", it is prudent to treat the clitoral fossa and sinuses with an actively growing bacterial broth purpose-made from normal equine external genital commensals, to encourage the establishment of a normal external genital microflora. In intractable cases, clitorectomy, performed under local infiltration anesthesia with the mare sedated and restrained in the standing position, may be required to resolve the problem.

The incidence of isolation of *P. aeruginosa* from Thoroughbred mares in the UK has been significantly reduced by the application of the HBLB's Code of Practice (*q.v.*).

NON-VENEREAL AEROBIC AND ANAEROBIC BACTERIAL ENDOMETRITIS

During estrus, the mare's cervix relaxes to allow intrauterine ejaculation by the stallion. All mares' endometria are therefore challenged at natural mating with the variety of microorganisms that normally inhabit the external genitalia of both mare and stallion. "Normal", genitally healthy mares are able to resolve this **acute endometritis** within 72 h, returning the endometrium to a healthy state by the time the fertilized ovum enters the uterus from the Fallopian tube at approximately Day 5 after ovulation.

Mares with perineal, vaginal, cervical or uterine structural or functional abnormalities, particularly those who are unable to clear uterine fluid from

their uteri, are unable to resolve this acute endometritis, which persists, resulting in **conception or gestational failure**. Such mares may also succumb to persistent acute endometritis spontaneously or following foaling or veterinary examination. Recurrent and/or persistent acute endometritis and **uterine fluid pooling** are thought to be important contributing causes of chronic endometrial disease, which leads to the almost linear decline in fertility potential that is well recognized in Thoroughbred broodmares.

Clinical signs may or may not include uterine fluid pooling (ultrasound scan), vaginal/vulvar discharge and shortened diestrus. Of the normal equine external genital microflora, the aerobes *Streptococcus zooepidemicus*, *Escherichia coli* and *Staphylococcus aureus*, and the anaerobe *Bacteroides fragilis* are most frequently isolated from endometrial swab samples in the presence of acute endometritis. Treatment with **intrauterine antibiotic irrigations** is indicated where there is concurrent cytologic evidence of acute endometritis (polymorphonuclear leukocytes in an endometrial smear, washing or biopsy sample). The choice of antibiotic preparation may be based upon **in vitro sensitivity tests**, but mixed infections with multiple species of aerobes and anaerobes are common and thus a broad-spectrum approach is usually appropriate. Particular care should be taken to avoid insoluble or irritant preparations/vehicles, which are likely to induce chronic endometritis, sometimes encouraging *Pseudomonas aeruginosa* or **fungal superinfection**.

Ceftiofur sodium, 1 g dissolved in 20 mL sterile water for injection administered IU daily for 3–5 days, has been found to be particularly useful as a non-irritant, no-residue, "first choice" approach. Mixed aerobic and anaerobic uterine infections are common and *B. fragilis* is the predominant equine uterine anaerobe, an organism that is frequently resistant to penicillin and aminoglycoside antibiotics. Culturing anaerobic bacteria is time consuming and so the use of an antibiotic with anti *B. fragilis* activity (e.g. ceftiofur sodium) is logical, helping to prevent persistent aerobe-negative endometritis. Following IU antibiotic treatments, 25 IU oxytocin may be administered IV to aid uterine clearance of fluids and the mare should be exercised, if possible.

These external genital microflora organisms are **opportunist pathogens** and thus predisposing factors such as pneumovagina, urovagina, cervical injury/incompetence or delayed post partum uterine involution must also be treated. Where there are additional signs of uterine fluid accumulation or pyometra, large-volume (3 L, repeated) **sterile saline irrigation**, with hydrogen peroxide added (2%), may be used prior to starting antibiotic treatment. Irrigation may be performed via a large-bore equine uterine flushing catheter. Following IU sterile saline uterine flushing and antibiotic treatments, 2.5 IU oxytocin may be administered IV to aid uterine clearance of fluids and the mare should be exercised, if possible.

MYCOTIC ENDOMETRITIS

The fungal organisms (*q.v.*) most commonly isolated from cases of equine acute endometritis are *Candida* spp., *Aspergillus* spp., *Mucor* spp. and *Allescheria boydii*. They are opportunist pathogens and interpretation of the significance of their isolation depends upon clinical and/or cytologic criteria. Fungal hyphae and/or spores should be demonstrable in endometrial smear, washing or

biopsy samples, with polymorphonuclear leukocytes. Fungal cultures are performed on Sabouraud's agar. Isolates are sometimes made on simple blood agar plates during aerobic bacterial screening.

Treatment is by **intrauterine irrigation** with large volumes of saline solution and 2% organic (povidone) iodine. Specific antifungal antibiotics such as nystatin, amphotericin, clotrimazole and econazole are available, but they are usually in tablet or pessary form designed for human use and are therefore not ideally suited for the treatment of mares. The administration of 3 g **ketoconazole** (15 × 200 mg tablets) orally daily for 10 days has been found to be a useful adjunct to IU treatment in some mares suffering from mycotic endometritis.

UTERINE IMMUNE AND/OR FLUID CLEARANCE INCOMPETENCE

Where demonstrable physical predisposing factors, e.g. pneumovagina (*q.v.*), have been corrected and there remains a history of recurrent acute endometritis with or without uterine fluid pooling, mares are specifically managed to try to prevent the development of persistent post-mating endometritis. Prior treatment with large-volume saline flush and/or antibiotic irrigation is essential to resolve active endometritis.

"**Minimal contamination breeding techniques**" (Box 13.1) have been found to be useful prophylactic techniques for mares with apparent **uterine immune incompetence**, aiding the resolution of normal transient post-mating endometritis and preventing persistent endometritis.

DEVELOPMENTAL, FUNCTIONAL, DEGENERATIVE AND NEOPLASTIC DISEASES OF THE OVARIES, UTERUS AND FALLOPIAN TUBES

Endometrial hypoplasia

Diffuse glandular under-development has been seen in endometrial biopsy specimens collected from barren maiden mares, sometimes in association

Box 13.1 Minimal contamination breeding techniques

1. The mare should have been successfully treated, if appropriate, and should be free of acute endometritis, prior to the use of these techniques.
2. She should be mated once only per estrous period, just prior to the anticipated ovulation of an apparently normally developing mature ovarian follicle, with the administration of hCG or GnRH to ensure that a second mating is not required.
3. A standard skimmed milk and glucose semen extender, with antibiotics added at concentration designed for this purpose, may be instilled into the mare's uterus just prior to mating, in mares with particular problems.
4. The uterus is flushed with 3 L sterile saline solution 12–24 h after mating then treated with 1 g ceftiofur sodium in 20 mL water for injection and 25 IU oxytocin IV.
5. The uterus is irrigated with 1 g ceftiofur sodium in 20 mL water for injection and 25 IU oxytocin is administered IV daily for the next 2 days.

with ovarian cyclic irregularities. Hypoplasia appears to be a feature of **relative genital immaturity** and usually resolves, without treatment, in time. Where the degree of hypoplasia is marked and ovarian size is minimal, or where the condition persists, the possibility of gonadal dysgenesis should be considered (*q.v.*).

Endometrial hyperplasia

Diffuse glandular hyperplasia with hypersecretion is a normal feature of endometrial biopsy specimens collected from mares during the post partum or post pregnancy failure period. Normal glandular architecture and secretory activity is usually achieved by 10–12 days, suggesting successful involution, but occasionally hyperplasia may persist for weeks if not months, when it is considered pathologic. Concurrent acute endometritis (*q.v.*) is frequently seen. Treatment with 50 IU oxytocin in 500 mL saline by slow IV drip has been used with good results.

In some cases, recurrent acute endometritis/pyometritis appears to produce **diffuse glandular hyperplasia**, possibly associated with recurrent premature luteolysis and hyperestrogenism. Successful treatment of the acute endometritis will reduce the signs of diffuse glandular hyperplasia.

Chronic infiltrative endometritis

Mononuclear cells, i.e. histiocytes/lymphocytes and plasma cells, are commonly seen diffusely and/or in focal stromal aggregations in endometrial biopsy specimens. The presence of these cells indicates a local immune response and therefore previous or ongoing antigenic challenge. No specific treatment is indicated.

A severe **granulomatous endometritis**, with large numbers of plasma and epithelioid-type cells, is occasionally seen in long-term, end-stage pyometra and is considered an indication for retirement.

Chronic degenerative endometrial disease

Glandular degenerative changes are seen in the form of functional or non-functional "nests", surrounded by lamellae of fibrous tissue or, less commonly, gland "cysts", lined by glandular epithelial cells and containing packed glandular secretion, in endometrial biopsy specimens. Periglandular, perivascular or, less commonly, **diffuse stromal fibrosis** is seen. Vascular degenerative changes may be identified. Pools of tissue fluid may be seen scattered in the stroma. Large and multiple lymphatic "lacunae", lined by lymphatic endothelial cells, may be seen in the stroma. It is unusual to sample an endometrial lymphatic cyst, using these biopsy techniques, but these are thought to have a similar pathogenesis.

These changes indicate **chronic degenerative endometrial disease** (sometimes called **endometriosis**). This is a normal progressive condition associated with aging and is thought to reflect long-term endocrinologic effects of repeated ovarian cyclic activity. Mares who are pregnant and have atraumatic parturitions and successful uterine involutions year after year develop these

chronic degenerative changes at a slower rate than do mares who have pregnancy "gaps" for whatever reasons. The performance mare that retires late to stud is notoriously difficult to start breeding and examination of biopsy samples often shows chronic endometrial degenerative changes that are considered to be well in advance of what would be expected for age-matched multiparous mares. In addition, the repeated stimulatory challenges of semen, microorganisms, external genital and environmental debris and fetoplacental antigens, and the repeated physical challenges of pregnancy, parturition and involution may accelerate the development, distribution and severity of these degenerative changes. The changes may significantly contribute to the **linear decline in fertility** seen in the Thoroughbred mare population and are frequently seen in mares that suffer repeated pregnancy failure or prolonged gestation with fetal dysmaturity.

Endometrial degenerative changes develop to a degree that is quite predictable and thus each biopsy specimen examined must be assessed in terms of the mare's **age and parity**. Where the degree of degenerative change is considered excessive, treatment with endometrial mechanical curettage may be attempted. The aim of this technique is to stimulate an increase in endometrial blood supply. Improvements in histopathologic appearance and fertility can be expected in 50% of mares <17 years and this technique is safer and more humane than chemical curettage.

In some cases, **recurrent acute endometritis/pyometritis** produces diffuse stromal fibrosis, possibly associated with recurrent premature luteolysis and hyperestrogenism. Successful treatment of the acute endometritis, followed by pregnancy, can sometimes reduce the signs of diffuse stromal fibrosis. Where there is concurrent acute endometritis, dimethyl sulfoxide may be added to the antibiotic mixture in an attempt to aid stromal penetration.

Cystic endometrial disease

Large **lymphatic cysts**, which project into the uterine lumen, and large lymphatic lacunae in the endometrial stroma may be found in many multiparous mares >14 years. Unless they are very large or are so extensive that they significantly reduce the functional endometrial surface area, resulting in gestational failure, they have little demonstrable effect on fertility. Large individual cysts that may interfere with normal early conceptual mobility or may confuse early pregnancy diagnosis may be **ruptured** by videoendoscope-directed laser surgery or snared and removed by videoendoscope-directed "hot-wire" thermocautery.

Myometrial degenerative disease

Myometrial incompetence and uterine postural considerations in aging mares are believed to play an important role in the failure of some multiparous mares to clear uterine fluids post mating and therefore predispose to the persistence of **post-mating endometritis**. Such mares are treated with 25 IU oxytocin IV after uterine sterile saline flushes, uterine irrigations with antibiotics and after mating (see Box 13.1).

Ventral uterine dilatations (areas of fold atrophy and myometrial stretching) are sometimes palpated in older multiparous mares. They may contain hypo-echoic luminal fluid accumulations or large endometrial cysts or lymphatic lacunae. It is possible that they may embarrass normal uterine clearance of luminal fluid and may have a role to play in some cases of recurrent acute endometritis. Treatment with 50°C hypertonic saline solution by intrauterine infusion, and/or 60 IU oxytocin in 500 mL saline solution by slow IV drip may improve myometrial tone and aid the clearance of pooled uterine fluid in such severe cases.

Endometrial atrophy

Diffuse glandular atrophy is seen in endometrial biopsy specimens of mares following prolonged ovarian inactivity and is therefore a normal temporary feature during winter anestrus. **True persistent endometrial atrophy**, with luminal epithelial and glandular atrophy, may be seen in aged mares, usually in association with senile ovarian malfunction. Rarely, it has been seen in younger mares following severe recurrent acute endometritis with *Pseudomonas aeruginosa* infection. No treatment is successful for persistent "senile" endometrial atrophy and retirement should be recommended.

Endometrial neoplasia

In contrast to some other species, endometrial neoplasia is relatively rare in the mare.

Leiomyoma/fibroleiomyoma tumors are usually small and benign, and have no primary effect on fertility. Treatment, by surgical removal, is only indicated where the tumor is large, when it may be pedunculated and cause persistent endometrial hemorrhage and secondary endometritis.

Rare cases of **adenocarcinoma** have been recorded in the literature. One mare had respiratory signs and post mortem examination confirmed pulmonary metastases.

Fallopian tube abnormality

Palpable or echographic abnormalities of the fallopian tubes are uncommon and bilateral blockage is very rare in mares. **Para-ovarian cysts** or other local developmental abnormalities may be incidental findings at rectal palpation or ultrasound imaging. They seldom have a specific effect on fertility.

Salpingitis

Mononuclear cell infiltrations of the submucosal layers of the fallopian tubes are as common as they are in the endometrium and again are presumed to be indicators of local genital tract immune responses to antigenic challenge. **Acute salpingitis** (polymorphonuclear cell infiltrations) is thought to be rare but may perhaps account for some failures of blastocyst transport in older mares with histories of recurrent acute endometritis.

Occlusive disease

Occlusive disease is thought to be very rare and then usually unilateral, not significantly depressing fertility.

Ovarian hypoplasia

Markedly small or absent ovaries in barren maiden mares suggest gonadal dysgenesis, definable by karyotyping. These mares are sterile. For reasons that can only be speculated upon, some mares appear to suffer delayed sexual maturity, showing poor ovarian follicular development, cyclic activity and ovulatory function until they are 6–7 yr old.

Ovarian cystic disease

True cystic ovarian disease, as seen in some other species, is uncommon in mares. Normal ovarian follicular size is very variable and many large "cysts" appear to ovulate normally, suggesting that they were normal follicles. Occasionally, mares develop large hyperechoic follicles that contain fibrin-like strands and are often referred to as anovulatory follicles. These may be **follicular cysts** and are often refractory to hormone treatments although they may not prevent the production and ovulation of other follicles on the same or the contralateral ovary. **Luteal cysts** may occur rarely in mares but it is difficult to make a precise diagnosis without histopathologic confirmation. **Ovulation fossa inclusion cysts** occur sometimes, usually in older mares, where multiple small follicles that have not matured and ovulated block the progress of other maturing follicles into and though the ovulation fossa. Treatment with repeated large doses of hCG or GnRH and then $PGF_{2\alpha}$ may resolve the problem in some cases.

Ovarian hematoma

Ovarian hematomas are difficult to define by palpation alone, but can be accurately diagnosed by their diffuse hyperechogenicity. Most cases resolve by **natural resorption**, require no treatment and have no lasting effect. In rare cases they can become very large, persist and cause abdominal pain necessitating ovariectomy. In even rarer cases, rupture of the hematoma may occur, resulting in fatal hemoperitoneum. Therefore, laparoscopic removal of persistent non-resolving ovarian hematomas is recommended.

Ovarian neoplasia

Granulosa/thecal cell tumor (*q.v.*) is the most commonly found equine ovarian neoplasm. The affected ovary is enlarged and palpably hard and is echographically polycystic, the cyst walls being relatively thick. The ovulation fossa is not palpable. The contralateral ovary is small and inactive. The mare may show **nymphomania, virilism** or **maternal behavior** depending upon neoplastic steroidogenesis.

Approximately 60% of affected mares have demonstrably **high circulating testosterone and estrone sulfate** levels. Many have **high circulating inhibin** levels but commercially available assays are not yet readily available for use in

most countries. Clinicians with access to assays are recommended to seek reference ranges from the laboratory concerned as assays vary between laboratories. Therefore, in most instances, equine granulosa cell tumors cannot yet be reliably diagnosed by blood hormone tests except where plasma testosterone and estrone sulfate or inhibin results are markedly elevated. **Gynecologic examinations**, with comparison of the size and ultrasonographic appearance of both ovaries, are required. Equine granulosa cell tumors are usually benign and, following unilateral ovariectomy, which now is usually performed by laparoscopic surgery, the contralateral ovary eventually regains normal function and the mare returns to fertile cyclic estrus.

Teratomas are unusual benign tumors and may contain teeth or hair. They are treated by unilateral ovariectomy.

Ovarian **adenocarcinomas** are aggressively malignant and cases invariably require euthanasia. Most exfoliate carcinoma cells and therefore peritoneal fluid analysis may aid diagnosis.

THE PREGNANT MARE

EARLY PREGNANCY FAILURE/EARLY FETAL DEATH

Early pregnancy failure (EPF) may arise from early fetal death (EFD) or fetal membrane abnormality. EFD is defined as loss of the conceptus before 150 days' gestation. Organogenesis is completed by 40 days, and pregnancy loss before this may be called **embryonic death**. No category of mares—lactating, barren or maiden—has been proven to be particularly susceptible. Lactating mares mated at "foal heat" are reported to have a relatively higher incidence, but not at subsequent estrous periods. Advanced age, >12 years, is reported to be related to a higher rate of EPF. Mares prone to uterine infection or those with advanced **chronic degenerative endometrial disease** are also reported to be more susceptible to EPF. In populations of Thoroughbred mares where the incidence of acute endometritis and advanced chronic endometrial degenerative disease is low, there is no obvious age or reproductive status bias and the majority of cases are suspected to be associated with genetic, developmental or functional abnormalities.

Incidence

Incidence rates from 5% to 45% have been reported for EPF. This wide range reflects the types of mares surveyed, the accuracy of pregnancy diagnosis and management conditions. Under modern stud management conditions, the incidence of EPF is reported to be 10–15%.

Etiology and pathogenesis

Malnutrition

Experimentally, maternal malnutrition has been shown to cause EPF between 25 and 31 days' gestation. Temporary starvation has been used in an attempt to encourage the reduction of adjacent twin conceptuses to a singleton, with a

success rate of approximately 60% reported by some authors and no significant effect reported by others.

Bacterial endometritis

Persistent acute endometritis (*q.v.*), established before mating, is often a cause of conception failure. However, **low-grade persistent endometritis** is an important cause of EPF. Low-grade endometritis may exist prior to mating or may result from inadequacy of uterine defenses to resolve the acute endometritis stimulated by natural service (*q.v.*). EPF may occur as a result of **direct fetal infection** or following **infection of the fetal membranes**.

Chronic degenerative endometrial disease

Recurrent endometritis/pyometritis appears to accelerate the development of chronic degenerative endometrial disease and produce diffuse stromal fibrosis. Repeated year-on-year pregnancy and atraumatic parturition, coupled with careful mare management with the application of minimal contamination techniques at mating, or artificial insemination where appropriate, may slow the progression of the condition (*q.v.*).

Genetic factors

Genetic factors are known to be causes of EFD in other species, and are thus suspected in the horse. These factors are not necessarily inherited directly from the parents, and may arise in the definitive gamete. **Chromosomal abnormalities** arising before organogenesis may cause EFD.

Maternal stress

Undue stress at any stage during pregnancy should be avoided. Increasingly horses, including pregnant mares, are **transported for long distances**. The period of pregnancy most susceptible to stress has not been identified, but it is generally recommended that transport stress should be avoided during the 20–45 day stage, when critical events such as transition from yolk sac to chorioallantoic placentation are occurring.

Endotoxemia

A pyrexic or septicemic process involving the release of endotoxins or inflammatory mediators into the mare's circulation may cause EFD. This is associated with a fall in circulating progesterone but it is not clear whether this is a primary or secondary phenomenon. The period most sensitive to the luteolytic actions of endotoxins is up to Day 45. After this time, additional progesterone is provided from secondary corpora lutea.

Mare reproductive loss syndrome (MRLS)

This extraordinary syndrome was seen in Kentucky and some other states of North America in 2001, 2002 and to a lesser extent in 2003. MRLS (*q.v.*) caused **dramatic losses** in the form of early fetal deaths and late fetal losses (*q.v.*) and appeared also to manifest in cases of **pericarditis** and **unilateral ophthalmitis**.

The early fetal deaths manifested as pregnancy failures during May, June and July, with ultrasonographic signs of fetal death and fetal fluid hyperechogenicity in those cases where the mare was examined during the period before expulsion of the dead fetus and its membranes. It is now believed that the unavoidable ingestion of **Eastern Tent caterpillars** that occurred following the massive increase in their population in 2001, contaminating feed and water containers, led to the mechanical transmucosal transmission of bacterial infection (most frequently α-hemolytic streptococci) and/or as yet undefined toxins. Control of the caterpillar population by removal of their habitats in the black cherry trees appears to have controlled the problem.

Diagnosis

Return to estrus

A relatively high rate of EPF is suspected to occur before 14 days but, as ultrasonographic pregnancy diagnosis is seldom used before 14 days, losses will not be detected and luteolysis and return to estrus occurs at the same time as in non-pregnant mares. If EPF occurs after 15 days, the primary corpus luteum may persist for 30–90 days, resulting in persistent diestrus. If EPF occurs after the production of endometrial cups (after 36 days), the mare may not return to fertile estrus until 90–150 days after conception.

Rectal palpation

Rectal palpation as a means of pregnancy diagnosis depends on the assessment of **uterine tone** and the presence of a **conceptual bulge**. Palpation findings in EPF depend on the interval between fetal or embryonic loss and collapse of the conceptual sac.

Ultrasonography

The use of **ultrasound imaging** has greatly improved the accuracy of pregnancy diagnosis and the detection of EPF. Pregnancy diagnosis is now possible as early as 9–12 days' gestation. EPF should be suspected in the following situations:

1. The **conceptual sac** is small for age. A high percentage (62–78%) of undersized vesicles (more than 1 or 2 standard deviations below the mean diameter for age) are lost before 25 days; others continue to grow but may be lost later. A 16–20 day conceptus should be at least 20 mm, and circular with an obvious echoic "specular" reflection at the sac boundary. A small endometrial cyst may be confused with a conceptus, but cysts are usually less regular in outline on scan image, and they may contain hyperechoic divisions. The conceptual sac becomes less circular in outline between 18 and 25 days due to increasing uterine tone and probably reduced tenseness in the yolk sac wall. Where cysts present a diagnostic problem, cyst mapping of the uterus may be used prior to mating. Alternatively, serial scanning and assessment of progressive size helps to differentiate a cyst from a conceptus.

2. The **fluid image** is irregular in outline and has a grainy/flocculent (hyperechoic) appearance. There may be signs of fetal disintegration and fetal membrane separation.
3. There is **edema** of the endometrial folds and uterine fluid is sometimes visible in the same or contralateral uterine horn.
4. An embryo with a **visible heartbeat** is not detectable after 22–25 days' gestation. After about 50 days the increased fetal size may hamper visualization of the heart, but fetal limb and body movements will help to confirm fetal viability.

Laboratory tests

Progesterone

Measurement of plasma or milk progesterone is a test of luteal function, and a level >2 ng/mL indicates the presence of a functional corpus luteum. **There is no reliable correlation** between peripheral progesterone concentrations and the viability of the conceptus. Although in most, if not all mares, peripheral progestogen levels fall in response to abnormality elsewhere in the fetoplacental unit, there is no convincing evidence to support the theory that primary progesterone deficiency is a cause of fetal loss in mares. Therefore, plasma progesterone levels **cannot be used** as a reliable means of assessment of fetal health.

Equine chorionic gonadotropin (eCG, PMSG)

A positive eCG result indicates endometrial cup activity, associated with the presence of a fetus at 35–40 days' gestation. However, eCG continues to be produced even after fetal death and circulating eCG will remain high until the endometrial cups are destroyed at 90–95 days. This scenario produces a false positive blood pregnancy test result in cases of EPF that occur after 30–35 days. The "window" for practical use of this test is therefore **45–95 days of gestation**.

Estrogens

A marked rise in circulating estrogens is detectable in the mare circulation after 90–100 days' gestation. These hormones are produced by the fetal gonads, and high levels of estrone sulfate (>160 ng/mL) are maintained from 120 days to term when a normal live fetus is present. Total urinary estrogen assay (**urine Cuboni test**) can similarly be used to confirm the presence of a live fetus after about 150 days' gestation.

Treatment

The most commonly applied "treatment" for EPF is exogenous progesterone or progestogen supplementation. As there is no convincing evidence that primary progesterone deficiency is a cause of fetal loss, **there is no rationale for the use of progesterone supplementation**. Nevertheless, large quantities of progestogens are administered to pregnant mares internationally, mostly for managerial reasons, sometimes with anecdotal claims of efficacy in individual cases.

However, once EPF has been reliably diagnosed, treatment is aimed at returning the mare to estrus and making sure that the uterus is in a condition for

optimal fertility at the earliest opportunity. Before 36 days, **$PGF_{2\alpha}$ treatment** will be effective in producing luteolysis and returning the mare to estrus, with relaxation of the cervix and expulsion of the fetus and membranes. **Uterine irrigation** with sterile saline solution and broad-spectrum antibiotics are recommended to assist in removal of uterine luminal debris. If the mare is to be mated again during the same breeding season, the use of minimal contamination breeding techniques (see Box 13.1, *q.v.*) is recommended, as the mare is considered somewhat more susceptible to persistent acute endometritis.

Once endometrial cups have formed, circulating eCG can prevent the effects of $PGF_{2\alpha}$ and repeated daily or twice daily injections may be needed to produce estrus. Estrous periods induced at this stage appear to have lowered fertility and most mares in this condition then demonstrate significantly greater susceptibility to persistent acute endometritis. In most cases it is better **not to attempt to mate the mare again** that breeding season.

Prophylaxis

As acute endometritis is an important cause of preventable EPF, attempts should be made to **avoid mating mares in this condition**. Cervicouterine cytologic and bacteriologic examinations and ultrasound scan examination to check for uterine fluid accumulation, performed in early estrus, will enable detection and characterization of uterine inflammation so that appropriate action can be taken. In cases with severe inflammation and bacterial infection, treatment and time for recovery is indicated. Where there are signs of low-grade inflammation, minimal contamination techniques, or uterine irrigation with sterile saline solution and broad-spectrum antibiotics following mating are indicated. Uterine irrigation with 3 L isotonic saline (at 37°C) daily for up to 3 days after mating has been used with some success. The **first flush** may be as early as 4 h following mating. Similarly, **antibiotic irrigations** can be used for up to 3 days after mating, starting on the following day. These techniques are aimed at assisting the uterine defense mechanisms by reducing the inevitable microbial contamination of the uterus that results from natural mating.

In mares with a history of repeated EPF, **endometrial biopsy** is indicated. An assessment of the histopathologic features can help to formulate a rational treatment regimen. It has been shown that paired biopsy techniques, the second following appropriate treatment and time for recuperation, provide a more accurate prognosis of fertility. Uterine biopsy is particularly useful for the assessment and quantification of chronic glandular degenerative change and stromal fibrosis. In cases where the degree of chronic endometrial degenerative disease is in advance of the mare's age, **endometrial curettage** may improve the condition of the endometrium in some cases. There is no doubt that repeated pregnancy throughout a mare's breeding career helps to slow her development of chronic endometrial degenerative disease and so successful gynecologic management helps to prevent EPF.

Aging gametes are known to be important causes of EFD in other species, and thus it is wise to time mating as close as possible to ovulation.

As early diagnosis of EPF or EFD is most useful, **serial pregnancy diagnoses** using rectal palpation and ultrasonographic examinations will enable

early detection of EPF, and examinations are recommended at the following stages:

1. 14 to 17 days after ovulation, when detection of twins facilitates the manual crushing of one. Further examinations at 20–25 days are then indicated to monitor progress of the remaining conceptus. In the case of adjacent twin conceptuses, the success rate for crushing one conceptus is lower, depending on the expertise of the operator. Monitoring the pregnancy for natural reduction of one twin is a risky option because, if not successful, the "window of opportunity" for successful manual reduction by crushing has been lost. Further examinations must then be made between 30 and 35 days; if twins are still present at this stage they can be eliminated by $PGF_{2\alpha}$-induced luteolysis before endometrial cup formation.
2. 25 to 30 days, when the presence of a single live fetus may be confirmed.
3. 40 to 45 days.
4. 60 to 90 days.

ABORTION

Abortion is defined as **expulsion of the fetus** before 300 days of gestation when, due to immaturity, it has little chance of survival, even with intensive care. Abortion is an important cause of wastage and reproductive failure in breeding horses.

Incidence

Incidence rates for abortion of 4–19% are quoted in the literature. This wide range is a result of variations in mare populations and their management, of accuracy and timing of pregnancy diagnosis, and because many abortions are not observed. UK surveys from the *General Stud Book*, which include only abortions that are observed later in pregnancy, result in a rate of approximately 2% of mares mated. Excluding abortion due to equine herpesvirus (EHV) and equine arteritis virus (EAV) infection (*q.v.*), where abortion storms may occur, abortions are generally sporadic.

Etiology

Infectious causes

Bacterial infections

A 5-year survey of post mortem examinations in Newmarket revealed that 1.4% of cases were associated with fetal bacterial septicemia, 2.4% with acute placentitis, 5.7% with chronic placentitis and 2.4% with posterior (cervical) pole placentitis.

Infective agents include *Streptococcus zooepidemicus, Escherichia coli* and *Staphylococcus aureus* (*q.v.*), usually causing placentitis, fetal septicemia and premature placental separation. *Salmonella* spp. infection (*q.v.*), once an important cause of abortion in mares, has disappeared from most parts of the world.

Leptospirosis (*q.v.*) causes placentitis and fetal septicemia in North America and Ireland but has not been reported in the UK. A focal placentitis associated with a nocardioform infection has been reported in Kentucky. It was a common cause of abortion for a few years but the incidence of this infection seems to have decreased, for reasons that have not been clearly explained.

Fungal infections

In the Newmarket survey, 0.5% of cases were associated with fetal fungal pneumonia and 0.5% with fungal placentitis. The majority of fungal abortions have been associated with *Mucor* or *Aspergillus* spp. Thick, mucopurulent placentitis is often a feature, sometimes leading to premature mammary development and purulent vaginal discharge. One case due to *Allescheria* spp. has been reported.

Viral infections

Some 6.7% of the Newmarket survey cases were associated with equine herpesvirus infections (*q.v.*).

Equine herpesvirus (EHV, rhinopneumonitis) and equine arteritis virus (EAV) may cause **abortion** in mares. EHV (types 1 and 4) commonly causes innocuous equine **respiratory infections**, but if the virus crosses the placenta it can cause fetal viremia and **fatal focal necrotic hepatitis** and/or pneumonia. A less common variant is now becoming recognized where EHV infection causes abortion following **endometrial and/or placental vasculitis**, following maternal viremia. In these cases there appears to be no fetal infection. EAV (*q.v.*) causes equine arteritis (EVA), which can cause individual or epidemic abortions associated with placental vasculitis, following maternal viremia.

Non-infectious causes

Twins

The Newmarket post mortem survey, involving both local and referred cases, revealed that 2.9% of cases were associated with twin pregnancy.

Before the widespread use of ultrasonographic imaging in equine pregnancy diagnosis, **twinning** was the most important cause of abortion in Thoroughbred mares, accounting for up to 29% of all abortions. Now that early detection of twins is possible, appropriate action can be taken to eliminate one conceptus and leave a singleton, or terminate the pregnancy and mate the mare again, as appropriate. Nevertheless, the occasional twin pregnancy evades detection.

Umbilical cord abnormalities

The Newmarket post mortem survey revealed that 46.2% of cases were associated with **umbilical cord vascular compromise**, clearly now one of the most important causes of abortion in Thoroughbred mares.

Developmental abnormalities or **excessive cord length** may constrict blood vessels and cause circulatory disturbances. It has been shown that excessive cord length (>90 cm) is associated with an increased incidence of vascular embarrassment leading to fetal death. Presumably a longer cord allows the fetus greater mobility, predisposing to cord accidents including strangulation

of the cord around the fetal neck, body or limbs, pinching of the cord between the fetus and the maternal pelvis, and excessive twisting of the cord.

Placentopathy

The Newmarket post mortem survey revealed that 8.1% of cases were associated with premature placental separation, 1.4% with posterior (cervical) pole placentopathy and 4.8% with other placental abnormalities.

An apparently non-septic posterior (cervical) pole ischemic placentopathy can cause abortion in mares, sometimes associated with excessive umbilical cord length and placental vascular inadequacy. **Premature placental separation** may occasionally be caused by endometrial and placental vasculitis associated with "atypical" EHV infections.

Nutritional deficiencies

Vitamin A and energy deficiencies have been suspected as causes of abortion.

Mare reproductive loss syndrome (MRLS)

Late fetal losses in MRLS (*q.v.*) manifest as **late term premature placental separations** ("red bag" deliveries) resulting in the birth of weak and often non-viable foals.

Other causes

The Newmarket post mortem survey revealed that 1.9% of cases were associated with maternal illness and that for 5.2% the cause of the abortion was not established.

Other probable but as yet incompletely defined causes include **endocrinologic dysfunction, chromosome or gross developmental abnormalities, maternal and/or fetal circulatory disturbances** caused by changes in maternal posture, fright or trauma. Certain surgical procedures (e.g. colic surgery) necessitate placing a pregnant mare in dorsal recumbency. In this position, the weight of the gravid uterus leads to aortocaval compression. There is a reduction in venous return to the heart, a reduction in cardiac output, and a significant drop in peripheral blood pressure resulting in reduced blood flow and oxygen delivery to the uterus. Maternal pulmonary gas exchange may also be impaired, compounding the fetal hypoxia. Precautions should be taken to **minimize anesthetic and surgical time**, especially time in dorsal recumbency, and maintain adequate maternal blood pressure (mean arterial pressure >80 mmHg). Intermittent positive pressure ventilation is recommended to improve pulmonary gas exchange. In general, the **unnecessary administration of drugs** during pregnancy should be avoided.

Pathogenesis

There are two principal pathways leading to expulsion of the fetus: **fetal death in utero preceding expulsion**, which occurs in cases of infectious abortion and non-infectious disturbances causing cardiac and circulatory failure; and **the abortion of a live premature fetus**, where the fetus may be expelled with its heart beating and may establish a respiratory rhythm for minutes or

even hours. In these cases the causal factors probably arise from the maternal side of the placenta, or from **fetal endocrinologic malfunction**.

Placental insufficiency, related to infective or non-infective causes, is an important cause of abortion. Twins are an example where reduced placental function leads to death of one fetus and eventually to abortion of both fetuses.

Clinical signs

Frequently there are **no premonitory signs** of impending abortion, and the foal is expelled with minimal effort, dystocia (*q.v.*) being unusual. The fetal membranes may be expelled with the foal or may be seen hanging from the vulva. Occasionally there is a prolonged third stage requiring therapeutic removal of the fetal membranes. A mucopurulent vulvar discharge is usually an indication of **chronic placentitis**, bacterial or fungal, or **premature placental separation**. In protracted cases, premature mammary development and lactation are frequently seen. A vulvar discharge may also be seen where fetal death has occurred in utero, although this usually results in rapid expulsion, and fetal mummification is rare in mares. Premature mammary secretion without vulvar discharge was often a sign of impending twin abortion but now that twin pregnancy is so uncommon it is more commonly seen with cases of placentopathy.

Diagnosis

Diagnosis of the cause of abortion depends on **detailed pathologic examination** of the fetus and its membranes. It is particularly important that a full examination is performed in every case so that EHV infection (*q.v.*) is not overlooked.

Bacterial infections

Bacterial abortions account for up to 13% of all equine abortions. Abortion due to bacterial placentitis can occur at any stage of gestation, but typically occurs after 5 months' gestation. There are three possible routes of access of the bacteria to the fetal tissues: **ascending infection** via the cervix resulting in caudal chorionitis—cervical incompetence will predispose to this situation, although the cervix often appears normal on examination; **hematogenous spread** via systemic infection of the mare—in this case the chorion is affected in a diffuse fashion; and **local spread** from deep-seated foci of endometritis.

The affected placenta is thickened and the maternal surface necrotic with areas covered in grayish exudate. Focal placental separation occurs. Pregnancy continues until the remaining area of functional placenta is insufficient to nourish the foal, and fetal distress or death precipitates expulsion. The infection generally involves 5–25% of the chorion, but in some cases gross placental lesions are minimal and microscopic examination of representative areas, including the cervical star, should be performed.

Infection may spread to the amnion via the allantois causing fetal lung pathology. In this case the causal organism can be cultured from the fetal stomach contents. Alternatively, the organism enters the fetus via the umbilical vein and lesions are seen in its liver. Typical signs of fetal septicemia are congested

mucous membranes and serosal surfaces, serous exudates and dark red/purple coloration of the muscles. Histopathologic changes will depend on the ability of the fetus to mount a cellular response to infection, and may be obscured by autolysis occurring between fetal death and expulsion.

Fungal infections

Fungi are responsible for up to 10% of all abortions in mares. The typical clinical presentation includes **premature lactation** and a **purulent vulvar discharge**. The pathology is usually confined to the placenta but may spread to the amnion, and occasionally to the fetus itself. The fetus is small and emaciated due to chronic placental insufficiency, and may be born alive but usually succumbs soon after birth.

Examination of the placenta reveals gross thickening, particularly at the cervical pole, and a brown/white sticky exudate. Histopathologic changes include **widespread necrosis of the chorionic villi**, an intense polymorphonuclear cell inflammatory response in the subepithelial chorionic tissue, multinucleate giant cells, and demonstrable fungal hyphae within the tissue. Amniotic lesions consist of irregular necrotic plaques. When fetal infection is present, small grayish-white nodules are seen scattered throughout the lung. Microscopically, fungal elements can be demonstrated by the use of special stains (e.g. periodic acid–Schiff and Grocott).

Equine herpesvirus (EHV, rhinopneumonitis)

EHV-1 and to a lesser extent EHV-4 (*q.v.*) are the only currently recognized forms of **contagious abortion** in the mare in the UK. In countries where EVA is endemic, this virus may cause multiple abortions following infection in a group of pregnant mares. The potential threat of an EHV-1 epidemic or "abortion storm" (not recognized with EHV-4) is such that precautions should be taken in every case of abortion until EHV-1 has been ruled out, as recommended by the HBLB Code of Practice (*q.v.*). The aborting mare should be isolated, a movement ban imposed and measures taken by personnel to limit spread. The fetus and fetal membranes should be submitted for post mortem examination and a diagnosis established as rapidly as possible.

Epidemiology

EHV infection during pregnancy, often linked to **foal-at-foot respiratory infection** at around 3 months' gestation, may result in abortion at 7 months onwards or the birth of a weak viremic foal at term. It is reported that susceptible **pregnant mares may abort** 3 wk to 4 mo after infection. The virus survives for about 14 days outside the body, and this may be extended to 40 days if it becomes dried onto organic matter. Late pregnant mares become **infected by contact** with aborted fetuses, fetal membranes and fluids, or aerosol shedding of virulent strains of the virus via the respiratory route from other individuals and may abort soon afterwards. The virus has been isolated from the respiratory tract of an apparently healthy foal during an outbreak. After abortion, the virus does not appear to persist in the reproductive tract but the **mare may shed virus via the respiratory route**.

Diagnosis

Abortion from EHV has its greatest incidence in gestational months 8 and 9, but has been recorded as early as 4 months. The infection is also responsible for stillbirth or neonatal illness/death. Typical gross changes seen in the fetal tissues at post mortem examination form an important means of early presumptive diagnosis, but these gross changes are highly variable in terms of severity and organ pathology, particularly in vaccinated mares. Definitive confirmation must be provided by microscopic examination of the fetal tissues, fetal and placental tissue EHV PCR tests, fetal and placental tissue EHV immunostaining and/or viral culture.

Some, but rarely all, of the typical gross lesions described below will be seen in the affected fetus or foal. Over half of EHV-1 abortions are born within intact fetal membranes. In other cases, rapid expulsion may occur and the membranes are delivered **villous side outermost**. Premature placental separation is not specific for EHV-1 infection, but it serves as a cautionary sign. The fetus usually appears to be in **good bodily condition** and good state of preservation. Jaundice of the mucous membranes, abdominal organs, footpads and joint surfaces is usually seen. Excessive amber-colored peritoneal, pleural and pericardial fluids are often seen.

White/yellow **pinhead-sized spots** under the liver capsule are an important diagnostic feature but their absence does not rule out infection. On gross section these lesions are found scattered throughout the liver parenchyma. The signs of jaundice, excessive amber-colored peritoneal and pleural fluids, gelatinous perirenal fat and the liver lesions have been found to be the most dependable gross findings, where they occur. The lungs may show subpleural edema, congestion, petechial hemorrhages and pneumonia. The spleen may be congested with petechial hemorrhages beneath the capsule and the lymphoid follicles may "stand out" in a granular manner.

Same day or overnight microscopic sections from formalin-fixed tissues are now obtained using modern microwave embedding processes. The diagnosis of viral abortion on microscopic examination depends upon the demonstration of typical eosinophilic **Cowdry type A intranuclear inclusion bodies**. The pathologic findings may differ between early (before 6 months) and later abortions. Before 6 months the fetus has either a limited or no ability to produce inflammatory and immune responses, and the lesions are characterized by widespread necrosis, whereas more mature fetuses can mount an inflammatory response.

The typical lesions are **hyperemia** and in some cases hemorrhage in the **liver**, with focal areas of cell necrosis with karyolysis and pyknosis. Inclusion bodies are seen in hepatocyte nuclei bordering the necrotic area. Inclusion bodies may also be seen in bile duct epithelia, blood vessel endothelia, fibroblasts and smooth muscle cells within the liver. There are varying degrees of congestion and pneumonia in the **lungs**, with necrotic inflammatory debris plugging the airways. Virus inclusion bodies are most frequently demonstrated in the lining epithelial cells of bronchi, bronchioles and alveoli. Necrosis of primary follicles with inclusion bodies is seen in the **thymus**, and in the **spleen** necrosis of splenic cores with inclusion bodies can be found. Similar foci of necrosis and inclusion bodies are often found in the adrenal cortex.

Definitive confirmation of EHV infection is made on the basis of specific PCR tests performed on fetal and placental tissues, backed up, if necessary, by immunostaining. **Virus culture** may be made from fetal viscera (fresh fetal lung, liver, spleen and thymus tissues in viral transport medium dispatched to a suitable virology laboratory without delay) but results may require 8–10 days in tissue culture.

Serologic studies may assist in investigating the epidemiology of an outbreak, but used alone are not a suitable means of diagnosis. Complement fixation tests (CFT) may be useful in differentiating infected from uninfected animals, so that they can be segregated from each other during an outbreak. CF antibody is normally detected 10 days after initial infection, and a fourfold increase in titer is seen. Virus neutralizing antibody persists for longer than CF antibody and may be used to demonstrate previous exposure. No association between susceptibility to infection and virus neutralizing antibody provided by previous infections has been found, and mares can become infected each year. This is, however, rare.

So-called "atypical" cases have been seen in Newmarket where the aborted fetus shows no histopathologic or viral evidence of EHV-1 infection but the placenta shows signs of infection (PCR and immunostain positive). Focal placentopathy and early placental separation is involved. Cases have been solitary, so far, usually in vaccinated mares. Their epidemiologic significance currently remains unclear.

Equine viral arteritis (EVA)

EVA is an acute contagious viral disease, characterized by fever, edema and abortion. The virus is transmitted between horses as a respiratory aerosol and via semen from seropositive stallions. The incubation period is 7–10 days. The existence of symptomless carriers serves as a reservoir of infection.

In contrast to EHV abortion (*q.v.*) where the mare shows no clinical signs of disease, EVA abortion (*q.v.*) occurs during the **acute phase of maternal infection** and the mare may show clinical signs of depression, fever (≥40°C), leukopenia, keratitis, palpebral edema, photophobia and dependent edema. In pregnant mares, fetal death is followed by abortion 7–10 days after the first signs of clinical disease. In some mares the clinical signs of maternal illness are so slight that they remain undetected.

Pathogenesis

It is believed that decreased blood supply to the placenta and fetus results in myometrial edema, tissue distension and loss of myometrial tonicity. There is mechanical compression of the blood vessels, placental detachment and delivery of a dead, moribund fetus.

Diagnosis

Diagnosis is based upon a detailed post mortem examination of the fetus and its membranes, revealing only signs of congestion and placental separation. Definitive diagnosis is obtained by specific PCR tests, viral culture of fetal tissues, and serologic tests on the blood of the infected mares. The serum neutralization test currently remains the international standard blood test but there is a clear need for a reliable ELISA test.

Treatment of abortion

The most commonly applied "treatment" is exogenous progesterone supplementation, but there is no scientific rationale to commend it. It is doubtful whether non-infectious abortion can be prevented or whether attempts to do so are indicated. Where fetal death is confirmed and/or when it is clear that abortion is inevitable, it is more appropriate to aid **speedy, atraumatic delivery** and to direct treatment toward returning the mare to optimal breeding condition as quickly as possible.

For **infectious abortion**, where a vulvar discharge is present, bacterial and fungal culture of the vulvar discharge may help characterize the infectious agent, so that systemic and/or local antibacterial or antimycotic agents can be employed. If there is pneumovagina (*q.v.*), appropriate vulvar surgery should be performed. If early treatment is applied, the pregnancy may be maintained closer to term, but in many cases where the foal is born alive it is weak and non-viable. Following expulsion of placental membranes affected by bacterial or fungal infection, the infection rarely persists in the mare's uterus. However, involution should be monitored, using cervicouterine bacteriologic and cytologic examinations at first post partum estrus to detect residual infection/inflammation. Uterine antibiotic/saline irrigations can then be employed as necessary.

Prevention of abortion

An inactivated EHV-1 and 4 vaccine (Duvaxyn EHV1,4) is available and licensed for use in pregnant mares against EHV abortion in the UK and some other European states, and its widespread use has reduced the incidence of abortions from EHV-1 and 4. The manufacturers recommend vaccination at 5, 7 and 9 mo of pregnancy each succeeding year. Ideally, in-contact horses on the stud farm should also be vaccinated using a priming course and a yearly booster. The vaccine does not prevent sporadic abortion but may help to prevent the occurrence of abortion storms. The use of another inactivated EHV-1 vaccine (Pneumabort-K) in Kentucky between 1950 and 1980 coincided with a reduction in diagnosed EHV-1 abortions from 25% to 10%.

An attenuated live virus (Bucyrus strain) EVA vaccine has been used in North America and has been found to produce a high degree of immunity. It is not recommended for use in mares in late gestation and it should be remembered that vaccination will complicate the diagnosis of EVA by serologic methods. Currently, a formalin-fixed EVA vaccine is licensed for use in Germany and is available in the UK under an Animal Test Certificate (ATC) and is similarly used in France and Ireland (usually for stallions rather than mares).

PARTURITION AND THE POST PARTUM MARE

PRE PARTUM CONDITIONS

The colic complex

Colic in a mare during her last trimester of pregnancy presents the clinician with a diagnostic challenge. **Gastrointestinal tract abnormalities** (*q.v.*) must

be eliminated by careful clinical examination, but the size and position of the fetus often makes optimal examination difficult. Some conditions of the genital tract can cause colic during this period.

Abortion/premature parturition may present as mild to moderate colic, with minimal premonitory signs such as mammary development. Vaginal examination reveals a moist, pink vagina, usually with loss of the cervical plug and relaxation of the cervix. In the early stages of abortion, rectal examination reveals the fetus to be engaged in the birth canal and there may be a **palpable pain response**. Veterinary intervention should be to facilitate an atraumatic delivery and then to provide post partum care of the mare, if required. All aborted fetuses should undergo a post mortem examination in order to eliminate EHV infection and the mare should be isolated until results are available.

Uterine dorsoretroflexion is seen in the last trimester of gestation. It usually presents as an acute moderate to severe colic, with inappetance, difficulty passing feces and in some cases abdominal straining. There is frequently vulvar and perineal swelling. On **rectal examination** a live fetus is characteristically palpable in a tight sac-like distension of the uterus, immediately under the hand, just cranial to the anus. Palpation of the fetus produces a marked pain response. Smooth muscle relaxant drugs (**butylscopolamine bromide** 0.2 mg/kg IV, or **clenbuterol** 0.8 μg/kg IV) should be administered in order to relax the myometrium and allow the fetus to return to a more cranial position in the abdomen, relieving the mare's discomfort. Food intake is reduced, and the mare given gentle exercise. Repeated administration of smooth muscle relaxants may be necessary in some cases. The pregnancy then usually proceeds uneventfully.

Uterine torsion is uncommon in mares. It usually occurs in **late gestation**, however it can occur at parturition. It presents as colic of varying severity, which may continue over several days. There is usually some **difficulty passing feces**. The condition is confirmed by rectal examination. It is often difficult to advance the arm in the rectum and the fetus is not palpable. Palpation of the broad ligaments will identify the torsion and indicate its direction. In cases of **anticlockwise torsion** the left uterine ligament is tight, runs ventrally and is caudal, the right ligament is slacker, runs from right to left and is cranial to the left ligament. It is possible to confuse the uterine ligaments with mesenteric bands associated with a large intestinal displacement, but in these cases the fetus is palpable. In mares, the vagina is very rarely involved, unlike cases of uterine torsion in the cow. Once a diagnosis has been made, **surgical correction** is indicated without delay in order to maintain fetal viability. This is performed either by standing flank laparotomy, sometimes requiring a two-surgeon, two-sided approach, or midline laparotomy in dorsal recumbency under general anesthesia in order to reposition the uterus. Where the fetus is already dead, confirmed if necessary by ultrasound imaging, Cesarean section is indicated.

Fetal hypermotility presents as **mild colic in late pregnancy**. It is associated with excessive violent movements of the fetus of unknown cause. Attempts by the fetus to correct an uncomfortable in utero position have been postulated. The condition appears to be more common in **first foaling mares** and older mares. Treatment with smooth muscle spasmolytics (e.g. **butylscopolamine bromide** 0.2 mg/kg IV) is usually effective. The possibility of fetal distress must be considered. If signs persist or if there are signs of premature parturition, a full assessment of the fetus with external transabdominal ultrasonographic

imaging should be performed and calcium and electrolyte levels of mammary secretion assessed.

Hydrops allantois is an uncommon condition seen in **multiparous mares**. Until the allantoic fluid reaches volumes in excess of 100 L there may be no clinical signs. The condition is seen in the last trimester of pregnancy, presenting as sudden marked abdominal distension, often with low-grade signs of colic, inappetance, dyspnea (particularly when recumbent) and difficulty in passing feces. On **rectal examination** the fetus is characteristically not palpable, and the uterus appears excessively distended and clearly fluid filled. Transabdominal ultrasound scan examination may be used to measure the allantoic fluid (>20 cm is abnormal). In cases of severe distension **prepubic tendon rupture** may occur, with associated pain and ventral abdominal swelling. The condition is progressive and parturition should be induced when the mare's clinical condition starts to deteriorate. Oxytocin may not be effective because the myometrium is over-stretched. **Prostaglandin E_2 pessaries** should be used to dilate the cervix to allow manual rupture of the allantochorion. Half the allantoic fluid should then be siphoned off. An **oxytocin drip** (20 IU) should then be administered to prevent cardiovascular shock associated with pooling in the splanchnic vasculature. In some cases supportive fluid therapy may be indicated.

Vaginal discharges

Vulvar and/or vaginal discharges are not uncommon in late pregnancy. Confusion can occur with urine staining or liquefaction of the cervical plug.

If vaginoscopic examinations reveal a vaginitis and cervicitis, **swab samples** should be collected for cytologic, bacteriologic and fungal examinations. Pus may be seen discharging though the cervix in cases of cervical pole placentitis. Topical treatment with appropriate antibiotics or specific antifungal preparations may be helpful, though in cases of placentitis the results are frequently disappointing. In cases where the fetus is viable and the pregnancy continues, the foal should be considered "high risk" and appropriate precautions taken at parturition.

Hemorrhage from **varicose vaginal vessels** is sometimes observed, but the quantities of blood lost are usually small and treatment is seldom necessary. These vessels are usually found dorsally at the level of the redundant hymen. If the problem persists, individual vessels can be identified via a "duck-billed" speculum held sideways and cauterized or coagulated with the application of swabs moistened with 5–10% formol saline.

Prolonged gestation

It is reported that 1% of pregnancies continue over 370 days, often resulting in a small foal. The condition is not uncommonly seen in aging mares with **advanced chronic degenerative endometrial disease**, where eventual parturition produces a dysmature foal. In other mares it has been postulated that a period of embryonic diapause may be involved.

If clinical examination of the mare reveals no abnormality, prolonged gestation is not an indication to induce parturition, as this may produce an at-risk

dysmature foal. External transabdominal ultrasonographic imaging can be used to evaluate the health of the fetus and its placental membranes.

Estrous behavior during pregnancy

Some mares repeatedly exhibit signs of estrus during pregnancy, which should be confirmed and the viability of the fetus assessed.

Rupture of the prepubic tendon

Tearing or complete rupture of the **prepubic tendon** may occur at its insertion to the pelvis, usually after the ninth month of pregnancy. The rupture usually occurs a little to one side of the midline and there is **gross ventral edema** associated with obstruction to venous drainage. Early induction of parturition and assistance at foaling due to reduced expulsive forces may be necessary in acute cases. In stabilized, non-painful cases, normal parturition usually occurs, the mare compensating for the lack of ventral abdominal tone by lying down and using the floor as abdominal support. Attempts at surgical repair using a synthetic mesh have been reported, but in rare cases of complete painful rupture the prognosis is hopeless.

Premature lactation

Premature lactation is not an uncommon condition and may be an indication of abnormality of the fetoplacental unit, most commonly placental separation and placentitis, or twin pregnancy with the death of one fetus. In some cases no obvious cause is proven.

The measurement of mammary secretion electrolyte levels may help to determine fetoplacental "readiness for birth". During the last 3 weeks prior to parturition there are marked changes, which are more diagnostically reliable in multiparous than in primiparous mares: **sodium** falls from 118 mmol/L to ≤30 mmol/L; **potassium** rises from 13 mmol/L to ≥30 mmol/L; **chloride** falls from 91 mmol/L to 33 mmol/L; **magnesium** rises from 3 mmol/L to ≥10 mmol/L; and **calcium** rises to ≥10 mmol/L.

External transabdominal ultrasonographic imaging should be performed to evaluate the health of the fetus. A 3.0 or 3.5 MHz linear array scanner is preferred. Normal fetal heart rate in the last 30 days of gestation is 76±8 bpm, with marked variations during periods of fetal activity.

If mammary development progresses and premature lactation occurs, the colostrum should be collected and IgG levels measured. If ≥70 g/L, the colostrum should be frozen for future administration to the newborn foal. If IgG levels are inadequate, the newborn foal should be given **good-quality donor colostrum** by bottle or stomach tube.

Orthopedic problems

Problems can develop in late gestation, particularly in overweight mares. Previous limb injuries may recur. **Strain injuries** to the hindlimbs are common due to increased weight on the suspensory apparatus and joints. These

require careful management with restricted exercise, support bandages and management of weight gain. **Laminitis** (*q.v.*) can occur in late pregnancy and may prove difficult to manage at that stage. Induction of parturition may be indicated on humane grounds. **Peripheral edema** of the hindlimbs is sometimes seen, apparently associated with poor lymphatic drainage and decreased exercise during late gestation. Gentle exercise and judicious use of phenylbutazone may be necessary to help the mare through to parturition.

INTRA PARTUM CONDITIONS

Dystocia

Dystocia is relatively uncommon in the mare. Most commonly, cases are associated with fetal deformity (e.g. hyperflexed forelegs), fetal death (active fetal movements are required to produce the correct birth posture) or twin presentation.

Foaling is a rapid and forceful event. **Early intervention** is necessary if the foal is to be saved. If delay is inevitable, appropriate advice to the attendants may affect the outcome. For example, in cases of **malpresentation** the mare should be kept up and walking to reduce further abdominal straining and prevent impaction of the foal in the birth canal; in cases of **premature placental separation** causing "red bag delivery", the allantochorion should be immediately ruptured manually and delivery assisted; **posteriorly presented foals** should be delivered as rapidly as possible, without undue force, in order to prevent umbilical cord compression; if the foal's foot or muzzle has caused a **rupture of the rectovaginal shelf**, but the foal is alive, delivery should be assisted without immediate concern for third degree perineal tearing, if unavoidable. If possible, the foal's limb or head should be replaced in the vagina before delivery to limit damage to a rectovaginal fistula; if the foal has **failed to rotate** into dorsal position the mare should be allowed to get up and down and roll in an attempt to correct the situation.

Careful examination of the mare and foal is essential to allow accurate diagnosis and treatment. The mare should be **restrained in the standing position** with one attendant holding her head and one holding her tail in order to maintain her in standing position. She will be distressed and uncomfortable and will attempt to get down, and examinations and manipulations may sometimes need to be made while walking slowly around the stable. The attendant at the head can help by holding the mare's tongue out of the side of her mouth to reduce the force of abdominal straining. **Copious lubrication is essential**. A thorough assessment should be made to determine the answers to the following questions: Is the foal alive? Are fore or hindlimbs presented? Is the foal deformed? Are twins presented? Is the birth canal adequately relaxed to allow vaginal delivery? Is the foal relatively oversized? Will an epidural anesthetic, by reducing abdominal straining, assist delivery?

Following careful assessment it is important to make an early decision whether Cesarean section or fetotomy (*q.v.*) is necessary.

For **assisted vaginal delivery**, the mare should be restrained standing to facilitate repositioning of the foal. Once this is achieved, the mare should be encouraged to lie down. The birth canal must be **fully relaxed before traction**

is applied, and plenty of lubrication is essential. Once repositioning has been completed, traction should be applied in unison with abdominal straining, and the foal pulled in a downward curving arc, one leg at a time to reduce width at the shoulders. Careful positioning of color-coded ropes may be helpful. In some circumstances, repositioning and vaginal delivery may be carried out under general anesthesia. Epidural anesthesia (*q.v.*) may be useful to abolish abdominal straining, and raising the hindquarters may also help.

Cesarean section, when performed by an experienced surgical team at an early stage, now generally carries a good prognosis for both mare and foal and is the preferred option when the foal is alive and where prolonged and difficult manipulation and traction would clearly endanger the health of both.

Fetotomy is a potentially **hazardous procedure** for the mare. It should only be used by experienced clinicians, in situations when it can be performed easily and safely, preferably external to the vulva. When economic considerations preclude Cesarean section and the foal is dead, this technique may be used to save the mare in spite of the risk of cervical damage. The mare should be sedated, an **epidural** anesthetic administered and smooth muscle relaxants, e.g. **isoxsuprine**, may be administered.

After an assisted foaling the mare should be examined for vaginal or cervical **lacerations**. Antibiotic therapy (including oral **metronidazole** to help prevent anaerobic infections) is advisable to reduce the risk of metritis (*q.v.*) and the mare should be exercised to assist uterine involution and to avoid pooling of uterine fluid.

Premature separation of the allantochorion

Sometimes the chorion separates prior to rupture at the cervical pole. The chorioallantois is presented as an intact velvety red sac at the vulvar lips ("**red bag delivery**"). Rapid manual rupture and assisted delivery are essential to save the foal.

Failure to lie down

Mares may sometimes foal in the standing position, particularly if attendants disturb them. Mares with musculoskeletal problems may be too uncomfortable to lie down. Once the situation is clear the mare should be restrained and the foal supported to prevent injury and premature rupture of the umbilical cord. Traction is usually necessary as contractions are less forceful in the standing position.

Uterine inertia

This is an unusual condition which may be more common in primiparous than multiparous mares. The mare remains relatively comfortable in persistent first stage labor, with a relaxed cervix, but does not initiate second stage. Parturition should be induced with 0.5 IU oxytocin administered in 1 L saline by IV drip, usually without complications.

Failure to strain

This may be due to heart, chest or orthopedic problems. The mare is uncomfortable in second stage labor but does not complete delivery because of diminished or failed abdominal straining. In some cases there may be no obvious cause. Assisted delivery by traction is necessary.

Relative fetal oversize

This may sometimes be seen in primiparous mares and may be due to inadequate pelvic relaxation. Any traction must be applied with great care not to damage either the foal, particularly at the chest, or the mare.

POST PARTUM CONDITIONS

A variety of maternal injuries and complications occur in association with the rapid and forceful equine birth process. These may be life threatening or may adversely affect future fertility.

Retained placenta

Normally, the equine placenta is fully and atraumatically released from the uterus within 1–2 h of the end of second stage labor. Retention may be diagnosed if release has not occurred by **the morning after parturition**. It is a relatively common complication that is most commonly associated with dystocia, abortion or Cesarean section, but may occur spontaneously. The nonpregnant placental horn is most commonly involved, especially at its tip. The recommended approach to removal is described in Box 13.2.

Vaginal hematomas

A hematoma may protrude though the vulvar lips, and can alarm attendants. When sizable, hematomas can produce abdominal straining. They can be drained or left to resolve according to individual circumstances. It is wise to provide systemic antibiotic medication to prevent secondary infection.

Uterine hemorrhage

Hemorrhage from the **uterine artery** is most commonly seen in older multiparous mares, but has been seen in primiparous mares. Dystocia (*q.v.*) does not appear to increase its incidence. Hemorrhage is not always fatal if it is contained within the broad ligament and associated tissues, but the mare will exsanguinate if the hematoma ruptures into the peritoneal cavity or the uterus.

Initial signs, seen within minutes or hours of parturition, are **acute moderate to severe colic** and sweating, with rapid pulse, which progresses to **cardiovascular shock**. The mare should be kept quiet with mild sedatives and analgesics. **Hypotensive tranquilizers** such as acepromazine or detomidine may help to encourage clotting to occur in some cases but may risk accelerating cardiovascular collapse (*q.v.*) in others. Fluid therapy with blood or

Box 13.2 Removal of retained placenta

- **Manual removal** should only be attempted with great care and should be abandoned if not immediately and easily successful. There is a considerable risk of causing chorionic microvillous retention, which can lead to **septic metritis**. Also there is risk of uterine wall damage and hemorrhage. Tearing the fragile placenta delays further natural release and increases the risk of leaving areas of placenta in the uterus. Sometimes the placenta appears to become impeded in the vagina; by gently collecting it together, lifting and rotating, release is easily completed.
- If gentle manual removal is not immediately successful, an **IV drip containing 50 IU oxytocin in 500 mL of sterile saline** should be administered over approximately 15 min. An IM bolus of 30–50 IU oxytocin may be effective when administered in the first 24 h after parturition. Repeated doses may be necessary beyond this period. These classically recommended doses of oxytocin are probably excessive, and 15–20 IU are probably as effective and more humane.
- If repeated IV drips of oxytocin are not successful then **large volumes (10–12 L) of warm water with dilute povidone–iodine** may be pumped into the allantochorionic space via a stomach tube. This distends the uterus and placenta, releases chorionic microvilli and stimulates uterine contractions and is usually effective within 30 min.
- **Systemic antibiotics** (including oral metronidazole to help prevent anaerobic infections) and flunixin (1.1 mg/kg IV to help minimize the effects of endotoxin release) therapy is indicated in most cases. If the placenta is retained for more than 8 h, bacterial multiplication is rapid and there is a risk of septic metritis and laminitis. Intrauterine antibiotic irrigations may also be useful in some cases.

plasma expander or hypertonic saline does not seem to alter the course of the condition and may be contraindicated as it often stresses the mare and increases blood pressure and further hemorrhage, delaying clotting. Treatment with hypertonic saline solutions has been reported to be useful in some cases. In mares that survive, the hematoma will be palpable for some considerable time.

Uterine rupture

Uterine rupture may follow dystocia or normal parturition. If the rupture is large, the mare will show signs of **peritonitis and cardiovascular shock** (*q.v.*), usually with a rapidly fatal outcome. If the uterine serosa remains intact the mare will show signs of colic but may survive with careful supportive treatment. Smaller tears may not become apparent until signs of peritonitis develop. Broad-spectrum systemic antibiotics (including **oral metronidazole** to help prevent anaerobic infections) and **flunixin** (1.1 mg/kg IV, to help minimize the effects of endotoxin release) therapy should be instituted, and early surgical repair considered. Small perforations sometimes only become apparent when localized peritonitis develops into a localized abscess and these may

respond to medical treatment with prolonged courses of antibiotics. Cautious IV sodium iodide therapy (0.4 mL/kg 16% aqueous **sodium iodide**, twice weekly for 4 wk) may be helpful.

Uterine prolapse

The cranial and lateral attachments of the equine broad ligament make uterine prolapse uncommon. It may occur at parturition but is more often associated with dystocia or placental retention (*q.v.*).

The mare should be sedated, an epidural anesthetic (*q.v.*) administered and broad-spectrum systemic antibiotics (including **oral metronidazole** to help prevent anaerobic infections) and **flunixin** (1.1 mg/kg IV to help minimize the effects of endotoxin release) therapy should be instituted. It is usually easier to replace the uterus with the mare's hindquarters raised. The uterus should be cleaned with a **dilute povidone-iodine solution** and examined carefully for lacerations, which should be repaired, before it is carefully replaced. The vulva should be temporarily sutured with heavy-duty suture material, allowing just enough opening for urination. IV oxytocin drips and large-volume intrauterine antibiotic irrigations are recommended to aid uterine involution and to prevent septic metritis (*q.v.*).

Thoroughbred mares may suffer from **hypovolemic shock**, and intensive care with IV fluid therapy may be required.

Cervical lacerations

Cervical lacerations may occur at foaling, most commonly associated with dystocia. **Mucosal splits** may heal completely with the aid of applications of local antibiotic ointment to prevent infection and adhesion formation. Lacerations involving the **muscular layer** interfere with closure of the cervical os and **profoundly reduce fertility**. Surgical repair is attempted after initial healing, with the mare sedated and restrained standing in stocks, under epidural anesthesia. After debridement, a three-layer closure is made (internal and external mucosae and muscularis) but this is never technically simple and reconstruction is seldom functionally ideal. Fertility, in most cases, remains depressed. Abortion and premature parturition, associated with posterior pole placentitis, are common sequelae.

Cervical lacerations can be prevented during fetal repositioning and assisted delivery if maximal cervical dilatation is encouraged, **copious lubrication** used and Cesarean section (*q.v.*) is considered as an alternative to fetotomy.

Vaginal rupture

Perforation of the dorsal vaginal wall by the **foal's foot** or muzzle during delivery occurs more commonly in primiparous than multiparous mares. It can also occur during obstetric manipulation. Cranial ruptures communicate directly with the peritoneal cavity, and the abdominal viscera may be damaged or may **prolapse** though the tear. Surgical repair is most readily attempted with the mare sedated and under epidural anesthesia (*q.v.*), restrained standing in stocks.

Broad-spectrum systemic antibiotics (including **oral metronidazole** to help prevent anaerobic infections) and **flunixin** therapy should be instituted to minimize the effects of endotoxin, and antibiotics should be administered into the abdominal cavity prior to closure. Traction of cervical stay sutures may improve exposure but the heavy post partum uterus makes full retraction difficult. The edges of the tear should be apposed using absorbable sutures, and a **Caslick's vulvoplasty** (*q.v.*) operation performed to prevent aspiration of air.

Retroperitoneal abscesses can develop secondary to vaginal lacerations that may have been overlooked. These often become chronic and require prolonged courses of appropriate antibiotic therapy. IV sodium iodide treatment (0.4 mL/kg 16% aqueous sodium iodide, twice weekly for 4 wk) has been very helpful in resolving some cases.

Endometrial hemorrhage

A persistent **hemorrhagic discharge** is observed for 3–4 days after parturition. **Oxytocin**, 50 IU in 500 mL of sterile saline, should be administered by IV drip over approximately 15 min or 15–20 IU IM, and may be repeated 2–3 times daily. If there is severe hemorrhage, exercise should be restricted and supportive treatment administered. Focal peri-uterine or endometrial hemorrhages are sometimes seen during ultrasound examinations at the first post partum estrus ("foal heat").

Delayed uterine involution

Delayed involution may be associated with grossly retained placenta, retained chorionic microvilli, uterine infection or lack of exercise. The mare may be dull with a poor appetite and signs of mild abdominal discomfort. There may be more serious signs of septicemia, toxemia and/or laminitis. There is usually a persistent hemorrhagic discharge that may be foul smelling. Vaginal examination will reveal a **downward tilt of the vagina**, often urine pooling and associated marked vaginitis. Rectal examination reveals the uterus to be voluminous. Ultrasound imaging reveals turbid fluid in the uterus.

When there is systemic involvement, parenteral antibiotics (including **oral metronidazole** to help prevent anaerobic infections) and **flunixin** therapy should be given. Large-volume **uterine lavage** should be used to remove accumulated exudates, and 20–50 IU oxytocin in 500 mL sterile saline should be administered over approximately 15 min to stimulate uterine contraction or 15–20 IU IM may be repeated 2–3 times daily. Exercise is also beneficial.

Pelvic fracture

Fractures (*q.v.*) most frequently occur in the iliac shaft or pubic symphysis following prolonged dystocia or a fall, during or after delivery. Confinement and supportive therapy allows repair in some cases but euthanasia may be indicated on humane grounds for others.

Metritis/laminitis/toxemia

This is an uncommon but **serious post partum complication**. Acute metritis may develop secondary to dystocia (*q.v.*), retained placenta or uterine contamination at or after delivery. The mare shows signs of depression, anorexia, pyrexia, congested mucous membranes and reluctance to move. The uterus is voluminous and filled with fetid brownish fluid, which may contain a small piece or pieces of placenta.

Treatment should include **systemic broad-spectrum antibiotic** (including **oral metronidazole** to help prevent anaerobic infections) and **flunixin** medication. The uterus should be irrigated using a **warm dilute povidone-iodine solution** and two stomach tubes. The lavage should be continued until the egress fluid is clear and may need to be repeated daily or twice daily until the uterus starts to involute, placental fragments and/or retained microvilli slough and are removed. Oxytocin, 15–20 IU administered IM, will help evacuate fluid from the uterus and hasten involution. A course of intrauterine antibiotics should be given. Early treatment for laminitis (*q.v.*), including sole supports or heart bar shoes, is important.

Gastrointestinal complications

Cecal rupture (*q.v.*) often involves an area of **avascular necrosis** at the cecal tip. The incidence is low (approximately 0.1%) and the cause is unknown, although chronic compression of the cecal tip between the fetus and maternal pelvis has been postulated. Parturition is often normal until second stage labor, when assisted delivery is required. Signs of colic, cardiovascular shock and acute peritonitis develop rapidly and euthanasia is required on humane grounds.

Constipation associated with bruising: Mares with severe bruising of the vagina and perineum may fail to pass feces for 24–48 h because of **perineal pain** and perhaps local neurologic impairment. Treatment with a **laxative** diet (preferably grass), exercise, 4 L liquid paraffin by stomach tube and analgesics are helpful. Periodic careful manual removal of the impacted feces may be required.

Colon torsion (*q.v.*) may be seen in the immediate post partum period. The degree of severity of signs is dependent on the degree of torsion and its duration. **Colic signs are usually severe** with abdominal distension, and signs of cardiovascular shock develop rapidly. Early surgical correction by emergency laparotomy is essential if irreparable colonic vascular damage is to be avoided.

Perineal injuries

Perineal injuries are classified according to their severity. **First-degree** lacerations consist of a tear of the dorsal commissure of the vulva and mucous membrane of the vestibule. Repair using Caslick's vulvoplasty operation (*q.v.*) is usually all that is required. **Second-degree** lacerations involve the vestibular mucosa, submucosa and perineal body. Caslick's vulvoplasty operation plus internal repair, as indicated, is used but if there is severe bruising and extensive tissue damage it may be appropriate to allow second intention healing to occur before final repair is completed. **Third-degree** lacerations involve

the ceiling of the vestibule, floor of the rectum, perineal septum, musculature and anal sphincter.

A minimum of 4–6 wk should be allowed for second intention healing, reduction in inflammation and wound contracture. During this period the wound should be kept clean, and broad-spectrum systemic antibiotic (including **oral metronidazole** to help prevent anaerobic infections) and non-steroidal anti-inflammatory treatment administered as necessary. As most cases are unsuitable for mating during the same breeding season, it is often preferable to delay repair until the foal is weaned. **Surgical repair** is usually performed in two phases, 4–6 wk apart. The mare is restrained standing in stocks, sedated and under epidural anesthesia. Systemic antibiotic and non-steroidal anti-inflammatory therapy is provided. The first stage involves reconstruction of the rectovaginal shelf and the second involves repair of the perineal body and vulva. The anal sphincter remains functionally incompetent.

Rectovaginal fistula involves an internal laceration though the rectovaginal shelf, the perineal body remaining intact. This can either be repaired by first converting to a third-degree laceration and then repaired as described above, or by splitting the intact caudal rectovaginal shelf cranially to and through the fistula, and then repairing the defect in the rectum transversely and the defect in the vagina longitudinally. The latter method has the advantage of maintaining the integrity and function of the anal sphincter. Some caudal rectovaginal fistulas will heal completely without surgical interference, given time, and others will become small enough to be repaired surgically via the vagina.

Chapter 14

Perinatology

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Chapter contents

INTRODUCTION

This chapter highlights the contributions of theriogenology, intensive care medicine and neonatology to the emerging clinical specialty of perinatology. Historically, research focused on infertility and early pregnancy loss in mares. The endocrinology of estrus and early pregnancy was investigated and strategies developed to manipulate estrus and ovulation. The introduction of **transrectal ultrasonography** allowed pregnancy detection as early as 15 days post ovulation with positive pregnancy diagnosis awaiting sonographic detection of a fetal heartbeat by Day 23. Ultrasonography improved the ability to detect **twin conceptions** early enough to allow crushing of one embryo as a means of ensuring a viable pregnancy with the remaining conceptus.

Endocrinologic confirmation of pregnancy has also been explored using maternal serum (and occasionally urine) concentrations of various hormones including pregnant mare serum gonadotropin, estrone sulfate, relaxin and progesterone. Unfortunately, most of these hormones are not sensitive enough markers of pregnancy loss, since elevated hormone concentrations frequently persist for variable intervals following embryonic or fetal death.

Impending **embryonic/fetal demise** is difficult to predict. Careful sonographic examination of the "embryo at risk" may reveal a small-for-date conceptus. An abnormally slow fetal heart rate during the **first trimester** suggests an unhealthy outcome. The value of attempts to intervene and maintain such pregnancies is controversial. If an **abnormal uterine environment** or **fetal chromosomal anomaly** is responsible for early fetal wastage, then intervention to try and maintain the pregnancy is probably unwise. An unhealthy in utero environment so early in gestation is likely to predispose to abnormal fetal growth and development. Conversely, intervention can be justified in pregnancies at risk due to extrauterine stresses such as **endotoxemia.** Progesterone supplementation and flunixin meglumine administration have been shown to exert a protective effect when given to mares before or soon after the onset of endotoxemia during early gestation (<90–120 days).

Mid-gestation appears to be the safest period for fetal development. The same maternal illnesses that may have terminated the pregnancy in early gestation as a result of luteolysis and progesterone deficiency are unlikely to have the same deleterious effect during the **second trimester** when the primary source of progestogens has become the fetoplacental unit. Drugs administered to the mare are more likely to have a teratogenic effect on the fetus during early pregnancy than during the second trimester when **organogenesis** has

already been completed. Causes of fetal death during mid-gestation are still poorly understood. Often pregnancy loss is not detected until weeks after it has occurred.

Late pregnancy remains the focus of most fetal monitoring techniques, with the goal being to recognize fetal compromise early enough to prevent irreversible damage. In women, the two most popular tests of fetal well-being during the **third trimester** are the **non-stress test (NST)** and **biophysical profile (BPP)**. The NST requires simultaneous, continuous monitoring of fetal heart rate and movement, and is based on the premise that fetal heart rate should accelerate in response to fetal movement. During a 20 min observation window, the healthy human fetus should experience two heart rate accelerations exceeding 15 bpm in amplitude above the baseline heart rate and lasting for at least 15 s. An NST meeting these criteria is termed **reactive** and is a reassuring sign of fetal well-being. The BPP involves a 30 min sonographic survey of fetal heart reactivity, muscle tone, body movements and breathing movements and an evaluation of **amniotic fluid volume (AFV)**.

Developmentally, **fetal muscle tone** is the first of these parameters to emerge. Fetal movement can be characterized by flexion and extension of the extremities and rolling movements of the torso. Three episodes of **fetal activity** during a 30 min period are considered normal. If fetal movement is observed, then muscle tone is considered to be present. Breathing movements in the human fetus develop during the end of the first trimester. At least 30 s of **fetal breathing** should be observed during the diagnostic window in late gestation. **AFV** is a measure of **fetal renal function** and general placental nutritive function. Amniotic fluid in women corresponds to allantoic fluid in mares, in that both contain fetal urine. Oligohydramnios (decreased AFV) in women has been associated with premature membrane rupture and hypoxia.

Each of the parameters is assigned a score of 2 (present) or 0 (absent). A significant decrease in AFV is considered an ominous sign even if the other parameters are still normal. As the BPP score decreases to $<6/10$ the incidence of perinatal complications and uteroplacental insufficiency increases.

During a transabdominal sonogram, the **placenta** is also evaluated for thickness, textural changes and premature separation. Fetal presentation and size are determined. Normal indices for the BPP in the equine fetus are being established.

While **transabdominal ultrasonography** may not become a routine screen for all pregnant mares, its use should be considered for those individuals with a history of previous perinatal loss, premature placental detachment, twinning or premature delivery (*q.v.*). Sonographic evaluation of fetal well-being can also be justified in those mares with unexplained or excessive abdominal enlargement, vaginal discharge, premature udder development or other severe systemic illness. If sonographic evaluation suggests fetal well-being, then therapy can be directed at maintaining pregnancy as long as possible to permit continued fetal maturation. If **fetal distress** is detected, then timely termination of the pregnancy can be coordinated with preparations to stabilize and treat a compromised neonate.

Management strategies for the abnormal pregnancy vary with the problem. A purulent vaginal discharge (*q.v.*) in a late pregnant mare may or may not result in placental insufficiency and the birth of a compromised and possibly

infected foal. Observation of a generalized increase in placental thickness and fetal fluid echogenicity raises the index of suspicion that **fetoplacental function** has been affected. Marked elevations in maternal concentrations of equine fetal protein provide biochemical confirmation of this condition. Such pregnancies need not be lost. Affected mares may be treated with antibiotics, and low (anti-endotoxic) doses of flunixin meglumine, progesterone and β-sympathomimetic drugs such as isoxsuprine hydrochloride to help maintain pregnancy. If signs of **fetal compromise** develop, induction is performed in a suitable intensive care environment (*q.v.*).

Sonographic determination of **anterior fetal presentation** (*q.v.*) in late pregnant mares provides reassurance that dystocia will not be a problem due to posterior presentation. Several studies have shown that after the ninth month it is extremely unlikely that the equine fetus will change its presentation between anterior and posterior.

Transabdominal ultrasonography may also provide insight into another common periparturient problem, **premature placental separation**. In most cases, it is unknown when the placenta begins to detach. Foals that are the product of premature placental separation are at increased risk for hypoxic organ damage. Although neonatal intensive care units have become quite adept at saving such foals, preventing or limiting fetal exposure to hypoxia is preferred. If significant areas of premature placental detachment are detected in a late pregnant mare, induction of parturition should be considered, rather than waiting for increasing hypoxia and fetal compromise to occur.

In utero determinants of **fetal size** are still being evaluated. If intrauterine growth retardation could be identified early in gestation, perhaps therapy could be directed at trying to improve uteroplacental blood flow. Intrauterine growth retardation is still being investigated in human medicine and perhaps the equine fetus might serve as a model for future research.

A successful **perinatal program** requires the collaborative efforts of those trained in reproduction and neonatology. A working knowledge of equine obstetric procedures and therapies for the more common periparturient emergencies is essential. **Enhanced neonatal survival** depends on a thorough understanding of foal physiology, an ability to recognize early signs of neonatal compromise, and the expertise, facility and equipment required to provide neonatal resuscitation and intensive nursing care. Successful management of the critically ill neonate requires rapid diagnosis and treatment of specific disease processes while addressing the unique metabolic demands and physiologic instability of the newborn.

The most serious threats to perinatal survival include septicemia, hypoxia and dysmaturity (*q.v.*). Treatment of these conditions post partum has become increasingly successful, but is still limited by how quickly the problem is recognized, how rapidly patient stabilization can begin, the economic restraints of the owner, and the limitations of the veterinary facility. Farm managers and foal owners must be fully informed of a sick foal's condition, the intensity of treatment required, and the possible sequelae. The decision to treat requires the **complete commitment** of both owner and veterinarian; otherwise, foal mortality will remain disappointingly high and many of the survivors will have their future performance limited by lingering disabilities associated with neonatal disease.

Frequently, disruptions in fetal maturation/adaptation begin prior to or during parturition. Recognition of the perinatal risk factors associated with **disturbed fetal development** allows the most important management change to occur: **increased surveillance** of a mare with a potentially abnormal pregnancy. Once the mare is identified as a high-risk candidate, more sophisticated periparturient monitoring techniques can be employed. Arrangements can be made to allow her to foal in a facility equipped to provide emergency care ranging from controlled parturition or Cesarean section (*q.v.*) to neonatal resuscitation and intensive care. Learning more about the perinatal events of an abnormal pregnancy will in turn improve reproductive management of the mare and care of the newborn foal. Successful integration of prenatal and neonatal care should reduce periparturient foal mortality in an economically sound manner.

ENDOCRINOLOGY OF THE PERIPARTURIENT PERIOD

GESTATION

To understand the endocrinology of the periparturient period, it is necessary to review the endocrinologic events of gestation (*q.v.*).

Progestogens

Progesterone (*q.v.*) plays a role in maintaining cervical and uterine tone, embryo motility, fixation and orientation, and uterine secretion of nutrients to the embryo. It is the only ovarian hormone necessary to maintain the first 70 days of pregnancy.

The primary corpus luteum starts to produce progesterone at ovulation and plasma concentrations rise >4 ng/mL within 6–8 days. The presence of the mobile embryo prevents the release of **endometrial prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$)** into the maternal circulation, thus preventing luteolysis. Progesterone concentrations decrease between Days 14 and 30. A second increase in plasma progesterone concentrations occurs again between Days 35 and 40 due to the resurgence of the primary corpus luteum (due to stimulation by equine chorionic gonadotropin). Additional follicles develop and ovulate between Days 40 and 70. The luteinization of these secondary follicles between Days 40 and 150 forms the secondary corpora lutea. Progesterone concentrations plateau near Day 60 of gestation at approximately 15 ng/mL.

There is great variation in plasma progesterone concentrations among normal mares during early gestation. Pregnancy should be maintained as long as plasma concentrations of progesterone are >4 ng/mL prior to 120 days of gestation. The luteal structures function until Day 150 and then progesterone gradually decreases to low plasma concentrations (1–2 ng/mL) at approximately 180 days. The ovaries have little activity throughout the remainder of gestation.

Between Days 30 and 60 of gestation, the conceptus begins to secrete progestogens, primarily pregnanes and 20-α-dihydroprogesterone. Concentrations gradually increase until Day 300 and then rise more sharply during the last month before parturition. The 5-α-pregnanes reach high concentrations

(some up to 2000 ng/mL) during late gestation. Progestogens decrease from as early as 2–3 days to as late as 4–12 h before parturition.

Both the stage of gestation and the assay specificity must be known to **interpret progesterone assay results** correctly for pregnant mares. Assays that have cross-reactivity between pregnanes and progesterones will have progestogen concentrations normally high in late gestation. Assays specific for progesterone will indicate low progesterone concentrations for normal mares in late gestation.

Equine chorionic gonadotropin

Trophoblastic cells from the chorionic girdle invade the endometrium to form endometrial cups. Endometrial cups secrete a glycoprotein called **equine chorionic gonadotropin (eCG)** (*q.v.*), formerly known as pregnant mare serum gonadotropin (PMSG).

Equine chorionic gonadotropin is present in the mare's blood between Days 35 and 120, with peak concentrations around Day 60. There is great variation among mares in the amounts of eCG produced and the timing of its production. Relatively small amounts of eCG are present in the urine and milk of pregnant mares. Demise of the endometrial cups is due to a lymphocytic immune reaction by the mare that destroys the endometrial cups.

Because use of exogenous eCG in cattle and sheep has both follicle-stimulating hormone (FSH) and luteinizing hormone (LH) activity that stimulates superovulation and ovulation, it was previously thought that eCG caused the development and ovulation of additional follicles in the mare to form secondary corpora lutea. However, many follicles are present on mare ovaries prior to the appearance of eCG and, therefore, it is not thought to have FSH-like activity in mares. Also, exogenous eCG does not increase follicular activity in mares. Equine chorionic gonadotropin does, however, have LH-like activity in mares and is luteotropic to the primary corpus luteum on Day 35, causing a resurgence of progesterone secretion prior to causing ovulation and/or luteinization of the secondary follicles of pregnancy. The primary and secondary corpora lutea also produce estrogens and, possibly, androgens.

Bioassays based on ovarian and uterine weight changes in immature rats were the first quantitative measurements of eCG. An LH radioimmunoassay can be used to estimate eCG because there is high cross-reactivity with LH. Immunoassays using anti-eCG serum-absorbed inhibition assay and hemagglutination inhibition assays are also available. Enzyme-linked immunosorbent assays (ELISA) are once again commercially available as a **pregnancy test** (*q.v.*) in the mare, although false positive results may occur because the endometrial cups are maintained until 120 days even if the fetus has died. False negative results may occur if the mare is tested before Day 35 or after Day 120 of gestation.

Estrogens

The equine conceptus is capable of estrogen production as early as Day 14 but increases in maternal circulation of estrogen (*q.v.*) are not seen until after Day 35. At 35–40 days, total plasma estrogens increase and a plateau of 3 ng/mL is reached on Days 40–60. Estrone sulfate is secreted by the fetoplacental unit

after Day 80 and steadily increases during the fourth month. High concentrations are maintained until the eighth or ninth month.

Conjugated equilin also increases during the fourth month and does not decrease until the last month of gestation. It is thought that the fetal gonads contain large amounts of estrogen precursors that the placenta subsequently converts to estrogens. Interestingly, estrogen concentrations decrease during the last month of gestation.

Interpretation of **estrogen assays** must be made carefully because estrogens of pregnancy exist in many forms and may be conjugated (bound to sulfates) or unconjugated (free in blood). The pregnant mare excretes huge amounts of estrogen in urine, principally **estrone** and **equilin**, which are used to produce commercial preparations of estrogen.

Assay of **estrone sulfate** can be used as a pregnancy test (*q.v.*) after the third month of gestation. Estrone sulfate assays can also be used to indicate fetal well-being because the fetus must be alive for concentrations to be elevated.

Estrogens are believed to have a positive effect on uterine, placental and fetal growth, perhaps through regulation of blood flow through the uterine and placental blood vessels and in the synthesis and storage of prostaglandin precursors in the endometrium and myometrium. During late gestation estrogens stimulate prostaglandin production, gap junction formation and oxytocin receptor synthesis. Gonadectomizing horse fetuses in mid to late gestation results in decreased maternal estrogen levels, weak ineffective labor associated with low prostaglandin levels, and the birth of dysmature foals.

Relaxin

The **placenta** is thought to be the sole source of relaxin in the mare. Placental secretion of relaxin (*q.v.*) begins on about Day 80 of pregnancy and peaks initially at approximately Day 175. A 50% decline occurs by Day 225, but concentrations then increase again gradually until parturition. Relaxin decreases the collagen content in the extracellular matrices of the pubic symphysis and uterine cervix, inhibits uterine contractility, and may play a role in mammary gland development.

Relaxin has been demonstrated to be an **indicator of fetoplacental health** in the late gestational mare. Low relaxin concentrations have been associated with varying types of placentitis and placental insufficiency.

Mares exposed to **endophyte-infected tall fescue** (*q.v.*) experience a decrease in circulating relaxin levels that coincides with placental dysfunction and fetal distress. When affected mares are treated successfully with **domperidone**, a D_2 dopamine agonist capable of reversing the signs of fescue toxicosis, the mares' clinical signs resolve and relaxin levels return to normal. This hormone represents a promising marker of fetoplacental function. No commercial assay for relaxin is currently available.

Prolactin

Prolactin (*q.v.*) concentrations rise markedly during the last week of gestation and remain high for 1–2 mo after parturition. Research in other species suggests that prolactin is involved with mammary development and lactation.

PARTURITION

The hormonal events controlling parturition (*q.v.*) affect **maturation of the fetus** and cause physical changes in the dam necessary to allow delivery, including relaxation of the pelvic ligaments and cervix, and uterine contractions. **Lactation and maternal behavior** are also influenced by hormones. In domestic farm animals, parturition is initiated by the fetus, but the mare can delay delivery temporarily if she is disturbed. Progestogen concentrations appear to decrease from 2–3 days before foaling.

Mare plasma $PGF_{2\alpha}$ concentrations are higher in late gestation ($\geqslant$270 days) than in early gestation. $PGF_{2\alpha}$ and 13,14-dihydro-15-keto-prostaglandin-$F_{2\alpha}$ (PGFM) dramatically increase during parturition, but concentrations are minimal within 1–2 days after parturition. Prostaglandin E_2 (PGE_2) concentrations gradually increase near term and are thought to play a role in cervical softening.

In sheep, the hypothalamus stimulates the anterior pituitary to produce ACTH that causes the fetal adrenal to increase secretion of cortisol during the last 48–72 h of gestation. Cortisol is thought to activate placental enzyme systems that convert progesterone to estrogen, which is needed for $PGF_{2\alpha}$ production and increase of oxytocin receptors. $PGF_{2\alpha}$ causes release of oxytocin from the posterior pituitary and softens the cervix. The oxytocin in turn stimulates myometrium contraction that results in delivery of the fetus.

The exact mechanism regulating parturition in the mare is not known, but it is thought to be similar to that in sheep. There is evidence that the fetus plays an important role. Equine fetal adrenals undergo **rapid hypertrophy** immediately before parturition and **fetal plasma cortisol** increases slightly near term. Concentrations of cortisol in the amniotic fluid also increase near term. In the mare, there is no change in plasma concentrations of glucocorticoids before parturition. Ovarian hormones are not necessary for parturition and pregnant, ovariectomized mares have normal parturitions. Exogenous progesterone will not prolong gestation.

In the mare, **$PGF_{2\alpha}$ and oxytocin** are involved with parturition but are not necessary for luteolysis. Oxytocin receptor formation seems to be controlled by estrogen–progesterone ratios and increased $PGF_{2\alpha}$ production. Oxytocin (*q.v.*) is only increased during **second stage labor** and until the placenta is passed. As oxytocin is a neurohormone under the control of the mare's central nervous system, this may be the mechanism by which she can "select" timing of delivery.

As the fetus and placenta are passed, steroid production by the conceptus is lost. Within 30 min of parturition, progestogen and estrogen concentrations in the mare decline precipitously. A **surge of FSH** occurs at the time of parturition, beginning a few days before and reaching a peak on or just before the day of parturition. Follicular development, therefore, soon resumes and estrogen concentrations increase during the first estrus (**foal heat**), which occurs approximately 7–11 days after foaling.

FSH (*q.v.*) concentrations then gradually decrease due to the inhibitory effect of the developing follicles associated with foal heat. However, LH (*q.v.*) concentrations are low prior to parturition due to the suppressing effect of progestogens. LH increases after the progestogens decrease following parturition. Further increases in LH concentrations occur due to estrogens produced by

follicles during foal heat. After foal heat ovulation, progesterone increases due to its production by the corpus luteum, and a normal estrous cycle ensues.

HORMONE ASSAYS

Before the 1960s, investigations on hormone regulations were performed with bioassays that measured changes in organ size or weights due to stimulation by a particular substance. In the late 1960s, competitive protein binding assays and later radioimmunoassays confirmed information learned from the bioassays. Very sensitive radioimmunoassays allowed for much more accurate determination of hormone concentrations.

Much work has been done to develop assays that do not require long, tedious laboratory techniques and radioactive isotopes. ELISA tests use highly specific monoclonal antibodies and involve enzyme-induced color changes that do not require radioactive agents. Assays can be performed quickly and outside laboratories that have to meet the regulated requirements for handling and disposing of radioactive materials. Some assays are in a simple dipstick form and give qualitative results indicating the presence or absence of the hormone. Quantitative results can be obtained using plate readers that give an accurate determination of hormone concentrations. **ELISA tests** are available for progesterone, equine LH and eCG. Interpretation of results must be made carefully, after following assay directions, using appropriate control standards, and with comparison to concentration ranges in normal mares for the particular reproductive stage.

PERIPARTURIENT COMPLICATIONS

VARICOSE VESSELS IN THE VAGINA

A distended blood vessel with possible hemorrhage may be seen in the vulva/vagina of the pregnant mare near term. Varicose veins are more common in **older mares**.

Etiology

During late gestation, the blood vessels supplying the genital tract enlarge; blood flow to the genitalia increases under the influence of estrogens, and retrograde pressure exerted by the weight of the fetus and uterus may compromise venous return in some areas, resulting in a varicose vein. Common sites for such varicosities are the hymen (transverse fold) and floor of the vagina. Occasionally, a varicose vein may rupture and cause frank bleeding that appears as a bloody **vulval discharge**. This clinical sign may cause great alarm to the novice mare breeder.

Clinical signs

A frank bloody vulval discharge may be present. The source of the bleeding is determined by **vaginal speculum** examination. If rupture of the vessel has not occurred, there may be no obvious clinical signs.

Treatment

Usually, no treatment is indicated. If severe hemorrhage occurs, the vessel may be ligated or cauterized. Light exercise may help improve circulation and lessen the occurrence of this problem. The condition will resolve after parturition.

UTERINE TORSION

Torsion of the uterus (*q.v.*) occurs during late gestation but is not usually associated with parturition as in the cow. The uterus rotates about its **long axis** and typically does not directly involve the cervix. The degree of rotation is quite variable and can range from 90 to >360°. The severity of clinical signs is related to the degree of torsion, and any gastrointestinal organ involvement or vascular compromise.

Etiology

Uterine torsion may be caused by the mare falling down or rolling or by increased activity of the fetus, but often there may not be any history of these events.

Clinical signs

The mare may appear as if she is in first stage labor. There may be restlessness, sweating, anorexia, frequent attempts to urinate, and signs of intermittent colic that is unresponsive to treatment. Severity of pain is related to degree of torsion and/or concurrent involvement of gastrointestinal viscera. Dystocia (*q.v.*) may be the presenting sign if uterine torsion occurs near term.

Diagnosis

On **palpation per rectum**, the broad ligament will feel very tense on one side as it is pulled under the pregnant uterus and the opposite side will seem to bulge up over the uterus. The uterine wall should be palpated carefully to assess the degree of congestion, necrosis or possible rupture.

Treatment

Uterine torsion can be corrected surgically, manually or by rolling. **Surgical correction** by rotation of the uterus can be made through a flank incision in a standing, sedated mare. If there is a suspicion that the uterus has been severely compromised and/or rupture has occurred, a ventral midline incision with the mare under general anesthesia (*q.v.*) is recommended.

If the mare is near term and the torsion not severe, **manual correction** per vaginam is possible provided the torsion is <270°. The mare should be prepared as for dystocia evaluation. The **cervix must be adequately dilated** and a portion of the fetus palpable. If the fetal membranes are intact they should be ruptured to release fluids and reduce the size and weight of the uterus. The fetus may be rocked to flip the uterus into normal position. The foal may then be delivered immediately. Parturition may be hastened by induction with **oxytocin** after the torsion has been corrected.

The mare can be **rolled** to correct uterine torsion. This procedure should not be used near term because of the increased risk of uterine rupture (*q.v.*). Anesthesia is induced using a short-acting injectable anesthetic and maintained with inhalation anesthesia (*q.v.*). The mare is placed in **lateral recumbency** with the side in the direction of the torsion down. The legs should be hobbled and ropes applied to the limbs. Place a **plank** (3.5 m long × 0.3 m wide × 5 cm thick) perpendicularly against the mare's back and flank. While one person kneels on the plank to hold the uterus in place, roll the mare such that her legs swing over her back in the direction of the torsion. Care should be taken to protect the mare's head from injury. Success of correction can be evaluated by **palpation per rectum** for the proper positioning of the broad ligament. If the torsion has not been corrected, the procedure can be repeated. Pregnancy should be monitored closely for several days.

Complications associated with correction of uterine torsion include premature placental separation with fetal compromise and/or death and abortion, uterine wall necrosis and rupture, peritonitis and recurrence of the torsion during the same pregnancy.

HYDROPS AMNII AND HYDROPS ALLANTOIS

Hydrops amnii (excessive accumulation of amniotic fluid) in the mare has been associated with foals with **hydrocephalus** (*q.v.*) and with **umbilical cord anomalies**. **Hydrops allantois** is an excessive accumulation of allantoic fluid that occurs during the last trimester of gestation. Although both conditions are rare in the mare, hydrops allantois is the more common of the two.

Etiology

Amniotic fluid is comprised of saliva and upper respiratory tract secretions and is cleared in part by fetal swallowing. Therefore any condition that impedes or results in **impaired fetal swallowing** may contribute to development of hydrops amnii. The exact cause of hydrops allantois is unknown but it is thought to be related to a **dysfunction of the chorioallantois** resulting in abnormal allantoic fluid maintenance. Some cases have been associated with fetal anomalies, heavy edematous placentas and umbilical cord disorders.

Clinical signs

Hydrops allantois is associated with dramatic and rapid enlargement of the abdomen over several weeks. Mares with hydrops amnii develop mild abdominal distension over a more prolonged time period of weeks to months. The increased volume of fetal fluids exerts pressure on the gastrointestinal tract and thoracic cavity and results in maternal anorexia, tachycardia, tachypnea, dyspnea, depression, colic, decreased manure production, difficulty walking and marked ventral edema (*q.v.*).

Advanced cases may develop ventral abdominal hernia or prepubic tendon rupture (*q.v.*). Other complications include uterine rupture and uterine inertia (*q.v.*). **Palpation per rectum** reveals a large, fluid-distended uterus. It is often difficult or impossible to feel the fetus. In the early stages of hydrops, an absolute diagnosis may be difficult to make. The condition is confirmed via **transabdominal ultrasonography**. Large volumes of clear fetal fluids are observed.

Treatment

Hydrops allantois tends to be more **life threatening** for the mare due to its **rapid onset** and the excessive volume of fluids that accumulate. Prognosis for both mare and fetus is grave unless the mare is at term. The fetus may be normal in these pregnancies, but survival depends on how late in the pregnancy the condition develops and how successfully the mare is supported during labor. Often the best chance for saving the mare is by **termination** of the pregnancy.

Hydrops amnii is often associated with fetal birth defects and/or umbilical cord anomalies. In cases of hydrops amnii the prognosis for the pregnancy is poor because **abortion and premature delivery** are common. Future fertility is often not impaired if there is no accompanying prepubic tendon rupture or ventral abdominal herniation.

If the mare is comfortable and close to term, fluid accumulation is mild to moderate and fetal viability is reasonable, then the mare can be supported with IV fluids supplemented with B vitamins and dextrose, a laxative diet, oral vitamin E and **altrenogest** (0.044–0.088 mg/kg PO q 24 h).

In advanced cases of hydrops, **parturition should be induced** to relieve pressure on the mare's internal organs and avoid prepubic tendon rupture, abdominal hernia formation or uterine rupture which can end a mare's reproductive career and increase the risk of colic post foaling. The mare's muscle enzymes should be monitored. Sudden increases in maternal **serum creatine phosphokinase (CPK)** concentrations herald increasing muscle damage and impending prepubic tendon rupture or hernia formation.

During delivery the sudden expulsion of large volumes of fetal fluids results in **hypotensive shock** (*q.v.*) in the mare. Manual rupture of the chorioallantois is often too blunt and results in rapid fluid expulsion. A sharp 20 to 32 French trocar catheter can be used to make a **puncture** through the chorioallantois to drain off allantoic fluid as **slowly as possible**. To prevent maternal shock, the mare should be **pre-treated** with at least 20 L of IV fluids. One to two liters of hypertonic saline or hetastarch (10 mL/kg) can be administered to improve oncotic pressure and combat hypotension.

Corticosteroids can also be given to treat shock (*q.v.*). **Oxytocin** is administered to stimulate uterine contractions, but uterine inertia should be anticipated and chains should be available to help extract the fetus as rapidly as possible to minimize peri partum asphyxia. Post partum, **flunixin** administration can improve maternal comfort.

Retained fetal membranes (*q.v.*) are common and are treated with repeated doses of oxytocin (10–20 IU IV/IM) q 3–4 h. The mare should be started on antibiotics and NSAIDs to reduce the risk of metritis, endotoxemia and laminitis (*q.v.*). Uterine involution may be delayed and additional oxytocin, IV calcium supplementation and uterine lavages may be indicated.

RUPTURED PREPUBIC TENDON AND VENTRAL ABDOMINAL HERNIA

Prepubic desmorrhexis (ligament rupture) and **abdominal hernia formation** are more common in older draft mares and other heavier breeds, but have been reported in other breeds including Arabs and ponies. Conditions that cause

severe distension of the body wall such as hydrops, twins, severe ventral edema, or trauma may result in rupture of the prepubic tendon or abdominal hernia. It may be difficult to distinguish between prepubic desmorrhexis and abdominal hernia (*q.v.*), and clinical progression of the two conditions is similar.

Etiology

The rupture tends to occur during the last 2 mo of gestation due to the excessive weight of the gravid uterus.

Clinical signs

Prior to rupture, the mare may be noted to be lying down frequently. A marked, thick, painful edema extending from the udder to the xiphoid region often precedes rupture of the prepubic tendon. Serum concentrations of **CPK** are usually elevated. After rupture has occurred, the mare will have a stiff, cautious gait and refuse to lie down. The mare will often assume a "**sawhorse**" **stance** with an elevation of the tail head and the ischial tuberosities. The udder and teats will be flattened and stretched cranially.

If rupture occurs suddenly, **intense pain and colic** may be accompanied by sweating, increased respiration, rapid weak pulse, internal hemorrhage and shock (*q.v.*) that often progress to death of the mare and fetus.

Management

Repair of the acute condition is not possible. Confine the mare to a stall, limit exercise, and avoid giving bulky feeds. The mare should be fitted with a **wide abdominal support** heavily padded over the back. Because abdominal contractions during parturition will not be effective, parturition should be induced when the mare is near term so that delivery can be assisted. Affected mares should not be expected to carry a pregnancy again.

Complications include death of the mare due to internal hemorrhage and/or bowel damage, ventral evisceration following rupture of the body wall, and colic after delivery associated with bowel trauma and intra-abdominal adhesions.

Minor rents in the body wall can be surgically repaired. Larger tears are not amenable to successful repair. Foals delivered from mares with hydrops or prepubic tendon rupture are at increased risk for problems associated with **chronic placental insufficiency** such as compromised growth and development and **hypoxic ischemic encephalopathy**.

Deliveries associated with these conditions are often difficult and protracted, thereby adding the additional insult of acute hypoxia to already stressed neonates. Many of these foals are weak, slow to stand and nurse, and unable to absorb adequate amounts of colostral antibodies, thereby rendering them more susceptible to early sepsis.

INDUCTION OF PARTURITION

The main advantage of induction is that it ensures the presence of assistance for mares that have a history of complications or that have experienced problems during gestation. It is very important to evaluate carefully the mare and her

reproductive status and to be sure that several criteria are met before making a decision to induce parturition. Poor timing of and preparation for induction of parturition can result in a premature foal and/or dystocia. Once owners have become accustomed to inducing parturitions, it may become difficult to convince them to wait when a mare is not yet ready.

Indications

1. Mares that have previously produced dead or severely hypoxic foals due to premature placental separation associated with delayed parturition.
2. Mares that have suffered problems during a previous foaling(s) such as dystocia, lacerations or other injuries, and that require professional assistance with delivery and immediate foal care.
3. Mares in which gestation is greatly prolonged beyond 12 mo and is associated with a very large fetus. NB Usually, mares with a prolonged gestation (>365 days) have small or normal size foals.
4. Mares in which there is the presence or possibility of rupture of the prepubic tendon.
5. Mares with hydrops.
6. Mares that have produced foals affected by neonatal isoerythrolysis, so the newborn foal may be prevented from ingesting colostrum before its red blood cells can be checked against the mare's serum.
7. Mares that have sustained pelvic fractures or other injury to the birth canal such that the canal is reduced and manual assistance during delivery is anticipated.
8. Preparation of nurse mares.

Criteria for induction

1. **Length of gestation.** Induction should only be performed when the fetus is mature enough to adapt to the environment outside the uterus. A minimum of 330 days usually ensures adequate fetal maturity at the time of induction if all other criteria are fulfilled.
2. **Adequate mammary development.** The udder should be enlarged and the teats distended with colostrum. In uncomplicated pregnancies, concentrations of calcium, sodium and potassium undergo distinct changes in pre partum mammary secretions associated with fetal maturity and readiness for birth. Calcium concentrations >40 mg/dL are associated with a mature fetus and values <12 mg/dL are associated with reduced fetal viability. As delivery approaches, sodium concentrations decrease to <30 mg/dL and potassium levels increase >35 mg/dL. **Water hardness test strips** can be used to monitor calcium concentration.
3. **Relaxation of the vulva and sacrosciatic ligaments.** Maximum relaxation occurs very close to foaling and can dramatically increase during the first stage of labor. The degree of these changes is quite variable among mares.

4. **Relaxation of the cervix.** The cervix should be soft and easily compressed, with some degree of dilatation. Cervical relaxation may normally occur as early as 1 mo before term or as late as first stage labor.

Methods of induction

Oxytocin (*q.v.*) is the most commonly used agent for inducing parturition. Parturition will occur rapidly and safely with small doses of oxytocin. Oxytocin, 20 IU administered IM, will cause a slow, quiet foaling. An IV bolus of 5–10 IU is also effective. Smaller IV doses such as 2.5–5 IU given every 20–40 min produce a more gradual onset of labor in late term mares and may reduce the risk of dystocia and premature placental separation that is observed with the use of larger doses of oxytocin.

Infusion of 60 IU oxytocin in 1 L of physiologic saline IV at a rate of 0.5–1 IU oxytocin/min produces parturition that **appears physiologically normal**. Second stage labor usually occurs 20–35 min after the start of infusion. Often, the mare will deliver while standing, which may be an advantage if one suspects that manual intervention will be necessary. Oxytocin may be continued until the placenta is passed.

Natural $PGF_{2\alpha}$ is not recommended for induction of parturition in the mare. Because of the strong uterine contractions it induces there is a high incidence of premature placental separation and fetal morbidity and mortality associated with its use. Some synthetic prostaglandins have however been used on a limited basis in mares. One synthetic $PGF_{2\alpha}$ that can be used is **fluprostenol sodium** (2.2 μg/kg). Doses of 1000 μg for mares and 250 μg for ponies administered IM are effective and signs of first stage labor will commence within 30 min of injection. Birth usually occurs within 2 h. There is some controversy over the safety and efficacy of fluprostenol for induction. Other synthetic prostaglandins that have been used in the mare are **prostalene** and **fenprostalene**. These drugs are dosed at 4 mg SC and 0.5 mg SC respectively. Studies using these drugs indicate that a viable fetus can be obtained approximately 4 h after administration.

Large doses of **corticoids** are necessary to induce parturition in the mare. Daily administration of 100 mg of dexamethasone for 4 days starting after Day 321 will induce parturition between 6.5 and 7 days after initiation of treatment. This delay between administration and delivery of the foal decreases the usefulness of this drug for induction. There is some thought that it may be beneficial to a potentially dysmature foal to administer corticosteroids for 2–3 days pre partum and then induce parturition with oxytocin.

PLACENTITIS

Placentitis (*q.v.*) describes inflammation of the fetal membranes and is a common **cause of reproductive losses** in mares. Most cases of placentitis are infectious in origin; the infection ascends by direct extension from the mare's lower reproductive tract or spreads hematogenously from the mare's systemic circulation. Acute placentitis may cause abortion or premature birth with or without infection of the newborn. Chronic placentitis can result in growth retardation of the newborn or death of the fetus.

Etiology

The most common cause of placentitis is **bacterial infection** that ascends from the dam's urogenital tract through a relaxing cervix. Early placental lesions are first detected around the cervical pole of the fetal membranes.

The bacteria most commonly isolated include *Streptococcus equi* var. *zooepidemicus*, *Escherichia coli*, *Enterobacter agglomerans*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* (*q.v.*).

In Kentucky, a slightly different form of placentitis has been recognized. It is characterized by **focally extensive inflammation** located predominantly at the junction of the uterine horns and the body of the placenta. The affected area is covered with thick, tenacious brown mucoid exudate and the underlying chorionic villi are necrotic, absent or reduced in size. This form is associated with infection by a group of Gram-positive, branching, filamentous nocardioform-like organisms.

A far less common route of infection is hematogenous as part of systemic disease in the dam. This form of placentitis is often diffuse in nature as seen with leptospirosis and *Corynebacterium pseudotuberculosis* (*q.v.*).

Clinical signs

Clinical signs of placentitis include **premature udder development, precocious lactation** and purulent or hemorrhagic **vaginal discharge** that may be evident on the mare's vulva, tail or inner thighs.

Despite even **voluminous vaginal discharge**, most mares with placentitis do not become febrile and do maintain a normal appetite. The dam's white blood cell count usually remains within normal limits. Transrectal ultrasonography can be used to detect early areas of placental separation and increased uteroplacental thickness in the pericervical area. Transabdominal ultrasonography can be used to evaluate other areas of the placenta to detect separation and thickening. If placentitis is severe enough to alter placental function and disrupt oxygen delivery then the fetus may demonstrate reduced fetal movement, loss of heart rate variability and persistent bradycardia.

Treatment

Samples of vaginal discharge should be cultured and Gram stains performed to identify the bacterial pathogens involved. The goal of maternal therapy is to treat the placental infection and maintain the pregnancy provided there is no evidence of severe fetal distress or demise and the mare remains healthy. Therapy includes **broad-spectrum antibiotics**, low dosages of **flunixin meglumine** (0.25 mg/kg IV q 8 h) to decrease inflammation and prevent prostaglandin-mediated induction of delivery, and **altrenogest** (0.044–0.088 mg/kg PO q 24 h) to quiet the myometrium and maintain cervical competency.

Clenbuterol has been administered as a **tocolytic agent** to suppress uterine contractions (0.8–1.2 μg/kg PO q 12 h) and reduce the risk of premature labor. Pentoxifylline (8.4 mg/kg PO q 8–12 h) has been used to support microcirculation. Oral vitamin E (5000–7000 U/day) can be fed for its antioxidant effect. If there is sonographic evidence of placental edema and thickening, IV dimethyl sulfoxide (DMSO) (0.5–1.0 g/kg administered as a 10% solution) can be administered for its anti-inflammatory and antioxidant properties.

The well-being of the dam and fetus should be monitored while treating placentitis. Tocolytic agents should be discontinued if fetal demise is suspected. **Termination** of the pregnancy should be pursued if the dam shows systemic signs of endotoxemia (*q.v.*). Delivery should be attended since there is an increased risk of premature placental separation, dystocia, retained placenta and the birth of a weak, hypoxic foal.

PREMATURE SEPARATION OF THE CHORIOALLANTOIS ("RED BAG")

Normally, at the end of the first stage of parturition, the chorioallantois bulges into the cervix and then ruptures in the area over the cervix (cervical star), releasing the allantoic fluid ("**first water**"). This lubricates the birth canal and allows passage of the foal. Normally, because the placenta is still attached to the endometrium and functioning, oxygen exchange continues. However, if the chorioallantois does not rupture, and the foal is delivered within this membrane, contact between placenta and endometrium is disrupted and fetal hypoxia occurs.

Clinical signs

If the chorioallantois fails to rupture at the cervical star and the second stage of labor commences, a "**red bag**" (prematurely separated chorioallantois) (*q.v.*) may appear at the vulvar lips as a velvety red membrane. It is not possible to predict to what degree placental oxygen exchange is compromised, but the foal may become anoxic and die or be born severely hypoxic.

Treatment

Premature separation of the chorioallantois is a medical emergency. The chorioallantois should be immediately ruptured by hand or with a blunt instrument and the foal manually delivered. Once the foal is out, rub it briskly with towels to stimulate deep breaths. The severity of asphyxiation depends on the degree and duration of placental separation and whether there is pre-existing placental disease.

Foals that are products of **premature placental separation** should be evaluated for asphyxia. Therapy includes oxygen administration and brisk rubbing to stimulate breathing. Foals that are not breathing require aggressive cardiopulmonary resuscitation (CPR) (*q.v.*).

Delivery also may be complicated by **meconium staining** of the fetus and fluids. Fetal hypoxia stimulates premature passage of meconium in utero. If this occurs, clear the foal's nose and mouth of meconium to reduce the risk of aspiration. Affected foals may benefit from oxygen via a mask or nasal cannula. **Meconium stained foals** should be monitored closely for signs of hypoxic ischemic encephalopathy (i.e. neonatal maladjustment syndrome) (*q.v.*).

DYSTOCIA

During normal parturition, the foal is delivered in an anterior longitudinal presentation, dorsal-sacral position with the forelimbs in an extended posture.

Deviations from this are the most common cause of a delayed or difficult birth. Other causes of dystocia are discussed elsewhere (*q.v.*).

Normal parturition is divided into three stages. During the **first stage**, uterine contractions occur, the fetus rotates from the dorsal-ventral or dorsal-lateral position it was in during gestation to a dorsal-sacral position, and the cervix dilates. The mare will be restless, sweat behind her elbow and flanks, urinate small amounts frequently, lie down and get up repeatedly, and appear to have colic. First stage labor lasts from 30 min to 4 h and early in this stage the mare can voluntarily delay parturition if disturbed.

Eventually, the cervical star of the chorioallantois ruptures and the allantoic fluid ("first water") is released. This marks the end of first stage labor. During the **second stage**, the fetus is expelled through the pelvic canal by continued uterine contractions and strong abdominal contractions. The second stage normally takes less than 30 min.

During the **third stage**, the uterus continues to contract and the fetal membranes are expelled within 15–90 min. If the placenta has not been passed after 3 h, treatment should be instituted.

If the second stage is not progressing normally, i.e. if after 15–20 min two forelegs and a nose are not seen at the vulvar lips, an examination should be performed to determine whether there is **malpresentation**. The mare's tail will already have been wrapped and the perineum should now be cleansed thoroughly. It is critical to maintain hygiene and use **plenty of lubrication**. The operator should thoroughly scrub arms and hands. Water-soluble methylcellulose lubricant is preferred because large volumes can be pumped into the uterine lumen using a sterile stomach tube and pump, if necessary. Petrolatum jelly may offer better protection to the vagina if a fetotomy is to be performed, but should be avoided if a Cesarean section (*q.v.*) is anticipated because it can be quite irritating to the peritoneal cavity.

It is preferable for the mare to remain standing during the initial examination. Care should be taken to prevent injury to the mare and operator. In many cases, restraint by a twitch or lip chain may permit initial examination.

Sedation should be avoided because it may depress the fetus. **Acepromazine maleate** (0.07 mg/kg IV) can be used to quiet the mare. If more sedation and analgesia are needed, 0.44 mg/kg **xylazine** IV followed in 5 min by 0.044 mg/kg **butorphanol tartrate** IV can be effective. **Caudal epidural anesthesia** (lidocaine 0.5–1.0 mL 2% per 100 kg body weight [BW]) may help stop straining by the mare. A possible 30 min delay to effect may be too long for it to be of assistance. It is important to evaluate the fetus and birth canal carefully in making the diagnosis.

Treatment

There are many causes of dystocia, including malpresentation, fetal–maternal disproportion, uterine abnormalities (such as torsion, inertia, ruptured prepubic tendon, pelvic and perineal abnormalities) and fetal abnormalities (such as skeletal malformation or fetal emphysema) (*q.v.*). The most common cause of dystocia in the mare is **fetal malpresentation**, particularly flexion of the anterior limbs or head and neck. This discussion of treatment will be confined to these common problems.

After a diagnosis of malpresentation has been made, a plan to correct the problem must be instituted. The birth canal and uterus should be **well lubricated** with a water-soluble lubricant. Great care should be taken to maintain **good hygiene** and avoid unnecessary contamination of the uterus.

Many malpresentations can be corrected with **mutation and traction**. Deviation of a fetus' forelimb is relatively common in the mare. The limb may be flexed at the carpus or extended back alongside the fetus' body. In such cases, the fetus should be repelled. The limb position can then be corrected by repelling the foot while rotating the carpus laterally. This manipulation reduces the longitudinal arc that the foot must traverse through the birth canal. Traction can be applied to the extremity by applying an **obstetric chain** dorsally above the fetlock with a second half loop over the pastern to extend the limb.

If the **head and neck** are deviated, first determine the position of the head. If the mare is in lateral recumbency and the head in a lateral posture, reposition the mare so that the head is above the fetal body. **Repulse the fetal body** to make room to manipulate the head and neck. Loop a chain around the neck and grasp the muzzle or eye orbits with finger, hook or snare to extend the head and neck. Sometimes it is helpful to flex and repel the limb on the side of the head deviation to provide more space for manipulation. Once posture is corrected, traction should be applied to both front legs and head by pulling out and down toward the mare's hocks as opposed to straight out behind the mare.

If the position cannot be corrected, it may become necessary to perform a **fetotomy** or **Cesarean section** (*q.v.*). To proceed with a fetotomy, amputation of the head and neck at the base of the neck may allow vaginal delivery of the fetus. Extensive fetotomy procedures often result in irreparable damage to the reproductive tract. Accordingly, it is generally felt that if difficult dystocias cannot be relieved using no more than two fetotomy cuts, a Cesarean section is warranted.

Because retained placenta and uterine contamination frequently occur in association with dystocias, broad-spectrum antibiotics and non-steroidal anti-inflammatory drugs (NSAIDs) should be administered.

UTERINE RUPTURE

Perforation of the uterus may occur with or without evidence of dystocia. Tears tend to occur either at the tip of a uterine horn or just cranial to the cervix. Death due to hemorrhagic shock may occur if the rupture is extensive. Contamination and hemorrhage into the abdomen may cause peritonitis (*q.v.*).

Clinical signs

The mare may be febrile, anorexic, endotoxic, have an elevated heart rate and be in shock (*q.v.*). The severity of illness depends on the degree of abdominal inflammation and hemorrhage. The tear is usually not palpable per rectum, but an atypically small and tonic uterus for the stage post partum may be felt. Palpation of the uterus per vagina frequently is sufficient to locate the laceration. **Transmural palpation** of the uterus (one hand per rectum and one hand per vagina) may help in evaluation of some tears, especially those that are partial thickness. The tips of the horns, which may be difficult to reach immediately after delivery of a foal, should be carefully evaluated. **Abdominocentesis** (*q.v.*) assists in the detection of peritonitis and hemorrhage.

Treatment

Uterine lavage is to be avoided if there is any suspicion of a **laceration**. Administration of broad-spectrum antibiotics and NSAIDs is necessary if **peritonitis** (*q.v.*) is present. Poor exposure of the uterine defect at laparotomy may make surgical repair difficult. However, if uterine contents continue to cause abdominal contamination, the laceration will need to be sutured. Some lacerations will heal on their own, but **adhesions** may occur, depending on the degree of peritonitis (*q.v.*).

UTERINE ARTERY RUPTURE

Older (⩾11 years) multiparous mares are prone to rupture of the **uterine artery** during late gestation or at parturition, but the exact cause is unknown.

Clinical findings

Hemorrhage may be free flowing in the abdomen or uterine lumen or can form a hematoma as blood is trapped within the broad ligament. If it occurs **at parturition**, the mare will continue to **sweat** and **appear anxious** after the foal has been delivered. Respiration and heart rates will be elevated and the mare may be weak and stagger. If hemorrhage dissects between planes of uterine tissue, the mare will tend to be more uncomfortable and show a more severe degree of **colic**. The mucous membranes will be pale and packed cell volume may decrease dramatically. Many mares may curl their upper lips frequently. If hemorrhage is severe enough, the mare will go into shock and die. Death is often sudden and can occur within half an hour of delivery or days later.

If hemorrhage is confined within the **broad ligament**, it may be possible to palpate and visualize the hematoma by ultrasonography per rectum. In acute conditions, these procedures may be contraindicated because they may exacerbate the mare's condition. Peritoneocentesis and uterine examination per vagina will help determine the location of the hemorrhage.

Treatment

It is recommended that the mare be kept as quiet as possible, in her own stall with the lights turned out, and exposed to minimum disturbance. Some sources recommend administration of **acepromazine** (0.01–0.02 mg/kg IV) to decrease anxiety and to lower blood pressure and help stop the bleeding. However, if blood pressure is already critical, the acepromazine may cause shock and death.

Transfusion of large quantities of blood may help, but it is difficult to administer sufficient amounts rapidly enough to be effective. **Oxytocin** (20 IU IM q 60 min) helps decrease myometrial hemorrhage and/or intrauterine bleeding only. Oxytocin should not be administered if there is a hematoma within the broad ligament. **Flunixin meglumine** (1.0 mg/kg IV q 12–24 h) should be given to decrease pain. Clinical reports indicate that **naloxone** (4 mg) may help a mare that is in shock and may prevent death. IV fluids can be administered if the mare shows signs of hypotensive shock.

Aminocaproic acid (10–20 mg/kg diluted in 1–3 L saline) administered slowly IV in the fluids may help reduce ongoing hemorrhage but should not

be administered during acute stages. IV formaldehyde has also been given to control hemorrhaging with anecdotal success. However, controlled studies using IV formaldehyde failed to demonstrate any significant effect on parameters of hemostasis. The recommended dose is 10 mL of 37% formaldehyde in 1 L of lactated Ringer's solution administered IV over 15 min. Higher doses may produce undesirable side effects including tachycardia, lacrimation, salivation and muscle fasciculations. **Antibiotic administration** is recommended for surviving mares to reduce the risk of secondary infection associated with bleeding into the uterus or peritoneal cavity.

Some cases have been saved by **surgical ligation** of the ruptured vessel. This is possible only if the affected vessel can be identified. Frequently, adequate exposure of the vessel is not possible and the mare may die under anesthesia during surgery.

Mares that recover from a uterine artery rupture are thought to be at a higher risk to experience more severe hemorrhage in subsequent pregnancies. Likewise, there are some mares that foal uneventfully during later pregnancies.

PERINEAL LACERATION

Perineal lacerations occur at the time of parturition.

Etiology/clinical signs

First-degree laceration involves tearing of the mucosa of the vestibule or vulvar lips. It often involves the dorsal commissure of the vulvar lips due to rapid stretching during expulsion of the foal or failure to adequately open a Caslick vulvoplasty (*q.v.*). **Second-degree** laceration involves mucosa and submucosa of the vestibule or vulva and perineal body musculature. **Third-degree** laceration involves vaginal mucosa, perineal body and anal sphincter. **A recto-vestibular fistula** is an opening between the vagina and/or vestibule and rectum that does not involve the anal sphincter or pudendal body. These conditions result when the foal's feet fail to pass the vestibular fold and are pushed dorsally through the vaginal wall into the rectum.

Treatment

A first- or second-degree laceration may be surgically repaired soon after foaling. If extensive tissue damage with subsequent necrosis has occurred, surgical repair should be delayed. Repair of third-degree lacerations or fistula is generally delayed until at least 1 mo after foaling or after weaning to give devitalized tissue time to repair. These repairs may require two to three procedures. Success requires proper preparation of the mare's fecal consistency by diet manipulation.

UTERINE PROLAPSE

Uterine prolapse (*q.v.*) rarely occurs in the mare because of the cranial attachment of the broad ligaments, and is more likely to occur following retained placenta or dystocia. Presence of the uterus, cervix or vagina at the vulvar lips is indicative of prolapse.

Treatment

The prolapsed uterus should be **carefully inspected** for lacerations and cleansed with **sterile saline**. Harsh antiseptics should be avoided. If the placenta is loosely attached, it should be possible to remove it. The uterus is then replaced into the abdomen, care being taken to position the uterine horns properly. The vulva is closed with heavy suture material to prevent re-prolapse. If the placenta is not easily removed, sufficient space must be allowed for the expelled portion to hang from the vulva.

NSAIDs such as **flunixin meglumine** (0.25–0.35 mg/kg IV q 8 h) or phenylbutazone (2.2–4.4 mg/kg q 12 h) are indicated together with broad-spectrum antibiotics such as penicillin (**benzylpenicillin potassium**, 22 000 IU/kg q 6 h) and gentamicin (**gentamicin sulfate**, 6.6 mg/kg q 24 h or 2.2 mg/kg q 6 h) until uterine involution has occurred. A low dose of **oxytocin** (10–20 IU) may help tone and decrease the size of the uterus.

RETAINED PLACENTA

The interval from delivery of the fetus to passage of the placenta (third stage labor) is short in the mare (usually ⩽3 h). The exact time when the presence of placenta becomes pathological (i.e. is a "retained" placenta) is variable (*q.v.*). Feral mares have been observed with placenta retained for up to 48 h without evidence of illness and have subsequently shown continued fertility by producing a foal within the ensuing 12 mo. In contrast, severe complications, even death, can be sequelae of placenta retained <8 h. Degree of difficulty of parturition, degree of contamination of and trauma to the reproductive tract, frequency of foal nursing, and physical activity may all influence the outcome.

Clinical signs

Diagnosis of **retained placenta** (*q.v.*) is by: (1) observation of the presence of fetal membranes hanging from the vulvar lips >3 h after parturition; or (2) examination of the passed membranes revealing that portions are missing that cannot be accounted for by trauma in the stall (mare stepping on them). The mare may become febrile and show signs of endotoxemia and laminitis (*q.v.*).

Treatment

If placental membranes are retained, the treatment schedule to be followed should be as in Table 14.1. If dystocia and uterine contamination have occurred, treatment with antibiotics and NSAIDs should be initiated soon after birth.

In some instances, the placenta is detached but remains within the uterus. In such cases, it is acceptable to lift and apply **gentle traction**. Otherwise, manual removal, and especially any kind of forced detachment, is contraindicated because hemorrhage may occur and small portions of chorion may be torn and remain in the uterus. Studies in cattle report that manual removal lowers subsequent fertility.

Infusion of the allantoic cavity with 10–12 L sterile saline will re-distend the uterus and cause release of endogenous oxytocin. Although this technique may be successful by physiologic mimicking mechanisms, extreme hygiene and care are necessary to avoid uterine contamination.

Table 14.1 Treatment schedule for retention of placental membranes

<3 h	No treatment
3–8 h	Bolus oxytocin 20 IU IM or IV; repeat q 2–3 h until passage is complete May give oxytocin saline with 500 mL calcium borogluconate added as IV drip administering 0.5–1.0 IU/min
<8 h	Continue oxytocin Administer broad-spectrum antibiotics such as penicillin (20 000 IU/kg IV q 6 h) and gentamicin (6.6 mg/kg IV q 24 h) Administer NSAID such as flunixin meglumine (0.25–0.35 mg/kg IV q 8 h) or phenylbutazone (2.2 mg/kg q 12 h)

POST PARTUM ENDOMETRITIS/METRITIS

Uterine involution is rapid in the normal mare and is histologically complete within 7–11 days, which coincides with the first post partum estrus ("foal heat") (*q.v.*).

Following parturition, most normal mares experience a **transient endometritis frequently associated with a β-hemolytic streptococcal infection** (*q.v.*). Such endometritis usually resolves spontaneously and only rarely requires therapy.

Etiology

If dystocia, significant uterine contamination, or retained placenta occurs, the fetus does not suckle, or the environmental situation prevents proper exercise for the mare, **metritis** may occur.

Clinical signs

Metritis differs from endometritis in that the myometrium is also inflamed. The mare may exhibit systemic signs of fever, anorexia, elevated heart rate, congested mucous membranes, endotoxemia and laminitis (*q.v.*). Physical examination of the uterus by palpation per rectum reveals an open cervix and enlarged flaccid uterus that may expel fetid, muddy brown fluid with manual pressure. The uterus does not respond to manual manipulation by contracting and increasing its tone as occurs in a uterus undergoing normal involution.

Treatment

The uterus should be **lavaged daily** with several liters of warm (45°C) sterile saline until the character of the effluent is similar to that of the sterile saline. Harsh antiseptics are to be avoided because they can exacerbate tissue inflammation.

Oxytocin (20 IU IV and 20 IU IM) may help to empty the uterus completely of its fluid. Exercise after administration of oxytocin will enhance the mechanical emptying of the uterus. Infusion of the uterus with antibiotics will do little in the presence of large amounts of uterine fluid.

Systemic broad-spectrum antibiotics (penicillin 22 000 IU/kg q 6 h, gentamicin 6.6 mg/kg q 24 h or 2.2 mg/kg q 6 h) and **NSAIDs** (flunixin meglumine 0.25–0.35 mg/kg IV q 8 h or phenylbutazone 2.2 mg/kg q 12 h) should be administered if the mare exhibits any systemic signs of illness.

CERVICAL LACERATION

Etiology

Cervical laceration can occur during an otherwise normal spontaneous delivery or during manipulation of the fetus during correction of a dystocia (particularly if a fetotomy was performed). There may be no clinical signs other than failure to maintain pregnancy.

Diagnosis

Thorough evaluation of the cervix requires **manual palpation per vagina** of the entire cervix during diestrus or while the mare is under the influence of exogenous progesterone. A laceration is likely to have occurred if a portion of the cervix is absent. Sufficient mucosa and muscular portions of the cervix must be present to form a competent cervical canal. Frequently, **cervical adhesions** may occlude the lumen or prevent adequate closure of the cervix.

Treatment

The treatment of choice is surgical repair; however, the endometrium should be evaluated for soundness prior to surgery. Surgery may be performed with the mare under epidural anesthesia or xylazine–morphine tranquilization (*q.v.*).

Lacerations can be repaired surgically by separating the luminal mucosa, muscularis and vaginal mucosa and suturing each respectively to re-establish a competent canal. Lacerations tend to recur at each subsequent foaling.

MANAGEMENT OF THE HIGH-RISK PREGNANCY

INTRODUCTION

Considerable attention has been focused on how to improve conception rates in the mare and how to save the **critically ill foal**. Once the mare is confirmed pregnant and there is no evidence of twinning, veterinary attention frequently wanes until parturition. Following delivery, sophisticated and aggressive intensive care strategies have been developed to improve survival rates of compromised foals. Many foals still die, not because their primary problem is untreatable, but because veterinary intervention was delayed, delivery was unattended, or neonatal compromise was not recognized in a timely fashion. **Close supervision** of a mare at risk for an abnormal pregnancy or difficult parturition allows earlier detection, treatment and/or possible prevention of neonatal disease.

The three periparturient events that have the most devastating effect on neonatal survival are **hypoxia**, **infection** and **derangement of in utero development**. Periparturient monitoring should focus on early recognition of these events to permit rapid post partum treatment of the affected neonate and investigation of therapy designed to ameliorate these conditions pre partum. Recognition of periparturient events associated with high-risk foals (Box 14.1) helps to identify mares that warrant close pre partum monitoring.

When considering problem pregnancies there are three populations of mares: (1) mares with histories of abnormal deliveries; (2) mares at risk for a problem

Box 14.1 Periparturient conditions associated with high-risk pregnancy

Maternal factors
- Severe systemic disease: colitis, hepatic disease, pneumonia/pleuritis
- Severe neurologic disease: equine protozoal myelitis, cervical cord compression, herpes myelitis
- Endocrinopathy: Cushing's syndrome, fescue toxicosis/ergopeptine toxicity
- Endotoxemia
- Abdominal surgery/general anesthesia
- Fever
- Anemia
- Severe hypoproteinemia
- Severe malnutrition
- Premature udder development/vaginal discharge/precocious lactation
- Hydrops allantois/amnii
- Prepubic tendon rupture
- Pelvic injuries
- Severe endometrial fibrosis
- Premature labor
- Production of poor quality colostrum

Placental factors
- Small placenta
- Placentitis: bacterial, fungal, nocardioform
- Premature placental separation
- Umbilical cord complications: umbilical cord torsion, excessively short cord
- Vasculitis, edema
- Thrombosis, infarction
- Placental insufficiency

Periparturient factors
- Induction of labor
- Dystocia
- Cesarean section
- Postmaturity syndrome
- Early umbilical cord rupture
- Premature placental separation (acute)
- Prolonged labor, uterine inertia

Fetal/neonatal factors
- Congenital anomalies
- Chromosomal anomalies
- Cardiopulmonary disease
- Inherited immunodeficiency disease
- Infection
- Prematurity/dysmaturity
- Twinning
- Failure of passive transfer

with the current pregnancy; (3) mares with no apparent risk factors that experience an abnormal periparturient event. Premature placental separation, dystocia, placentitis and premature delivery (*q.v.*) are examples of recurrent problems some mares experience during successive pregnancies. Regardless of the mare's past reproductive history, the following conditions during late gestation increase the risk of an abnormal pregnancy outcome: severe maternal illness and debilitation, general anesthesia, acute abdominal crisis, vaginal discharge, premature udder development or excessive abdominal enlargement. Mares in the first two groups are candidates for more **intensive periparturient monitoring** to evaluate maternal and fetal well-being. These high-risk mares should be assured of an attended delivery in a facility capable of providing assistance during parturition, post partum resuscitation and stabilization of the newborn foal.

Management strategies for the high-risk mare involve the use of physical and biochemical parameters to assess the health of the fetoplacental unit.

PERIPARTURIENT ENDOCRINOLOGY

The exact mechanism regulating parturition in the mare is unknown. Current concepts of hormonal regulation of gestation are discussed in detail elsewhere (*q.v.*).

During early pregnancy, **progesterone** (*q.v.*) is produced by the primary and secondary corpora lutea. The placenta begins to produce progesterone during the first trimester and eventually becomes the sole source of this hormone after the corpora lutea have ceased to function between Days 150 and 200. The developing fetus and placenta produce other progestogens, primarily α-pregnanes and pregneninolone, which contribute to support of the pregnancy beginning around Day 60.

Understanding the role of progesterone and maintenance of pregnancy during late gestation is confounded by the fact that there is cross-reaction between the α-pregnanes and progesterone. Most progesterone assays measure only progesterone and not fetoplacental progestogens. Yet both groups of metabolites contribute to maintenance of pregnancy.

During the first trimester, several clinical conditions have been associated with **inadequate maternal progesterone** concentrations and pregnancy loss. Mares with **endometritis** may experience premature luteolysis and low progesterone concentrations. **Severe stress**, such as fatigue or food deprivation, may cause decreased progesterone levels and jeopardize pregnancy. Endotoxemia and surgical manipulation of the uterus result in abortion via $PGF_{2\alpha}$ secretion, compromised luteal activity and inadequate progesterone production. **Progesterone supplementation** (0.044–0.088 mg/kg PO q 24 h) in these instances can certainly be justified. Administration of flunixin meglumine (0.25 mg/kg IV q 8 h) is beneficial due to its ability to inhibit prostaglandin production.

Elevated **estrogen concentrations** are present in maternal blood and urine during the second half of gestation with peak values obtained during the 7th and 8th month followed by a gradual decline thereafter. There are two main groups of estrogens in the mare: common phenolic estrogens (estrone and estradiol 17β) and ring β-unsaturated estrogens (equilin and equilenin). Fetal gonads also provide estrogen precursors such as dihydroepiandrosterone

(DHA) that are converted by the placenta to the final estrogen products. Since normal estrone sulfate concentrations (≥2 ng/mL) after Day 40 require a viable fetus, **estrone sulfate measurement** may be helpful in monitoring fetal viability. An accurate reference range for estrone sulfate concentrations throughout pregnancy remains to be developed.

Gonadectomized foals from estrogen-deficient mares are dysmature at birth. Labor in these mares is weak and inefficient and associated with low prostaglandin levels. Estrogens appear to play a role in normal fetal development, an effect that may be mediated by alteration of uteroplacental blood. A correlation between fetal distress, growth retardation and death and changes in maternal and urinary estrogen concentrations has been suggested. Further investigations remain to be performed before these relationships are fully understood.

FETAL ELECTROCARDIOGRAPHY

Fetal electrocardiography (ECG) can be used to confirm pregnancy and monitor fetal viability after Day 150. Twinning produces two separate heart rate patterns. **Fetal cardiac arrhythmias** occur with a variety of abnormal pregnancies. Severe bradycardia often indicates hypoxemia and impending fetal demise.

The limb lead electrode (LA) is placed on the dorsal midline of the mare in the mid-lumbar region. The other limb lead electrode (LL) is placed approximately 15–20 cm cranial to the mare's udder on the ventral midline. Alcohol or ECG gel should be used to improve skin contact with the electrodes. The hair should be clipped prior to lead placement. Maternal ECG deflections are larger and slower and usually have a different polarity than those of the fetus. Fetal ECG polarity is variable and depends on fetal position. A poor fetal signal may result from fetal movement, improper electrode placement or electronic noise. See also Chapter 8, page 455.

TRANSABDOMINAL ULTRASONOGRAPHY

Transabdominal ultrasonography allows non-invasive monitoring of fetal development and assessment of fetal well-being during mid and late gestation. Due to the deeper tissue penetration required to image the fetus in late gestation, transducers with lower frequencies of 2–4 MHz are used. In preparation for scanning, the mare's ventral abdomen is cleaned and clipped. A viscosity coupling gel is applied to the abdomen and transducer. This abdominal approach can be used after the gravid uterus contacts the ventral abdominal wall after Day 150 of gestation but is used most frequently during the second and third trimesters.

Twins can be detected at any stage of pregnancy but are more difficult to locate during late gestation. The heart rate, presentation and position of each twin should be noted. During late pregnancy the entire gravid uterus must be explored systematically. Twins located **one on top of the other** may be mistaken for one fetus. In addition to visualizing only one fetus, it is helpful to identify the empty non-fetal horn to eliminate the possibility of twins.

Ultrasonographic assessment of fetal well-being incorporates a variety of fetal parameters into a biophysical profile. In humans this profile includes measurements of fetal heart rate, reactivity, movement, tone and breathing

patterns, and measurement of amniotic fluid volume. The placenta is examined for changes in thickness and texture and the clarity of fetal fluids is evaluated. Measurements of various fetal body parts including head circumference and femur length have resulted in elaborate in utero growth charts for various stages of gestation.

The size of the equine fetus makes some of these measurements impossible. Parameters that can be assessed in the horse include fetal heart rate (at rest and after spontaneous activity), frequency and vigor of fetal movements, aortic diameter, fetal breathing movements, measurements of placental thickness, and gross evaluation of allantoic and amniotic fluid volumes and clarity. Reliable indices of fetal size have yet to be established. Limited studies have been performed relating fetal size to measurements of fetal aortic diameter, fetal orbit diameter, biparietal diameter and thoracic girth.

Placental separation can be detected with careful methodical scanning. It is important to remember that not all of the placenta can be visualized during transabdominal examination. Transrectal ultrasonography should be used to evaluate the allantochorion in the pericervical area.

During late gestation, all fetuses exhibit some movements ranging from limb flexion to rotation about the long axis of the body. Brief periods of fetal inactivity may be associated with normal sleep patterns. Prolonged periods of inactivity ($\geq$40 min) are rare and suggest fetal distress.

Fetal **heart rates** average between 60 and 100 bpm during late gestation with transient bouts of tachycardia (25–40 bpm above baseline) observed during or immediately after fetal activity. **Persistent bradycardia** is associated with fetal distress and is mediated by a vagal response to hypoxemia (*q.v.*). **Severe tachycardia** and arrhythmias have been associated with fetal stress and sepsis (*q.v.*). **Maternal sedation** will affect fetal heart rate.

Placental thickness can be estimated by measuring the uteroplacental unit and averages between 0.8–1.3 cm. Abnormally thickened placentas have been associated with placentitis and edema. Transrectal ultrasound using a 5 MHz linear transducer provides an excellent image of the allantochorion in the area of the cervical star. An increased measurement during mid to late gestation (>7 mm prior to 270 days of gestation, >8 mm between Days 271 and 300, >10 mm between Days 301 and 330, and >12 mm after Day 330) suggests **placental failure** and **impending abortion**. Pockets of fluid accumulation between the placenta and uterine wall are compatible with premature placental detachment.

Fetal **aortic diameter** measurements have been used to predict fetal weight and size. The aortic diameter for near-term thoroughbred foals is approximately 2.0–2.2 cm. An abnormally small fetus detected in late gestation is compatible with an inaccurate breeding date or some form of **intrauterine growth retardation (IUGR)**. Possible causes of IUGR include perinatal infection, congenital anomalies, uteroplacental insufficiency and inadequate maternal nutrition.

The maximum ventral fetal fluid pocket depths average 8 cm for amniotic fluid and 13 cm for allantoic fluid. Excessive fetal fluid accumulation is observed in cases of hydrops. The amniotic and allantoic fluids normally become more echogenic during the last months of gestation. Free floating, swirling particles in the fluid are usually composed of mineral deposits and mucoproteins. Abnormal **particulate matter** in either fluid compartment may include blood,

meconium or inflammatory debris such as white blood cells and protein. Hemorrhage suggests loss of placental integrity. Meconium signifies fetal distress, often due to hypoxia. Inflammatory debris suggests in utero infection.

Pre partum **fetal asphyxia** may result in **renal compromise** and decreased urine production leading to a reduction in allantoic fluid volume. Dramatic decreases in fluid volume may predispose to abnormal umbilical cord compression pre partum and during birth resulting in fetal compromise. Decreased allantoic fluid volume has been associated with poor neonatal outcome and chronic hypoxia.

PRE PARTUM MAMMARY SECRETIONS

Electrolyte concentrations in pre partum mammary secretions begin to change prior to parturition. A rise in the **calcium** concentration in the precolostral milk is the most reliable indicator of impending delivery. Calcium levels >40 mg/dL have been associated with fetal maturity. A scoring system using colostral calcium, sodium and potassium concentrations helps predict "readiness to give birth" and can help determine an appropriate time for elective induction or Cesarean section. Table 14.2 lists the parameters for the scoring system.

Variations of water **hardness test strips** are used to measure the calcium concentrations in pre partum mammary secretions to predict the likelihood of foaling. These strip tests are marketed under a variety of names: Predict-A-Foal Test (Animal Health Care Products, Vernon, CA 90054, USA) and Sofcheck (Environmental Test Systems Inc., Elkhart, IN 46514-0659, USA). Causes of false negative results using the calcium milk strip test include severe maternal malnutrition and premature delivery. Causes of false positive results include placental infection and premature lactation. Occasionally, normal mares with normal deliveries have abnormal test results. The milk strip test is not foolproof and should be used only as an aid in predicting "readiness for birth".

FETAL FLUID ANALYSIS

Amniotic fluid (AF) can be aspirated directly from the amniotic sac immediately prior to rupture during parturition. Pre partum, amniocentesis can be performed during late pregnancy using a 20 G needle with a trocar and an ultrasound-guided, transabdominal approach. The ideal location is the **AF pocket** located between the front legs and thorax of the fetus. This area is usually visualized best just cranial and lateral to one side of the dam's mammary gland. Mares may require **light sedation** and can be pre-treated with flunixin

Table 14.2 Scoring system for electrolyte concentrations in mammary secretions

Calcium (mg/dL)	Sodium (mEq/L)	Potassium (mEq/L)	Points for each electrolyte
⩾40	⩽30	⩾35	15
⩾28	⩽50	⩾30	10
⩾20	⩽80	⩾20	5

Total score ⩾35 suggests probably safe induction.
Adapted from Ousey, J.C., Dudan, F., Rossdale, P.C. Equine Veterinary Journal *16: 259.*

meglumine. A sharp needle is essential to allow clean penetration of the free-floating, echogenic amniotic membrane separating allantoic and amniotic fluid compartments.

Allantocentesis can be performed using a similar procedure. Fetal fluid collection remains a research tool and is not used routinely in clinical cases.

Cortisol and creatinine concentrations have been examined in amniotic fluid in relation to fetal maturation and gestational age. Preliminary results in the horse are inconclusive.

Phospholipid components of surfactant, lecithin (L), sphingomyelin (S) and phosphatidylglycerol (PG), are measured in amniotic fluid to predict fetal lung maturation and the risk for neonatal respiratory distress syndrome. In women, L:S $\geq$2.0 and the presence of PG in amniotic fluid are associated with fetal lung maturity and a low incidence of respiratory distress syndrome. Once again, preliminary results in the horse are inconclusive.

Fetal fluid samples can also be cultured for bacteria and viruses. Samples stored frozen for several weeks have yielded positive cultures for herpes and equine viral arteritis viruses. Fetal fluid cytology can be used to detect infection. Fetal karyotyping can be performed, but is rarely used in clinical practice.

Neonatal serum creatinine concentration

Markedly **elevated serum creatinine concentrations** in foals less than a few hours of age have been associated with clinical signs of **birth hypoxia**. Since the placenta essentially functions as an in utero kidney for the fetus, it is not surprising that certain forms of placental dysfunction might result in **fetal azotemia**. Peri partum hypoxia can also cause primary renal tubular damage resulting in persistent neonatal azotemia post partum.

Neonatal serum glucose concentration

Presuckle hypoglycemia (glucose <35 mg/dL) immediately following birth is suggestive of placental dysfunction and hypoxia. Persistent hypoglycemia during the first 48 h post partum suggests immature insulin response and marginal glucose reserves. Hyperglycemia (glucose >180–200 mg/dL) is associated with hypoxia-induced pancreatic endocrine dysfunction, sepsis-induced release of glucagon, catecholamines and cortisol resulting in peripheral insulin resistance (*q.v.*).

Equine fetal protein

Alpha-fetoprotein (AFP) is a glycoprotein produced primarily by the fetal liver. Other sites of synthesis include the yolk sac, placenta and fetal gastrointestinal tissues. AFP is closely related to albumin. Its function is unclear, but may include the role of a transport protein. This fetal specific protein has been identified in numerous mammalian species including sheep, cattle, pigs and horses. The highest concentrations are in fetal serum, fetal urine and fetal CSF. Decreasing amounts are present in fetal fluids and the sera of pregnant females.

AFP is secreted via fetal urine into amniotic fluid in women and into allantoic fluid in horses. Trace amounts of AFP enter the maternal circulation

transplacentally or by direct diffusion. In pregnant women, elevated AFP concentrations are associated with open neural tube defects, multiple births, fetal demise, fetal distress, congenital defects, low birth weight, placentitis and spontaneous abortion. Abnormally low levels have been associated with poor fetal outcome and chromosomal defects. Today AFP testing in women is used primarily to screen for open neural tube defects during the second trimester.

In pregnant mares, elevated equine fetal protein (EFP) concentrations have been associated with **premature placental separation**, the birth of **maladjusted foals, twinning, placentitis** and **uterine trauma**. The highest values are observed in mares with placentitis and recent or impending fetal demise. The test is a microtiter plate ELISA. In normal pregnant mares, serum EFP concentrations range between 4 and 10 units/mL. Normal values are currently being established for amniotic and allantoic fluids. Foal EFP concentrations are dramatically higher than those of their dams and decrease to adult levels within 100 days post partum.

APGAR SCORE

The APGAR score is used to evaluate the degree of **birth asphyxia** immediately post partum. APGAR stands for *A*ppearance, *P*ulse, *G*rimace, *A*ctivity and *R*espiration (see Table 14.9, page 819). These parameters should be assessed continuously during the first 5–15 min of life to help determine the degree of birth asphyxia and need for neonatal resuscitation.

OTHER SURVEILLANCE METHODS

Mares under observation for signs of foaling should be checked frequently by trained attendants. Closed-circuit, stall-mounted television cameras facilitate periparturient monitoring. Other currently available delivery detecting devices include Foalert, Breeder Alert and Birth Alarm. The alarm system on all of these devices can also be connected to the phone lines and set to dial automatically specified numbers such as those of the veterinarian, farm manager, etc. The Foalert involves suturing a transmitter attached to an actuating magnet to the lips of the vulva. When the foal enters the birth canal, the vulva lips are parted, the magnet is activated and the alarm is transmitted to a pocket pager and the phone system. The Breeder Alert utilizes a monitor attached to the halter that activates the paging system whenever the mare lays down in lateral recumbency for >30 s. The Birth Alarm uses a transmitter attached to an anti-roll surcingle device that activates an alarm or paging system when the mare lays down in lateral recumbency.

EVALUATION AND MONITORING OF THE HIGH-RISK MARE

Any mare considered at increased risk of a problem pregnancy should receive a **complete physical examination**. Treatment of concurrent medical or surgical problems should proceed with maternal and fetal well-being in mind. Any maternal event that reduces uteroplacental circulation and/or oxygenation poses an immediate threat to fetal well-being.

The diffuse epitheliochorial equine placenta is a more permeable barrier than the cotyledonary ruminant placenta. Oxygen, pH and glucose gradients between fetus and dam are far less in the mare than in the sheep or cow. In the ruminant, wide swings in maternal oxygen concentrations produce comparatively little change in fetal oxygenation. However, due to the more efficient oxygen exchange in the mare's placenta, maternal hyperoxia and hypoxia are accompanied by even greater changes in fetal oxygen levels.

While **maternal hypoxia** represents a relatively greater threat to the equine fetus, oxygen supplementation in the mare has the potential to improve dramatically certain forms of fetal hypoxia. Because of the more efficient transplacental glucose exchange in the mare, prolonged periods of maternal hypoglycemia must also be avoided. Force feeding or glucose supplementation should be considered for pregnant mares that are completely anorexic.

The **reproductive tract** can be evaluated initially by palpation and ultrasonography per rectum to appreciate fetal movement, gross body position and cervical tone. Sonographic visualization and measurement of the fetal orbit confirms anterior presentation and provides a rough estimate of fetal size. Transabdominal ultrasonography provides a more rewarding assessment of fetal well-being, fetal position and gross changes in placental integrity. When no fetal movement can be detected on rectal palpation, transabdominal ultrasonography can evaluate fetal viability by observing the absence or presence of fetal heart rate.

Although maternal **hypertension** is a serious complication in women, it has not been documented to occur in the mare. It is plausible that hypertension may develop in mares suffering from severe laminitis or other painful conditions. Blood pressure is easily monitored using a pneumatic cuff, the Doppler technique and the middle coccygeal artery. Severe untreated hypertension may impair uteroplacental profusion.

Pre partum mammary secretions should be evaluated for rising calcium concentrations as a sign of impending parturition as soon as secretions are easily obtained from the gland. Monitoring frequency should increase to every 24 or 48 h when calcium concentrations begin to rise.

Near-term mares should be evaluated daily for signs of vulva elongation, sacroiliac ligament relaxation and degree of mammary development.

PERI PARTUM INTERVENTION

Pharmacologic intervention pre partum remains conservative in the mare. Seriously ill or stressed mares during the first trimester are candidates for pregnancy loss due to **progesterone deficiency** and benefit from exogenous progesterone administration to maintain progesterone concentrations >4 ng/mL. Only two forms of progestogen are readily available for use in the mare. Progesterone in oil requires IM injections of 150 mg daily. **Altrenogest**, a synthetic progestin, can be given orally at a dose of 0.044 mg/kg. Once begun, progesterone supplementation should continue through to Day 100. Progesterone administration after the first trimester remains controversial.

The abortifacient effect of **endotoxemia** (*q.v.*) in mares early in pregnancy is mediated indirectly through $PGF_{2\alpha}$ secretion, compromised luteal activity and inadequate progesterone secretion resulting in fetal death. **Flunixin meglumine**

(1.1 mg/kg IV) administered prior to or immediately after the onset of endotoxemia is believed to prevent early pregnancy loss by inhibiting synthesis and release of $PGF_{2\alpha}$. Successful treatment depends on early recognition or a high index of suspicion of endotoxemia.

A second mechanism that may be involved in endotoxin-induced fetal death and abortion is **compromised uteroplacental perfusion** associated with the systemic inflammation, cardiovascular collapse, hypotension and coagulopathies associated with endotoxemia. Therefore, administration of **flunixin meglumine** is a reasonable therapy for any pregnant mare at risk for endotoxemia.

In women, β-adrenergic agonists such as ritodrine, terbutaline and isoxsuprine have been used to improve uteroplacental blood flow and to prevent premature contractions. The use of these agents for these purposes in the pregnant mare is still experimental.

Mares examined for a potential **high-risk pregnancy** should have a database completed as outlined in Box 14.2. A careful history helps identify what problems to anticipate.

Box 14.2 Database for high-risk pregnancies

Signalment
- Age
- Breed

Past reproductive history
- Number of previous pregnancies
- Outcome of past pregnancies: if abnormal, classify as pre partum, intra partum, or post partum complications
- Length of gestation(s), date of delivery(ies), sex of foal(s)
- Results of most recent uterine biopsy/culture

Current reproductive history
- Date last bred
- 340 day due date
- Description of current medical problems
- Recent drug administration
- Presence of vaginal discharge or premature udder development
- Vaccination

Initial work-up and pre partum monitoring
- Physical examination
- Body weight
- Rectal palpation
- Vaginal examination (only if indicated clinically)
- Transrectal ultrasonography
- Transabdominal ultrasonography
- Blood pressure
- Mammary secretion electrolyte concentrations (as soon as secretions easily obtained)

Box 14.2 continues on page 798

Box 14.2 Database for high-risk pregnancies [continued]

- Daily evaluation of pelvic ligament relaxation, udder development, vulva elongation
- Frequent visual observation for signs of parturition (with or without the aid of television monitors and labor detection devices)

Post partum evaluation: mare

- Evaluation of placenta: description, weight, histopathology
- Specific gravity of colostrum
- Palpation/ultrasonography per rectum to evaluate uterine involution

Foal

- Physical examination
- White blood cell count, differential
- Fibrinogen
- Glucose
- Creatinine
- Blood culture if foal, placenta or delivery is abnormal
- Arterial blood gas if foal is weak or shows signs of respiratory distress
- IgG concentration between 12 and 18 h of age

Special **management guidelines** for various periparturient conditions are presented in Table 14.3. Frequent surveillance of a late pregnant mare is essential to ensure that delivery is attended. All the supplies required for a rectal examination, vaginal examination, epidural, correction of a dystocia and neonatal resuscitation should be readily available (Box 14.3).

Vaginal delivery is the preferred route of parturition. However, **induction of parturition** should be considered when abnormal conditions such as a non-reassuring biophysical profile or ultrasonic evidence of premature placental separation (*q.v.*) exist. A history of severe dystocia, or an obstructed pelvic canal secondary to previous trauma, urge consideration of an elective Cesarean section (*q.v.*). Other indications for induction or Cesarean section are presented in Box 14.4.

Whenever delivery is being artificially controlled, the mare should be as close to her physiologic due date as possible without jeopardizing fetal or maternal health. Gestation length beyond 320 days, pelvic ligament relaxation, udder development with colostrum-like secretions in the gland, and cervical dilatation are all encouraging signs that termination of the pregnancy will result in a close-to-term foal.

If a premature foal is anticipated, the most life-threatening neonatal condition is **respiratory distress** due to **primary surfactant deficiency**. Post partum intratracheal instillation of artificial or bovine origin surfactant is being evaluated for such foals.

During late pregnancy, satisfactory induction has been achieved using a slow, **continuous infusion of oxytocin** at a rate of 1 IU/min. Delivery frequently ensues within 30–40 min after beginning the oxytocin drip. The infusion is slowed to 0.5 IU/min after birth until the placenta is passed. Small IV/IM boluses of 2.5–5.0 IU oxytocin given every 20–30 min have also produced a gradual onset of labor and delivery.

Table 14.3 Management guidelines for selected causes of high-risk pregnancies

Maternal condition	Effect on pregnancy	Monitoring/treatment
Endotoxemia	Compromised uteroplacental perfusion; PG mediated abortion	Anti-endotoxin plasma; fluid therapy; flunixin meglumine; ±progesterone; transabdominal US
Abdominal surgery/ general anesthesia	Compromised uteroplacental perfusion; anesthetic depression of fetus	Minimize duration of surgery; flunixin meglumine; progesterone; maintain adequate maternal PaO_2, BP; transabdominal US
Severe neurologic disease	Difficult delivery; possible trauma to mare or foal	Attended delivery; safe footing for mare; sling support if necessary
Severe hypoproteinemia	Compromised uteroplacental circulation	Fluid support; plasma; transabdominal US; high nutritional plane
Placentitis/purulent vaginal discharge/ premature lactation	In utero fetal infection; PG-induced premature delivery	Systemic broad-spectrum antibiotics; flunixin meglumine; progesterone; transabdominal US; immediate post partum neonatal evaluation; bloodwork, cultures
Pelvic injuries	Dystocia due to abnormal pelvic inlet	Assisted delivery; elective Cesarean section
Hydrops allantois	Fetal/uteroplacental compromise; maternal hypotension, cardiopulmonary collapse post partum; prepubic tendon rupture	Transabdominal US; induced, controlled delivery; maternal fluid and O_2 support; abdominal belly wrap
Poor colostrum production	Neonatal FPT; increased risk of neonatal sepsis	Evaluate colostrum quality; provide alternate source of colostrum or plasma transfusion
Postmaturity syndrome	In utero fetal growth retardation and chronic hypoxia	Transabdominal US; induced delivery; evaluation of maternal endocrine function; uterine biopsy
History of premature placental separation	Fetal hypoxia	Transabdominal US; maternal O_2 therapy; induced delivery; neonatal resuscitation

FPT, failure of passive transfer; PG, prostaglandin; US, ultrasonography.

Box 14.3 Supplies for foaling cart

Obstetric equipment

- Rectal sleeves and lubricant
- Clean, stainless steel bucket
- Cotton and bactericidal scrub for cleaning purposes
- Tail wrap
- Sterile nasogastric tube, pump, obstetric lubricant for use during dystocia
- Sterile lubricant and gloves for vaginal exam
- Light source for vaginal exam
- Obstetric straps or chains and handles
- Lidocaine, 18 G needles, 10 mL syringe for epidural

Box 14.3 continues on page 800

Box 14.3 Supplies for foaling cart [continued]

- IV catheters, fluid administration sets
- Xylazine, butorphanol for mare restraint if needed

Minimal resuscitation equipment

- Oxygen source: O_2 tank, wall source, oxygen
- concentrator
- Intranasal oxygen cannulas and oxygen tubing
- Ambu bag or oxygen demand valve
- Cuffed nasotracheal tubes (7–11 mm diameter, 55 cm long)
- Sterile lubricant and gloves
- Suction pump and tubing
- Towels
- Heat source
- IV catheters, fluid administration sets with coiled extension sets
- Liter bags of balanced electrolyte and dextrose-containing fluids
- Emergency drugs: adrenaline/epinephrine, calcium, bretylium, lidocaine, bicarbonate

Box 14.4 Management of parturition

Indications for induction

- History of premature placental separation and the birth of dead or hypoxic foals
- Sonographic evidence of fetal death or severe distress, large areas of placental separation
- Prolonged, unproductive first stage labor that fails to progress, uterine inertia
- Severe maternal illness that threatens fetal well-being
- Post-date pregnancy with evidence of severe fetal distress or growth retardation
- Prepubic tendon rupture
- Hydrops amnii or allantois

Indications for Cesarean section

- Severe dystocia
- Recurrent history of severe dystocia
- Pelvic injury resulting in obstruction of the birth canal
- Life-threatening gastrointestinal compromise in the dam necessitating exploratory celiotomy

If **Cesarean section** (*q.v.*) is indicated, it is important to keep the duration of fetal anesthesia to a minimum and to avoid intraoperative episodes of severe maternal hypotension or hypoxemia. Newborn foals experiencing **respiratory distress** from narcotics administered to the mare should receive an appropriate dose of a reversing agent such as **naloxone** (0.01–0.02 mg/kg IV). Ventilatory support and careful monitoring of body temperature are required by many anesthetized newborns.

The **placenta** should be evaluated grossly and microscopically for evidence of infection, premature detachment and other anomalies.

PHYSICAL EXAMINATION OF THE NEONATAL FOAL

HISTORY

Evaluation of the **health of a foal** should begin with a thorough reproductive history and physical examination of the mare. The breeding dates should be used to calculate an accurate gestational age. The normal length of gestation in the mare ranges from 320 to 365 days with a mean of 340 days. A gestational age of <320 days indicates prematurity.

Signs of **immaturity** include soft, silky haircoat, domed forehead, flexor tendon laxity, floppy ears, general weakness, low body weight and incomplete ossification of carpal and tarsal bones.

Foals that exhibit signs of immaturity but are of correct gestational age are **dysmature**. Dysmaturity is associated with placentitis, congenital abnormalities, drug exposure and other diseases. IUGR can result in dysmaturity or a foal that is small for its gestational age.

A history of abnormal events surrounding this pregnancy or others in the past may identify a foal at increased risk for the development of disease. Factors associated with compromise of the neonate include placentitis, premature separation of the placenta, twinning, Cesarean section, dystocia and vulvar discharge (*q.v.*).

PHYSICAL EXAMINATION OF THE MARE AND PLACENTA

One of the first signs of **poor nursing behavior** in the foal is a turgid and sometimes painful udder in the mare. These mammary gland changes are also compatible with **mastitis** (*q.v.*) so the milk should be examined. If the udder appears small and flaccid and little milk can be expressed, the mare may not be producing enough milk.

A foal may nurse as frequently as four to seven times an hour but should sleep in between feedings. Foals that are constantly at the udder are most likely not getting enough milk. A history of a mare dripping milk prior to parturition implies the mare has lost valuable colostrum. An equine Colostrometer (Lane Manufacturing Inc., Denver, CO, USA) or modified refractometer (Eclipse refractometer) can be used to measure the **quality of colostrum** based on specific gravity. Colostrum with a specific gravity ⩾1.060 is considered good quality. If the mare's colostrum is of poor quality, then tested colostrum from another mare should be fed via a bottle or nasogastric tube prior to 12 h of age and preferably before 4 h of age.

In addition to examining the foal, the **placenta** should also be evaluated for signs of edema and infection. Examination of the fetal membranes can provide insight into the type and duration of in utero insult the fetus may have experienced. A normal placenta should weigh approximately 10% of the foal's BW. Heavier than normal membranes may be caused by **edema** or **placentitis** (*q.v.*) that may be acute or chronic in nature. A foal exposed to a brief bout of placental insufficiency/hypoxia has a better prognosis than a foal exposed to

chronic hypoxia. Full-term foals deal with chronic hypoxia more effectively than premature foals.

Since most intrauterine bacterial infections begin as an **ascending placentitis** of the chorioallantois, the area of discoloration and thickening originates at the cervical star and extends up the body of the placenta. Acute cases of placentitis may require histopathologic examination for a diagnosis. Cases of chronic placentitis are usually recognized by thickening and discoloration of the chorion. β-Hemolytic streptococci and *E. coli* are among the most common bacterial pathogens associated with placentitis. **Diffuse placentitis** is associated with hematogenous spread of infection such as is seen with **Leptospira** infection (*q.v.*).

It has been hypothesized that **nocardioform placentitis** may develop from a focal endometritis that was present prior to pregnancy. **Fungal placentitis** often presents with a sticky brown mucoid exudate covering parts of the chorion and is often associated with a small, emaciated foal. Sabouraud's agar should be used to isolate suspected fungal pathogens. A direct smear of the exudate can be examined with Gomori's methenamine silver stain. *Aspergillus* and *Mucor* species (*q.v.*) are the most fungal pathogens isolated. Systemic fungal infection of the foal is relatively rare.

When submitting samples of the placenta for microscopic examination, sections should be taken from the fetal and non-fetal horns, the body of the placenta, the region around the cervical star, any abnormal areas of the chorion, and the amnion.

The placenta should be examined for signs of hypoplastic chorionic villi, meconium staining or placentitis. **Hypoplastic chorionic villi** appear as pale, thin, shiny plaques in the chorion. Large areas can result in decreased placental exchange and have been associated with fetal growth retardation. In the case of twins, the opposing areas of placenta will have no villi.

Meconium staining imparts an orange-brown tinge to the amniotic membranes as well as the foal. Meconium staining is a sign of **fetal distress** prior to or during parturition. **Aspiration of meconium** by the foal can lead to severe respiratory compromise.

Placentitis (*q.v.*) is recognized by a thickening and discoloration of the placenta most often involving the area of the cervical star. Foals exposed to in utero infection may appear normal at birth and have a normal leukogram, but have an elevation in **plasma fibrinogen** levels indicative of chronic (≥2 days) inflammation (Table 14.4). It is important to remember that even though the placenta may appear normal, microscopic pathology can result in decreased placental exchange.

Adenomatous hyperplasia of the allantois may appear as hyperplasia and hypertrophy of the epithelial cells of the allantois with the formation of intraepithelial glands. More severely affected membranes may have raised firm tan nodules on the allantoic surface of the chorioallantois. These lesions consist of dilated, anastomosing glands surrounded by loose, collagenous stroma. Inflammatory changes are thought to be secondary to the adenomatous dysplasia. The cause of this lesion is not known, but it is seen with chronic placentitis, placental edema and fetal diarrhea.

Umbilical cord abnormalities may also affect the fetus. Granular debris and golden meconium particles on the amniotic portion of the cord suggest local inflammation. An excessively long umbilical cord (normal range 36–83 cm)

Table 14.4 Normal hematology values for neonatal full-term foals

	1 day of age	7 days of age
Red blood cells ($10^6/\mu L$)	8.2–11.0	7.4–10.6
Mean cell volume (fL)	36–46	35–44
Mean cell hemoglobin concentration (g/dL)	32–40	35–40
Hemoglobin (g/dL)	12–16.6	10.7–15.8
Packed cell volume (%)	32–46	28–43
Total leukocytes ($10^3/\mu L$)	4.9–11.7	6.3–13.6
Neutrophils ($10^3/\mu L$)	3.36–9.57	4.35–10.55
Lymphocytes ($10^3/\mu L$)	0.67–2.12	1.43–2.28
Monocytes ($10^3/\mu L$)	0.07–0.39	0.03–0.54
Eosinophils ($10^3/\mu L$)	0–0.02	0–0.09
Basophils ($10^3/\mu L$)	0–0.03	0–0.18
Platelets ($10^3/\mu L$)	129–409	111–387
Total plasma protein (g/dL)	5.2–8.0	5.2–7.5
Fibrinogen (mg/dL)	100–400	150–450

Reproduced with permission from Harvey, J.W. (1986) Normal haematologic values, in Korterba, A.M., Drummond, W.H., Kosch, P.C. (eds) Equine Clinical Neonatology. *Lea & Febiger, Philadelphia, pp. 561–570.*

may result in **strangulation** of the fetus with evidence of edema and vascular occlusion around the head and neck. If there is **excessive twisting** of the cord there may be compromised fetal circulation and/or obstruction of the urachus. **Urachal obstruction** may contribute to urachal patency or bladder rupture. An unusually **short cord** is prone to premature rupture and hemorrhage and may predispose the foal to hypoxic injury. Umbilical cord anomalies can also be associated with cases of **hydrops amnii** (*q.v.*).

RESPIRATORY SYSTEM

The foal's respiratory rate should be obtained prior to entering the stall. The **normal respiratory rate** of the foal just after birth is 60–80 breaths/min but decreases to 20–40 breaths/min within the first day of life. Although most foals have a normal respiratory pattern, some foals, when in a deep sleep, will exhibit periods of **apnea** followed by a series of rapid breaths. No nasal discharge should be present.

Auscultation of the lungs reveals air moving over the entire lung field without crackles or wheezes. Foals' lungs are louder and harsher than adult lungs as a result of a thinner chest wall. Areas of dullness or changes in pitch or character of lung sounds as auscultation continues ventrally indicate areas of **consolidation** or **atelectasis**.

Signs of respiratory distress due to **lung immaturity** (lack of surfactant, increased chest wall compliance, etc.) or **pneumonia** (*q.v.*) include nostril flare, increased respiratory effort, rib retraction and inspiratory or expiratory noises.

Foals on the brink of respiratory failure begin to grunt at the end of expiration as a form of physiologic "PEEP" (*p*ositive *e*nd *e*xpiratory *p*ressure) in an attempt to keep alveoli inflated. Affected foals also demonstrate **paradoxical respiration** associated with collapse of the chest wall during inspiration due to respiratory muscle fatigue and increasing lung stiffness.

Thoracic auscultation in the foal can be misleading, as it may be normal despite severe pathology. If the clinician identifies signs of respiratory distress or has a suspicion of respiratory disease, **thoracic radiographs** should be taken and **arterial blood gas analysis** considered.

Periodic apnea and **abnormally slow respirations** are often the result of metabolic disturbances (e.g. hypoglycemia, hypocalcemia), hypothermia, advanced prematurity or hypoxia-induced suppression of the respiratory center. **Tachypnea** is often a response to pain or stress. If birth was difficult, check carefully for **fractured ribs**. In addition to palpating crepitus over the broken ribs, a faint clicking sound can be heard during inspiration on the side of the chest with the rib fracture(s). Affected foals often exhibit grunting during expirations and may prefer to lie on the unaffected side if rib fractures are unilateral.

Congenital defects of the respiratory system include various malformations of the nares, larynx, and trachea including stenotic nares, choanal atresia, subepiglottic cyst, collapsing trachea and guttural pouch tympany (*q.v.*).

CARDIOVASCULAR SYSTEM

The **rectal temperature** of a normal newborn foal is 37.2–38.9°C (99–102°F) and the **heart rate** ranges from 70 to 100 bpm. Heart rhythm should be regular; however, a **sinus arrhythmia** may be present for the first few hours after birth.

A healthy foal's distal extremities should be warm with easily palpable pulses. Normal blood pressure values are: systolic 144 ± 15 mmHg, diastolic 74 ± 9 mmHg, mean 95 ± 13 mmHg. **Thready pulses** herald cardiovascular collapse. **Hypotension** is associated with septic and hypovolemic shock, severe asphyxia and advanced prematurity.

During the first day following delivery the foal's heart rate should increase to >100 bpm and then stabilize between 90 and 100 bpm. A **jugular pulse** can be present in the distal one third of the jugular groove when the foal hangs his head or is in lateral recumbency.

A **systolic murmur** (*q.v.*) is frequently heard over the left heart base during the first 5–7 days of life and is usually associated with a closing **ductus arteriosus**. In these individuals the **patent ductus arteriosus (PDA)** (*q.v.*) is benign since birth-induced changes in intracardiac and pulmonary pressures result in a reversal of blood flow. A **PDA** presents with either a continuous machinery murmur or a holosystolic murmur loudest on the left side, which may persist for 1–4 days. Pathologic causes of a persistent murmur include PDA, VSD (ventral septal defect) and other valvular defects. A foal with a pathologic PDA suffers hypoxia since fetal circulatory pathways are maintained.

Mucous membranes should be pink and moist with a capillary refill time of 1–2 s. Signs of **septicemia** include injection or congestion of mucous membranes, a bright pink toxic ring around the teeth, jaundice or petechiation of mucous membranes and inside of the pinnae. **Jaundice** may also be a sign of **neonatal isoerythrolysis** or liver disease and EHV-1 infection (*q.v.*).

Tachycardia, unless associated with pain or excitement, is often an early sign of sepsis. Tachycardia has also been associated with hypocalcemia. **Bradycardia** may be associated with hypothermia, hyperkalemia and hypoglycemia.

GASTROINTESTINAL SYSTEM

The **suckle reflex** is present within 20 min of birth. In their first attempt to nurse, most foals explore the mare to find the udder but should nurse within 2 h. Healthy foals consume 15–25% of their body weight per day divided into many frequent feedings. Neonates nurse as frequently as every 10–20 min. **Loss of the suckle reflex** or inability to find the mare's udder can occur with **neonatal maladjustment syndrome**, sepsis or prematurity (*q.v.*).

A small percentage of foals will drip milk from the nose during the first few days of life with no associated pathology. Milk streaming from the nostrils following nursing is compatible with a **cleft palate** or dysphagia as a result of neonatal maladjustment syndrome, subepiglottic cyst, white muscle disease and occasionally prematurity (*q.v.*) and should be investigated. Inability to swallow milk adequately can lead to **aspiration pneumonia** and is evidenced by coughing or a rattling in the trachea after nursing.

Auscultation of the abdomen normally reveals borborygmi bilaterally. Abdominal distension indicates a mechanical or functional gastrointestinal obstruction. **Meconium**, the first feces a foal passes, should be passed in the first 24 h of life and appears as dark brown fecal balls compared with the softer light tan manure of a foal consuming mare's milk. Meconium is a combination of cellular debris, secretions and amniotic fluid swallowed by the foal during gestation and retained in the rectum and small colon. Ingestion of colostrum aids in the passage of meconium although many foals require an enema to prevent impaction. Passage of melena is associated with **clostridial enteritis** (*q.v.*) and **hypoxic–ischemic bowel injury**.

Distension of the small and/or large bowel results in generalized abdominal enlargement that is readily apparent due to the foal's thin body wall. Abdominal distension and colic may be associated with ileus, peritonitis, hypoxic gut damage, meconium impaction, or other intestinal obstruction such as intussusception and volvulus (*q.v.*).

Congenital defects affecting the gastrointestinal tract include atresia coli, atresia recti and atresia ani (*q.v.*). The all-white offspring of Overo spotted paint horses suffer from fatal **congenital ileocolonic aganglionosis**. This condition is termed Overo lethal white foal syndrome (OLWFS) (*q.v.*) and results in atrophy of the distal small intestine and colon. Affected foals retain meconium and demonstrate progressive colic beginning on Day 1 as a result of fatal functional intestinal obstruction. There is no cure for the disease, which is caused by a mutation in the endothelin B receptor. Genetic testing is available at the University of California Davis Veterinary Genetics Laboratory (http://vgl.ucdavis.edu). American Paint Horses with "frame Overo" coat pattern are heterozygous for the mutation.

UROGENITAL SYSTEM

Time to **first urination** is approximately 8 h. Colts generally urinate before fillies. Some colts normally do not drop the penis to urinate for the first week post partum due to a **persistent frenulum**. Urination should be observed to rule out a **patent urachus**.

The **umbilicus** should be small and dry. Swelling around the umbilical stump may be associated with hemorrhage, urine accumulation, hernia formation or

infection. Umbilical cords that have been ligated or cut seem more prone to secondary infection. Excessive use of **concentrated iodine** solutions also results in an increased incidence of **omphalitis** and premature sloughing of the stump, which increases the risk of a patent urachus (*q.v.*). An inflamed or moist umbilical stump suggests infection and/or urachal patency. The internal umbilical remnants (e.g. two umbilical arteries, umbilical vein and urachus) can be palpated through the abdominal wall in some recumbent foals if they are relaxed.

The best way to evaluate internal umbilical remnants is with transabdominal ultrasound using a 5–7.5 MHz transducer. The umbilical vein is followed from umbilical stump cranially along the ventral midline to the liver. The diameter of the umbilical vein should be <1.0 cm. The umbilical stump is visualized and the two umbilical arteries and urachus are traced caudally to the bladder. The combined view of the two arteries and urachus just caudal to the stump should have a diameter $<1.5 \times 2.5$ cm. Both arteries should be examined at their attachment alongside the bladder. Each artery should have a diameter <1.0 cm. Omphalitis usually affects more than one structure within the umbilicus. At the first sign of umbilical infection the foal should be started on **broad-spectrum antibiotics** and the umbilicus should be disinfected using dilute iodine or chlorhexidine solution.

Observing the foal urinate cannot completely rule out ruptured bladder (*q.v.*). Signs of **uroperitoneum** include depression, dysuria and abdominal distension with a fluid wave. Transabdominal ultrasonography provides a rapid, non-invasive method of confirming the diagnosis. Uroperitoneum produces large volumes of non-echogenic fluid within the peritoneal cavity and surrounding the "floating" intestines and collapsed bladder.

Urine specific gravity in the foal is low due to a high-volume liquid diet and incomplete development of the kidney, resulting in decreased concentrating capacity compared with the adult.

Testes may not be descended at birth but the scrotum should be palpated for scrotal hernia. An **inguinal hernia** describes herniation of bowel or omentum through the deep inguinal ring into the inguinal canal. A **scrotal hernia** describes hernial contents that have passed through both deep and superficial inguinal rings into the scrotum. Most hernias are indirect, which means the vaginal process or tunica vaginalis forms the hernial sac. Rupture of the tunica vaginalis results in a direct hernia.

The best way to **evaluate inguinal and scrotal hernias** is with the foal in lateral recumbency. If the hernial contents can be reduced by gently milking the intestines and omentum back into the abdomen, the hernia may close spontaneously within 3–6 mo. To reduce scrotal hernias, gentle tension is placed on the testicle and the hernial contents are milked back up into the abdomen. The owner should be shown how to manually reduce the hernia several times daily. Hernias require surgical closure if the hernia continues to enlarge, fails to close spontaneously within 3–6 mo, or is no longer reducible.

The vulva should be evaluated in fillies to detect congenital defects.

NERVOUS SYSTEM

The nervous system of the foal is still continuing to develop after birth; therefore results of a neurologic examination of the foal differ from those of an adult horse (*q.v.*). The foal should stand within 30 min to 2 h of birth.

Foals spend much of their time sleeping and at times can be difficult to rouse, but once awake they should be bright, alert and responsive to stimuli.

The **suckle reflex** is present by 20 min after birth. Foals will make a nodding motion of the head when searching for the udder. When restrained, a foal will have periods of strong body tone interspersed with periods of sudden relaxation of all four limbs causing him to flop up and down. Head and neck carriage are upright and angular.

Healthy foals stand with an erect, angular head and neck carriage and a base-wide stance. Gait and limb movements are often exaggerated and limb reflexes are hyper-reflexive. When recumbent, foals have strong resting extensor tone and a crossed extensor reflex is present when a withdrawal reflex is elicited for up to 1 mo of age.

Hypotonia, seizures and hyperesthesia are often associated with **hypoxic–ischemic encephalopathy**. Jitteriness is a sign of mild hypoxia. More severe hypoxia results in progressive hypotonia. Such foals are more difficult to arouse from sleep. With more global CNS hypoxic–ischemic damage foals exhibit signs of grand mal seizures followed by periods of post ictal stupor. Septic meningitis is a less common cause of seizures. Affected foals display concurrent signs of sepsis including mucous membrane and scleral injection, depression and tachycardia.

Congenital defects of the brain and spinal cord include cerebellar abiotrophy, occipito-atlanto-axial malformation, hydrocephalus, hydrencephaly and hypomyelinogenesis (*q.v.*).

OPHTHALMIC SYSTEM

Although foals have adequate vision at birth, a consistent **menace response** may be absent during the first week of life. Pathologic causes of an absent menace response include cerebral edema associated with birth asphyxia, septic optic nerve neuritis and ocular defects such as detached retina and optic nerve hypoplasia (*q.v.*).

A **pupillary light response** is present unless the foal's pupils are dilated due to excitement or stress. Fixed, dilated pupils may also be associated with severe midbrain swelling and are observed in comatose foals suffering from head trauma or severe hypoxic–ischemic encephalopathy.

Ventromedial strabismus may be present during the first 2 weeks of life. The hyloid artery remnant can be seen coursing from the optic disk to spread on the posterior lens capsule, sometimes resembling a spider web. Suture lines can be seen in the center of the lens and should not be mistaken for cataracts. The normal neonatal lens may appear **cloudy** for the first few weeks of life. Persistent **pupillary membranes** may be visible (e.g. lens to iris, iris to cornea) and can result in small pigment nests on the anterior lens capsule. These persistent strands are reported more often in Thoroughbreds. No treatment is required. The persistent strands break down within 12 mo.

Examination of the eyes should rule out other congenital ocular anomalies including entropion, retinal detachment or hemorrhage, cataracts and microphthalmia (*q.v.*). Acquired or congenital **entropion** (*q.v.*) is the most common congenital ocular anomaly. Acquired entropion is associated with self-trauma, dehydration or prematurity and the lack of periorbital fat. Entropion should

be corrected promptly before serious corneal ulceration and keratitis develop. Manual eversion of the eyelids several times daily followed by topical application of topical antibiotic or ocular lubricant may resolve mild cases. Another short-term treatment consists of SC injections of **procaine benzylpenicillin** (1 mL) into the lower eyelid. Most foals with entropion will require placement of vertical or horizontal mattress sutures in the lower eyelid to correct the problem. The affected eye should be stained with **fluorescein** (*q.v.*) to detect concurrent corneal ulceration.

Uveitis, hypopyon, hyphema and scleral injection (*q.v.*) may also be associated with septicemia. Nystagmus and retinal hemorrhages may be observed in hypoxic foals. Scleral hemorrhage is usually the result of birth trauma and can take several weeks to resolve.

MUSCULOSKELETAL SYSTEM

The musculoskeletal system of the newborn foal should be examined for **fractures** of the long bones, ribs or mandible as a result of periparturient trauma.

Signs of **septic arthritis** (*q.v.*) include lameness, heat, swelling or pain on palpation of the joints. Joints in the neonate have an increased range of motion compared with the adult. The sole of the front foot can touch the caudal triceps in many foals.

The most common angular limb deformities are **contracted tendons** and **flexor tendon/periarticular laxity**. In cases of contracted tendons (*q.v.*), the tendons are not truly contracted, but rather the effective functional length of the musculotendinous unit is too short to allow normal leg extension. Fetlock and carpal contractures are the most common. Radiographs should be taken of limbs with severe deformities to be certain primary bone malformation is not the cause.

Mild **flexural deformities** respond to physical therapy and weight bearing. Judicious use of analgesics helps encourage conservative exercise. Heavy support bandages, splints and **oxytetracycline therapy** (1–3 g IV diluted in 100–500 mL of saline q 24 h for a maximum of three treatments) are more aggressive forms of therapy. High dosages of oxytetracycline have been shown to produce tendon relaxation in neonates, although the precise mechanism is uncertain. During oxytetracycline therapy the foal's renal function should be monitored. **Splints** should be reset frequently to prevent pressure sores.

All forms of therapy are more effective if there is concurrent weight bearing on the affected limbs. Severely affected foals are in pain and are often unable to stand unassisted. These cases require **analgesics** (e.g. ketoprofen 1.1–2.2 mg/kg IV q 24 h; phenylbutazone 2.2 mg/kg IV, PO q 12–24 h), **anti-ulcer medication** (e.g. omeprazole 4 mg/kg PO q 24 h; ranitidine 8 mg/kg PO q 8 h; cimetidine 6.6 mg/kg IV q 6 h or 20 mg/kg PO q 6 h, famotidine 2.8 mg/kg PO q 24 h) and assistance when nursing. Rupture of the lateral extensor tendons may complicate management of forelimb contractures.

Tendon laxity, if mild, can be treated conservatively with restricted exercise on good footing. Most foals have mild laxity that improves during the first 48–72 h following delivery. More severe cases benefit from shoes with heel

extensions. Affected foals should have restricted exercise until the soft tissue laxity improves. Excessive exercise and fatigue on weak tendons can result in soft tissue trauma and sesamoid bone fractures (*q.v.*).

Angular limb deformities (*q.v.*) may occur as a result of impaired cartilage nutrition due to abnormal cartilage thickening. If uneven bone growth occurs, deviation of the normal leg axis results. Anything that produces uneven pressure across growth plates can cause angular limb deformities. Such stresses include joint laxity, in utero malpositioning, excessive trauma due to large body size, excessive activity, impaired cuboidal bone ossification or opposite limb lameness. Deformities may be present at birth or acquired shortly thereafter. Most foals are born with mild carpal valgus conformation and subtle tendon laxity that self-correct within the first week of life.

CLINICAL PATHOLOGY

Good restraint is essential when obtaining a blood sample from the foal in order to prevent vessel trauma and decrease stress. The jugular veins are the largest accessible veins in the foal; however, the cephalic and saphenous veins are also common sites for venepuncture. The site should be prepared with alcohol prior to routine venepuncture. Sampling for blood cultures is a sterile procedure requiring aseptic preparation of the skin.

Sites for **arterial blood gas** sampling include the great metatarsal, brachial, femoral and facial arteries. Due to risk of severe hematoma formation, sampling from the carotid arteries should be reserved for those foals in which peripheral pulses are too weak to obtain a sample elsewhere. Once the artery has been identified by pulse palpation, the site should be prepared with an antiseptic solution. Blood should be drawn into a heparinized syringe and all air bubbles removed. The sample should be analyzed immediately or sealed and placed in an ice bath. The sample can be stored in this way for up to 5 h without significant changes in PaO_2. After the needle is withdrawn, pressure is applied to the artery for 3 min to prevent hematoma formation.

Reference ranges for hematology, biochemistry and blood gas values are presented in Tables 14.5–14.7.

If there is any suspicion about a newborn foal's well-being, the following database should be obtained: packed cell volume (PCV), total protein concentration, white blood cell count and differential, fibrinogen concentration and serum concentrations of IgG, creatinine and glucose. The use of **portable analyzers** has made stall-side determination of IgG, glucose, creatinine and fibrinogen concentrations easy, fast, accurate and affordable.

Newborn foals are born with an average PCV between 39% and 48%. The PCV decreases during the first 24 h as a result of colostrum ingestion, the osmotic effect of absorbed colostral proteins and blood volume expansion. PCV is affected acutely by **hydration status** and blood loss or destruction. Poor nursing behavior quickly results in dehydration and an increase in PCV. A low PCV accompanied by icterus and hemoglobinuria is indicative of hemolysis (e.g. **neonatal isoerythrolysis**, *q.v.*) or **disseminated intravascular coagulation** (DIC) associated with sepsis. A low PCV is also observed following **umbilical cord hemorrhage**. Decreased red cell production causes slower,

Table 14.5 Normal clinical chemistry values for neonatal full-term foals

	1 day of age	7 days of age
Glucose (mg/dL)	121–233	121–192
Blood urea nitrogen (mg/dL)	9–40	4–20
Creatinine (mg/dL)	1.2–4.3	1.0–1.7
Total bilirubin (mg/dL)	1.3–4.5	0.8–3.0
Conjugated bilirubin (mg/dL)	0.3–0.7	0.3–0.7
Unconjugated bilirubin (mg/dL)	1.0–3.8	0.5–2.3
Cholestrol (mg/dL)	110–562	139–445
Triglycerides (mg/dL)	30–193	30–239
Albumin (g/dL)	2.5–3.6	2.7–3.4
Total globulin (g/dL)	1.5–4.6	1.6–3.9
Alkaline phosphatase (IU/L)	861–2671	137–1169
Glutamyl transferase (IU/L)	18–43	14–164
Sorbitol dehydrogenase (IU/L)	0.6–4.6	0.8–8.2
Aspartate aminotransferase (IU/L)	146–340	237–620
Alanine transaminase (IU/L)	0–49	4–50
Creatinine kinase (IU/L)	40–909	52–143

Reproduced with permission from Bauer, J.E. (1986) Normal blood chemistry values, in Koterba, A.M., Drummond, W.H., Kosch, P.C. (eds) Equine Clinical Neonatology. *Lea & Febiger, Philadelphia, pp. 602–614.*

Table 14.6 Normal serum electrolyte concentrations for neonatal full-term foals (mean ± 2 SD)

	1 day of age	7 days of age
Na^+ (mEq/L)	141 ± 18	142 ± 12
K^+ (mEq/L)	4.6 ± 1.0	4.8 ± 1.0
$C1^-$ (mEq/L)	102 ± 12	102 ± 8
TCO_2 (mEq/L)	27 ± 6	28 ± 4
HPO^{4-} (mg/dL)	5.6 ± 1.8	7.4 ± 2.0
Ca^{2+} (mg/dL)	11.7 ± 2.0	12.5 ± 1.2
Mg^{2+} (mg/dL)	2.4 ± 1.8	2.0 ± 0.6

Reproduced with permission from Bauer, J.E. (1986) Normal blood chemistry values, in Koterba, A.M., Drummond, W.H., Kosch, P.C. (eds) Equine Clinical Neonatology. *Lea & Febiger, Philadelphia, pp. 602–614.*

Table 14.7 Normal arterial blood gas values for neonatal full-term foals in lateral recumbency (mean ± SEM)

	2 hours of age	7 days of age
PO_2 (mmHg)	66.5 ± 2.3	86.9 ± 2.2
PCO_2 (mmHg)	47.7 ± 1.7	46.7 ± 1.1
pH	7.362 ± 0.012	7.374 ± 0.014
Base excess (mmol/L)	0.9 ± 1.0	1.4 ± 0.9
Bicarbonate (mmol/L)	25.0 ± 0.9	25.6 ± 0.8

Reproduced with permission from Stewart, J.H., Stewart, R., Rose, J., Barko, A.M. (1984) Respiratory studies in foals from birth to seven days old, Equine Veterinary Journal *16: 323–328.*

subtle changes in PCV. Premature foals tend to have a slightly lower PCV at birth. An elevated PCV >50% may be associated with chronic in utero hypoxia resulting in **neonatal polycythemia**.

Presuckle total protein (TP) concentration varies between individuals from 3.5 to >5.0 g/dL. Total protein concentration increases following colostrum ingestion due to immunoglobulin absorption and during dehydration. Without knowing the presuckle values, it is impossible to use TP to measure IgG absorption. Low TP values <3.5 g/dL are suggestive of a **failure of passive transfer** (FPT). Hypoproteinemia may also be associated with protein loss from the gastrointestinal and urinary systems.

Neutrophil numbers increase during late gestation to an average of 5000–6000/μL at birth. Immediately after birth a stress-induced cortisol release results in an increase in neutrophil numbers. Neutropenia (<2000/μL) is associated with septicemia and is accompanied by toxic changes within the neutrophils and increasing numbers of bands. At birth the neutrophil–lymphocyte ratio (N:L) should be >2–3. An inversion of the N:L ratio, without signs of sepsis, is compatible with prematurity and an underdeveloped hypothalamus–pituitary–adrenal axis. Lymphocyte counts may be <1000/μL in newborns, but should increase within the first few days of life. Persistent lymphopenia is a sign of **combined immune deficiency** (CID), severe stress, bacteremia or viremia.

Fibrinogen concentration increases slowly over 2–3 days following an inflammatory insult and reflects chronic rather than acute infection. Most healthy foals have values <200 mg/dL. Hyperfibrinogenemia at birth suggests in utero sepsis.

Healthy foals that have absorbed adequate colostrum have serum IgG concentrations well above 800 mg/dL within the first 18–24 h of life. IgG <200 mg/dL is termed failure of passive transfer (FPT). IgG between 200 and 400–800 mg/dL is considered partial FPT.

In the newborn foal **creatinine concentration** serves as a crude estimate of placental function pre partum. Neonatal azotemia has been associated with abnormal placentas and the birth of hypoxic or septic foals. Newborn foals should have a creatinine concentration <3.5–4.0 mg/dL.

Foals are born with relatively low blood **glucose** concentration (40–80 mg/dL). **Presuckle hypoglycemia** (glucose <35 mg/dL) immediately following birth is suggestive of **placental dysfunction** and hypoxia. Glucose concentration should increase in normal foals following birth as a result of colostrum ingestion and insulin release. Persistent hypoglycemia during the first 48 h post partum suggests immature insulin response and marginal glucose reserves. **Hyperglycemia** (glucose >180–200 mg/dL) is associated with hypoxia-induced pancreatic endocrine dysfunction, sepsis-induced release of glucagon, catecholamines and cortisol resulting in peripheral insulin resistance.

COMMON FOAL DISORDERS

MECONIUM IMPACTION

Meconium (*q.v.*) is composed of swallowed amniotic fluid, cellular debris and intestinal secretions and is dark brown to black in color. Due to the firm and

tenacious consistency of this material even normal foals must strain to pass the first manure. Meconium passage normally occurs within 24–36 h post partum and is followed by soft, tan-colored, **milk feces**.

Etiology

There is an increased incidence of **meconium impaction** in colts due to their narrow pelvic canal. Impaired gastrointestinal motility associated with asphyxia, sepsis or dysmaturity (*q.v.*) predisposes to meconium retention. Prolonged recumbency and dehydration are additional risk factors.

Clinical signs

Clinical signs associated with **meconium impaction** include tenesmus, frequent tail flagging, colic and loss of nursing vigor. If the impaction persists, abdominal distension develops contributing to the foal's discomfort. During episodes of **severe tenesmus**, the umbilicus may begin to bleed, the urachus may reopen and drip urine, and rectal prolapse (*q.v.*) may occur.

The diagnosis is frequently made based on a history of straining to defecate unsuccessfully, digital rectal evaluation and response to enema administration. Certain cases may require abdominal radiography, with or without a barium enema, to demonstrate the fecal impaction. Gas and/or fluid frequently accumulate proximal to the site of obstruction. **Transabdominal ultrasonography** has been used to identify firm fecal material within the distal colon. Other conditions that may be confused with meconium impaction include uroperitoneum, urachitis, cystitis, congenital defects such as atresia coli, and other causes of intestinal obstruction and colic such as large bowel volvulus, foreign body obstruction and intussusception (*q.v.*).

Treatment

Mild impactions respond to **gravity enema** administration using 0.5–1.0 L warm, soapy water or water mixed with rectal lubricant. Solutions containing docusate sodium should be used with extreme caution, due to its irritation of rectal and colonic mucosa. **Retention enemas** using 150 mL of a 4% solution of acetylcysteine (6 g acetylcysteine powder in 150 mL water) and administered through a cuffed urinary Foley catheter (left in place for 20–40 min) help dissolve refractory impactions. Retention enemas can be repeated several times without adverse affect.

If the impaction persists, oral laxatives can be administered in conjunction with oral fluids. Mineral oil (120–240 mL) administered via nasogastric tube is the safest and most commonly used laxative. Castor oil (15–30 mL) and docusate sodium (10–15 mL) should both be used cautiously due to their **extremely irritant** nature. Severe gastroenteritis has been induced in foals by misuse of both of these agents. **Increased exercise** is also beneficial. In chronic cases of meconium impaction, aggressive IV fluid therapy should be initiated. Only rare cases will require surgical intervention.

PATENT URACHUS

Normally the urachus closes spontaneously at birth or shortly thereafter and atrophies to become a scar on the apex of the bladder. The urachus may fail to

close following birth (**congenital patent urachus**) or may reopen post partum (**acquired patent urachus**). As long as urachal patency persists it represents a source of irritation and a potential route of infection.

Etiology

Congenital patency can result from urachal over-distension secondary to torsion of the umbilical cord in utero or during parturition. **Acquired patency**, the most common form, is usually associated with inflammation of the umbilicus and coincides with sloughing of the necrotic umbilical stump. Factors associated with acquired urachal patency include prolonged recumbency associated with urine scalding and umbilical irritation, ligation or cutting of the umbilical cord, and any neonatal condition producing increased intra-abdominal pressure such as tenesmus associated with constipation or dysuria due to cystitis, urachitis, urachal diverticulum, uroperitoneum or bladder catheterization.

Clinical signs

A patent urachus (*q.v.*) often results in a thicker than normal umbilicus that remains moist due to continuous or intermittent discharge of urine. The umbilicus may be warm and painful if inflammation is present. A 7.5 MHz ultrasonographic transducer (linear ray or sector scan) can be used to image a patent urachus as a fluid-filled structure located along the ventral midline next to the umbilical arteries. Communication between the urachus and bladder apex is best seen in the longitudinal view. Positive contrast radiography can also be used to demonstrate some urachal disorders.

Treatment

Local cautery of the urachus using silver nitrate applicators and 2% iodine aids closure in mild, uncomplicated cases. If tenesmus due to constipation or dysuria associated with cystitis (*q.v.*) is delaying urachal closure due to transient bouts of increased abdominal pressure, then these conditions must be treated concurrently. Constipation can be treated with enemas and laxatives.

Straining to urinate due to cystitis can be relieved using **phenazopyridine** (4 mg/kg PO q 8–12 h), a systemically administered diazo dye with local anesthetic effects on bladder mucosa.

If transabdominal ultrasonography reveals significant omphalitis complicated by focal areas of abscessation and/or marked urachal enlargement, then surgical resection of the umbilical remnants is indicated. Until the urachus closes or the umbilical remnants are resected the foal should be maintained on **broad-spectrum antibiotics**.

HYPOGAMMAGLOBULINEMIA

Overwhelming bacterial infection is one of the leading causes of neonatal foal mortality. One of the risk factors for septicemia is **hypogammaglobulinemia**. Although immunocompetent at birth, foals are immunologically naïve and rely on passive transfer of colostral immunoglobulins and non-specific host defense mechanisms for protection against infection during the first 2 mo of life. Complete failure of passive transfer (FPT) is generally defined as serum

IgG concentrations ≤200 mg/dL. Partial FPT is defined as serum IgG levels between 200 and 800 mg/dL.

Etiology

Foals are born virtually **agammaglobulinemic** due to the diffuse epitheliochorial placenta of the mare that prevents maternofetal transfer of antibodies. The mare produces colostrum containing predominantly IgG during the last 2–4 wk of gestation. The foal absorbs colostral immunoglobulins via specialized epithelial cells within the small intestine. Absorption declines rapidly within 12 h of birth and **ceases completely** 24–36 h post partum. Most normal newborn foals attain serum IgG concentrations >800 mg/dL following colostrum ingestion.

The incidence of FPT is estimated to be between 3% and 25% and is affected by a variety of management practices. Causes of FPT include: (1) poor quality colostrum; (2) failure to produce adequate volumes of colostrum; (3) premature lactation; (4) failure of the newborn foal to ingest adequate colostrum within the first 12–24 h post partum; (5) ineffective intestinal absorption of IgG; (6) increased protein catabolism associated with sepsis.

Poor quality colostrum may be associated with advancing maternal age, maternal obesity, individual or breed variation, season and climate, poor prenatal maternal vaccination, premature delivery, premature lactation or agalactia. Failure to ingest adequate amounts of colostrum within the first 24 h of life may be due to neonatal weakness, musculoskeletal problems (e.g. tendon laxity, tendon contracture), abnormal behavior (e.g. hypoxic–ischemic encephalopathy), or foal rejection by the dam.

Peak colostrum absorption occurs within the first 10 h of life. Early feeding of colostrum not only ensures optimal IgG absorption, but may reduce the risk of infection from ingested pathogens by accelerating gut closure. Foals suffering from hypothermia, hypotension, severe hypoxia, prematurity or intestinal disease should not be expected to have normal gut function. Such foals require a **plasma transfusion** to ensure adequate IgG levels (*q.v.*).

Although most studies strongly suggest that FPT is a major predisposing factor for neonatal sepsis, there is evidence to suggest that on well-managed stud farms serum IgG levels in foals are not related to the incidence or severity of disease or to neonatal survival rates. The observation that many septic foals are hypogammaglobulinemic does not necessarily clarify the issue. Low serum IgG levels may predispose to infection or may be the result of increased protein catabolism associated with overwhelming sepsis.

The clinical significance of FPT must be determined on an individual basis and take into account environmental and management factors. Few would argue that foals at serious risk for sepsis or already showing signs of infection benefit from having serum IgG concentrations in the normal range (i.e. IgG >800 mg/dL). IgG supplementation is recommended for any foal with a serum IgG <200 mg/dL regardless of its health status or environment.

If the foal's IgG is between 200 and 800 mg/dL, **IgG supplementation** (*q.v.*) should be considered if one or more of the following conditions exist:

1. Gestation length <320 days or signs of prematurity/dysmaturity

2. Difficult delivery (e.g. dystocia, premature placental separation, meconium staining)
3. Grossly abnormal or heavy placenta (>11% foal's BW)
4. High environmental stresses including overcrowding and poor farm hygiene
5. Anticipated transportation off the farm within 7–10 days of foaling
6. Failure to stand and nurse within 3 h of delivery
7. Abnormal physical examination within 24 h of birth; significant abnormalities include generalized weakness, injected mucous membranes, poor suckle, severe angular limb deformities, enlarged umbilicus, patent urachus, colic, meconium retention, increased respiratory effort or other signs of localized infection.

Diagnosis

Serum IgG levels are routinely evaluated in foals between 12 and 24 h of age. Commonly used tests for **IgG assessment** include zinc sulfate turbidity, latex agglutination, glutaraldehyde precipitation and ELISA.

Treatment

If FPT is diagnosed within the first 18 h of life, **additional colostrum** can be administered. Ideally, a foal should receive at least 1 L of good quality colostrum. Oral administration of concentrated or lyophilized **equine IgG products** results in wide variations in serum immunoglobulin concentrations. **Bovine colostrum** provides some protection, but will not protect against exclusively equine pathogens. **Equine plasma** may be administered orally within the first 18–24 h of life or IV at any age. The recommended plasma dose depends on the foal's body weight, the severity of hypogammaglobulinemia, the IgG concentration in the plasma product, and whether or not the foal is already septic. The administration of 20 mL/kg of normal equine plasma (1 L for a 45 kg foal) routinely raises serum IgG concentration by 200 mg/dL in a healthy foal when given IV. Oral administration of plasma results in variable immunoglobulin absorption.

Clinically ill foals experience **increased IgG catabolism** and require additional plasma. In addition to providing antibody, plasma provides electrolytes, complement, opsonins, increased oncotic pressure and volume expansion, and it improves neonatal neutrophil function.

If equine plasma is not commercially available, the ideal donor is an adult horse, preferably a gelding, that has been **blood typed** (*q.v.*) and found to be negative for isoantibodies to the major equine RBC blood types (particularly A and Q alloantigens). Plasma should be administered at **room temperature** using a blood administration set and delivered at a rate of 1 L over 1–3 h. The foal should be monitored for a variety of transfusion reactions, examples of which are listed in Table 14.8.

The incidence of FPT can be reduced by observing periparturient mares closely for adequate mammary gland development and premature lactation. Good quality colostrum should be thick and sticky with a specific gravity >1.060 as measured on an equine Colostrometer.

Table 14.8 Types of immediate transfusion reactions

Type of reaction	Signs	Cause	Treatment
Acute hemolysis	Hemoglobinemia; hemoglobinuria	Incompatibility between donor plasma and recipient's RBCs	Discontinue transfusion
Non-hemolytic, febrile reaction	Fever, chills	Response to donor protein, antigens or WBC fragments	Antipyretics
Allergic reactions	Urticaria	Recipient's reaction to soluble antigens in donor's plasma	Slow transfusion; antihistamines
Anaphylactic reaction	Respiratory distress; hypotension; shock		Stop transfusion; epinephrine/adrenaline
Circulatory overload	Pulmonary edema; hypertension; cardiac failure	Volume overload	Slow or stop transfusion; diuretics

PERI PARTUM ASPHYXIA (NEONATAL MALADJUSTMENT SYNDROME)

Peri partum asphyxia affects multiple organ systems. Unfortunately, the popularized name, **neonatal maladjustment syndrome** (NMS), focuses attention on the more clinically obvious behavioral and neurologic signs associated with hypoxia-induced CNS damage (*q.v.*).

Asphyxia during late pregnancy and/or delivery causes a decrease in tissue perfusion and oxygenation in the newborn foal and results in a spectrum of clinical signs that include neurologic deficits ranging from hypotonia to grand mal seizures, gastrointestinal disturbances ranging from mild ileus and delayed gastric emptying to severe, bloody diarrhea and necrotizing enterocolitis (NEC) and renal compromise accompanied by varying degrees of oliguria.

Based on the neurologic deficits that include loss of affinity for the dam, seizures, abnormal vocalization and aimless wandering, affected foals have been called "dummies", "convulsives", "barkers", and "wanderers". NMS is a common term used to describe this condition. **Hypoxic–ischemic encephalopathy** (HIE) is a more precise medical term describing the CNS disturbances that include edema, necrosis and occasional hemorrhage.

Etiology

Asphyxia is caused by impaired oxygen delivery to cells and usually results from a combination of hypoxemia and ischemia. Other potential metabolic derangements include hypercarbia and metabolic acidemia. Fetal compensatory mechanisms to increasing asphyxia include bradycardia, decreased oxygen consumption, anaerobic glycolysis and circulatory redistribution resulting in increased blood flow to the heart, adrenals and brain and diminished flow to lungs, gut, spleen, kidneys, liver and muscle. The nature and extent of tissue

injury depend on the age of the neonate (full term or premature), and the duration and severity of asphyxia (acute or chronic, partial or complete).

An important mediator of ischemic tissue damage is the fast excitatory neurotransmitter, **glutamate**. At high extracellular concentrations, glutamate acts as a neurotoxin and mediates opening of ion channels that permit sodium to enter cells followed by an influx of chloride ions and water resulting in osmotic lysis and immediate neuronal death. Glutamate also mediates delayed cell death by provoking calcium influx through depolarization-induced opening of calcium channels and by direct stimulation of N-methyl-D-aspartate (NMDA) receptors that open additional calcium channels. High intracellular levels of free calcium result in activation of enzyme systems, generation of free radicals, and impaired mitochondrial function resulting in delayed neuronal death.

The wide variation in **CNS damage** associated with peri partum hypoxia illustrates how the type of asphyxia and age of fetus influence the final outcome. Mature fetuses dying of severe asphyxia demonstrate hemorrhagic softening involving primarily the cerebral cortex and hemispheral white matter. Immature fetuses dying of asphyxia show damage involving structures deep within the hemispheres. Partial prolonged asphyxia produces injury primarily in the hemispheres accompanied by significant brain edema. Acute, total asphyxia damages the brainstem and spinal cord and is less commonly associated with brain swelling.

Chronic hypoxia associated with placental insufficiency produces fetal growth retardation in a fashion reflecting redistributed blood flow. The brain is spared, but other organ systems are not, resulting in a small, runted fetus with a relatively large head. This disproportional growth is typical of IUGR. Chronic hypoxia stimulates fetal adrenals and enhances maturation of many fetal organs, including the lungs.

Perinatal asphyxia may be associated with a rapid, seemingly uncomplicated delivery of a term foal, dystocia, premature placental separation or Cesarean section. Peri partum asphyxia may not alter the delivery process itself, making it difficult for owners to understand how an outwardly normal birth could produce an abnormal foal. Specific peri partum causes of neonatal asphyxia are listed in Box 14.5.

Clinical signs

Pre partum, transabdominal ultrasonography can be used to evaluate fetal response to asphyxia by observing the following biophysical variables: fetal movement, breathing and heart rates, and fetal amniotic fluid volume. Chronic hypoxia can produce decreased renal blood flow, decreased fetal fluid production, depressed fetal limb and respiratory movements and bradycardia. Acute asphyxia may produce transient bouts of tachyarrhythmias. Post partum, a modified **APGAR score** (Table 14.9) can be used to evaluate severity of fetal stress and birth asphyxia.

Peri partum hypoxia produces a wide range of clinical signs, according to the organ system(s) involved. Mild hypoxia causes jitteriness and hyperexcitability and may go unrecognized. Moderate hypoxia results in stupor, somnolence, lethargy and hypotonia that may be accompanied by epileptiform

Box 14.5 Peri partum conditions associated with neonatal foal asphyxia

Maternal factors
- Endotoxemia
- Severe hypotension, shock
- Severe anemia
- Hypoproteinemia
- Abdominal surgery/general anesthesia
- Hydrops
- Prepubic tendon rupture
- EHV-1 infection
- Fescue toxicosis

Placental factors
- Placentitis
- Placental insufficiency
- Small placenta
- Placental vasculitis, edema
- Placental thrombosis, infarction
- Umbilical cord complications

Periparturient factors
- Premature placental separation
- Dystocia, prolonged labor
- Induction of labor
- Cesarean section
- Early umbilical cord rupture

Fetal/neonatal factors
- Congenital cardiac anomalies
- Surfactant dysfunction
- Severe pulmonary disease
- Persistent fetal circulation
- Twinning

seizures and episodes of extensor rigidity and opisthotonus during recumbency. Moderate hypoxia is also associated with loss of suckle, dysphagia, decreased tongue tone, odontoprisis, central blindness, mydriasis, anisocoria, nystagmus and head tilt. Limb deficits and generalized spasticity are less common.

Premature foals exposed to moderate hypoxia are more likely to experience "subtle seizures" characterized by paroxysmal events including eye blinking, eye deviation, nystagmus, pedaling movements, a variety of oral–buccal–lingual movements such as intermittent tongue protrusion, sucking behavior, purposeless thrashing, and other vasomotor changes such as apnea, abnormal breathing patterns and changes in heart rate. Tonic posturing is another subtle seizure activity characterized by symmetric limb hyperextension or flexion and is often accompanied by abnormal eye movements and apnea. Severe

Table 14.9 Modified APGAR scoring system

Sign	0	1	2
1. Heart rate	Absent	<60 bpm, irregular	>60 bpm, regular
2. Respiratory effort	Absent	Slow, irregular	<30 breaths/min, regular; can whinny
3. Muscle tone	Limp, lateral recumbency	Some voluntary flexion of extremities	Active motion; sternal recumbency
4. Reflex irritability			
Nasal stimulation	No response	Grimace	Sneeze/cough
Ear tickle	No response	Weak ear flick	Ear flick/head shake
Thoracolumbar stimulation	No response	Head/neck motion	Head/neck/limb motion

Interpretation of score results
Score 7–8: minimal asphyxia; no intervention required.
Score 5–6: mild asphyxia; stimulate, rub, extend limbs; suction.
Score 3–4: moderate asphyxia; respiratory acidosis; positive pressure ventilation; intravenous fluids.
Score ⩽2: severe asphyxia; respiratory and metabolic acidosis; positive pressure ventilation; aggressive circulatory support; bicarbonate administration.

hypoxia results in marked CNS depression, coma, and loss of central regulation of respiration, blood pressure and temperature, leading to death.

Renal dysfunction is common, but mild signs such as transient oliguria may be easily overlooked. Hypoxic **gut damage** produces colic, ileus, abdominal distension, gastric reflux, ulceration and diarrhea. **Cardiopulmonary complications**, including surfactant dysfunction, pulmonary hypertension, myocardial infarcts and persistent fetal circulatory patterns, can result in respiratory distress and cardiac failure. **Endocrine disorders** are difficult to identify but involve damage to the adrenal glands, pancreas and parathyroids. Hepatocellular necrosis and biliary stasis may also occur accompanied by **clinical jaundice**.

Few laboratory results are pathognomonic for birth asphyxia. Hematology reveals a normal or stress leukogram. Many foals suffer FPT due to **inadequate colostrum ingestion**. A mixed metabolic/respiratory acidosis develops in response to shock, poor perfusion, increased anaerobic metabolism and respiratory dysfunction. Elevated concentrations of **liver enzymes** reflect hepatocellular necrosis. Renal dysfunction produces hyponatremia, hypochloremia and azotemia. Marked elevations in **serum creatinine** concentrations immediately post partum have also been associated with placental dysfunction rather than primary neonatal renal disease. Elevated **serum creatinine kinase** concentrations are associated with ischemic muscle damage. Severe respiratory compromise produces hypoxemia and hypercapnia. Clinicopathologic conditions associated with peri partum asphyxia are summarized in Table 14.10.

Differential diagnoses for a weak, lethargic foal believed to be suffering from asphyxia should include septicemia, prematurity/dysmaturity, and other metabolic derangements such as hypoglycemia, hyper- or hyponatremia, and hypocalcemia (*q.v.*).

Treatment

Anticonvulsive therapy is crucial to control seizures in order to prevent recurrent episodes of CNS ischemia and hypoxia and to reduce the risk of neonatal

Table 14.10 Clinicopathologic conditions associated with peri partum hypoxia

Organ system	Sign	Lesion
CNS	Hypotonia/hyperesthesia, abnormal behavior, apnea, seizures, coma	Cerebral edema; ischemic necrosis; occasional CNS hemorrhage
Renal	Anuria, oliguria, generalized edema, azotemia, hyponatremia, hypochloremia	Tubular necrosis
Gastrointestinal	Colic, ileus, abdominal distension, diarrhea (±blood), gastric reflux	Ischemic necrosis, necrotizing enterocolitis, ulceration
Respiratory	Respiratory distress: tachypnea, dyspnea, rib retractions, decreased tidal volume; apnea, hypoxemia, hypercapnia, respiratory acidosis	Hyaline membrane formation, atelectasis, meconium aspiration, pulmonary hypertension
Cardiac	Arrhythmias, murmurs, hypotension, generalized edema, weak peripheral pulses, hypoxemia	Persistent fetal circulation, myocardial infarcts, valve insufficiency
Hepatic	Icterus, hyperbilirubinemia, elevated hepatocellular and biliary enzymes	Hepatocellular necrosis, biliary stasis
Endocrine		
Adrenals	Weakness; low serum cortisol	Necrosis, hemorrhage
Parathyroid	Hypocalcemia	Necrosis, hemorrhage

self-trauma. **Diazepam** (0.1–0.2 mg/kg IV) is used initially to stop seizures quickly because of its rapid onset of action but repetitive doses should be avoided to reduce the risk of respiratory depression. Due to its short duration, diazepam should be followed by **phenobarbital** (2–10 mg/kg slowly IV q 8–12 h) to control severe or recurrent seizures. Phenobarbital should be given slowly to minimize respiratory depression. Foals receiving phenobarbital should have their body temperature, blood pressure and respiratory rate monitored. If diazepam and phenobarbital are not available, **pentobarbital** (3–10 mg/kg IV to effect) can be used.

Naloxone (0.01–0.02 mg/kg IV) has been used as an opiate antagonist to diminish CNS depression. **Thiamine** (10–20 mg/kg q 12 h) can be added to the IV fluids to help preserve aerobic brain metabolism. Thiamine deficiency has been associated with intracellular and extracellular edema and neuronal cell death due to glutamate-induced and NMDA receptor mediated excitotoxicity. Xylazine should be avoided since it can cause transient hypertension with exacerbation of CNS hemorrhage. Acepromazine should be avoided also since it lowers the seizure threshold.

Cerebral edema occurs in some HIE foals. IV DMSO (0.5–1.0 g/kg) is administered as a 20% solution to help reduce brain swelling and intracranial pressure as well as to decrease inflammation and platelet aggregation. DMSO should be used cautiously in hypotensive neonates. The osmotic diuretic, **mannitol** (0.25–2.0 g/kg given as a 20% solution IV over 15–40 min), has been used to treat cerebral edema and to scavenge free radicals. To avoid exacerbation of cerebral edema, IV fluid administration should be conservative and **fluid balance monitored** in anuric or oliguric patients. Low doses of magnesium

sulfate administered as a continuous infusion have been used to reduce the hypoxia-induced increase in oxygen free radical generation. Other medications used for their antioxidant properties include ascorbic acid (vitamin C) and alpha-tocopherol (vitamin E).

Controversy surrounds the benefits of **glucose administration** to neonates during the early post-hypoxic period. Possible benefits include a reduced incidence of CNS infarction, attenuated brain damage, and some degree of neuroprotection by stimulating insulin release and reducing glycolysis, free radical formation and glutamate-mediated injury. However, hyperglycemia can augment hypoxic brain injury. Therefore, it is best to avoid extremes in glucose concentration.

Fluid therapy should be monitored closely to avoid over-hydration and hyper- and hypo-osmolar states. Low levels of **dopamine** (1.0–5.0 μg/kg/min) stimulate dopaminergic receptors and improve renal blood flow and urine production. Moderate doses stimulate β_1 receptors to increase heart rate and strength of contraction, which help improve renal perfusion by correcting mild cases of hypotension. High doses of dopamine compromise renal and gastrointestinal perfusion and should be avoided. **Furosemide** (0.25–0.5 mg/kg IV q 30–60 min administered during dopamine infusion or constant rate infusion [CRI] 0.25–2.0 mg/kg/h) works synergistically with dopamine to promote diuresis. Serum electrolytes should be monitored during diuretic therapy.

Ileus associated with hypoxic gut damage can result in bowel distension and colic (*q.v.*). To reduce the risk of **necrotizing enterocolitis (NEC)**, asphyxiated foals should have enteral feeding withheld until intestinal motility has returned. Reassuring signs include manure passage, normal borborygmi and stable vital signs (temperature, blood pressure). **Enteral feeding** should be started cautiously with fresh mare's milk or colostrum. Foals with severe gastrointestinal dysfunction should have enteral feeds withheld and should be started on **parenteral nutrition** using a hypertonic solution containing dextrose, amino acids and lipid emulsion. Since intestinal ischemia may predispose to **ulceration** (*q.v.*), H_2 blockers (cimetidine, ranitidine), proton pump inhibitors (omeprazole), or cytoprotective agents (sucralfate) are recommended.

Mild to moderate hypoxemia can be treated by increasing the amount of time the foal spends in **sternal recumbency** or **standing** and by administering modest flows of **humidified intranasal oxygen** (2–8 L per min). Foals suffering severe hypoxemia and hypercapnia (PaO_2 <40 mmHg, $PaCO_2$ >65 mmHg) require positive pressure ventilation.

Respiratory stimulants are used to treat periodic apnea and abnormally slow breathing patterns associated with central depression of the respiratory center. **Caffeine** (loading dose 10 mg/kg PO; maintenance dose 2.5–3.0 mg/kg PO q 24 h) is used most frequently to stimulate the respiratory neuronal activity and increase receptor responsiveness to elevated carbon dioxide concentrations. Overdosing with respiratory stimulants leads to excessive CNS, myocardial and gastrointestinal stimulation resulting in agitation, seizures, tachycardia, hypertension, colic and diarrhea. Caffeine is the safest of the methylxanthines to use.

Maladjusted foals (*q.v.*) are at increased risk for FPT due to their abnormal nursing behavior. Serum IgG levels should be evaluated to ensure adequate

passive transfer of colostral antibodies. The foal's serum IgG should be >800 mg/dL by 18–24 h of age. If IgG <800 mg/dL, **colostrum** and/or **plasma** should be administered to treat hypogammaglobulinemia. Adequate nutrition must be provided until the foal is able to nurse normally from the mare.

It is reasonable to expect to see stabilization of CNS signs within the first 48–72 h following delivery followed by gradual improvement in neurologic signs within the first 3–5 days. Some foals may not regain the ability to nurse from the mare for 7–10 days or longer.

Treatment of the hypoxic foal must address all organ systems involved. A therapeutic plan designed to treat the variety of complications associated with hypoxic tissue damage is outlined in Box 14.6. Approximately 60–80% of foals affected with HIE recover.

Box 14.6 Therapeutic plan for hypoxia-induced disorders in foals

CNS dysfunction

- Seizure control: diazepam (0.11–0.44 mg/kg IV), phenobarbital (2–10 mg/kg IV q 12 h; monitor serum levels), pentobarbital (2–10 mg/kg IV)
- Avoid xylazine; causes transient hypertension and exacerbates CNS hemorrhage
- Avoid acepromazine; lowers seizure threshold
- IV DMSO (0.5–1.0 g/kg IV given as a 10–20% solution over 1–2 h; can repeat q 12 h); stabilizes membranes, prevents platelet aggregation, maintains vascular integrity, scavenges free radicals during reperfusion
- IV mannitol (0.25–1.0 g/kg IV over 15–20 min q 6–12 h); osmotic diuretic; contraindicated with cerebral hemorrhage
- Magnesium sulfate CRI: 50 mg/kg/h diluted to 1% and given slowly as a CRI over 1 h, then decreased to 25 mg/kg/h as a CRI for 24–48 h
- Ascorbic acid (vitamin C): 50–100 mg/kg/day; antioxidant
- Alpha-tocopherol (vitamin E): dose not established; 500 units PO/day has been recommended
- Thiamine: 10 mg/kg IV q 12 h; support cerebral metabolism

Renal dysfunction

- Monitor fluid in/urine out to avoid over-hydration and evaluate renal function
- Dopamine CRI (2–10 μg/kg/min); improves renal blood flow and urine output
- Furosemide CRI (0.25–2.0 μg/kg/h)
- Mannitol (0.25–1.0 g/kg IV q 6–12 h); osmotic diuretic
- Dobutamine CRI (2–10 μg/kg/min); use if cardiac dysfunction and hypotension are contributing to poor renal perfusion

Gastrointestinal dysfunction

- Nasogastric decompression; percutaneous large bowel trocarization
- Prokinetic drugs for delayed gastric emptying: erythromycin (2 mg/kg PO/IV q 6 h); metoclopramide (0.25–0.4 mg/kg slow IV infusion q 6 h); bethanechol (0.03 mg/kg SC q 8 h, 0.16–0.2 mg/kg PO q 8 h); do not administer prokinetic drugs if there is evidence of severe ischemic bowel damage or obstruction

Box 14.6 continues on page 823

Box 14.6 Therapeutic plan for hypoxia-induced disorders in foals [continued]

- Anti-ulcer medication: ranitidine (8–10 mg/kg PO q 6–8 h; 1–2 mg/kg q 8 h), cimetidine (20 mg/kg PO q 6 h; 6.6 mg/kg IV q 6 h), omeprazole (4 mg/kg PO q 24 h), antacids
- In cases of severe asphyxia, hypotension and hypothermia, delay enteral feeding until gut motility is restored; begin parenteral nutrition
- Broad-spectrum bactericidal antibiotics

Cardiac dysfunction

- Dopamine, dobutamine to treat systemic hypotension and reduced cardiac output (dopamine: 1–15 μg/kg/min CRI; dobutamine: 1–20 μg/kg/min CRI)
- Avoid over-hydration
- Diuretics (furosemide) to treat edema associated with cardiac failure (0.5–1.0 mg/kg IV)
- Digoxin (0.02–0.35 mg/kg PO q 24 h) if cardiac failure is evident

Secondary infection

- Colostrum
- IV plasma
- Broad-spectrum bactericidal antibiotics

Dehydration and poor nursing behavior

- Cautious fluid therapy: maintenance rate: 4–5 mL/kg/h
- IV dextrose: avoid hyperglycemia
- Enteral feeding: 10–25% of foal's BW per day of mare's milk, artificial replacer, or goat's milk
- Parenteral nutrition to replace or supplement enteral feeds if gut function is compromised

Respiratory function

- Mild hypoxemia: increase time foal spends in sternal recumbency or standing; intranasal, humidified oxygen at 2–10 L/min
- Moderate to severe hypoxemia/hypercapnia ($PaO_2 < 65$ mmHg, $PaCO_2 > 65$ mmHg): provide positive pressure ventilation
- Intratracheal surfactant administration to treat surfactant dysfunction
- Respiratory stimulants: caffeine (loading dose: 10 mg/kg PO; maintenance dose: 2.5–3.0 mg/kg PO q 24 h) to treat periodic apnea and improve diaphragmatic contractility

Prognosis is determined by duration and severity of clinical signs and quality of nursing care. Foals with the poorest prognosis develop septicemia, fail to show any signs of improvement in neurologic function within the first 5 days of life and remain comatose and difficult to arouse. Poor prognostic signs include refractory hypotension and oliguria, signs of severe brainstem damage including loss of thermoregulatory control and profound apnea, and seizures that persist past 5 days of age despite anti-convulsant therapy.

Rare, long-term CNS sequelae include unusual docility as adults, vision impairment, residual gait spasticity and recurrent seizures. Recovered foals usually show no residual neurologic deficits.

PREMATURITY

Prematurity suggests **curtailed gestational length** (⩽320 days) as the cause of fetal underdevelopment. Immaturity and dysmaturity imply an **abnormal intrauterine environment** (e.g. placentitis, hydrops, twinning, and placental insufficiency [*q.v.*]) that has resulted in retarded growth and/or development. Dysmature foals can have shortened, normal or prolonged gestation lengths. Some premature foals demonstrate comparable immaturity of all organ systems, while others show prematurity of some organs and selective, accelerated development of other systems. The difference depends on whether the foal was the product of simply a shortened gestation and otherwise normal intrauterine environment or was the result of chronic in utero disease contributing to abnormal fetal development.

Intrauterine growth retardation (IUGR) is pathologic and is due to genetic causes or epigenetic causes that affect placental function. IUGR results in a newborn that has a relatively large head and small body. In humans, most forms of IUGR are suspected to occur during the third trimester and are associated with placental vascular lesions, maternal starvation, twinning, intrauterine infections due to bacterial or fungal pathogens and chronic hypoxia. **Small for gestational age** (SGA) defines a foal that is smaller than normal for its gestational age. The relative weight of the term foal to its dam is approximately 10%.

Etiology

Causes of prematurity include any condition that adversely affects the intrauterine environment and fetal development or precipitates early delivery. **Placental abnormalities** associated with premature delivery include placentitis, premature membrane rupture, premature placental separation and hydrops (*q.v.*). **Fetal factors** include congenital anomalies and twinning (*q.v.*). Maternal conditions that predispose to early delivery include incompetent cervix, severe illness and chronic debilitation, general anesthesia and viral infection. Another unfortunate cause of prematurity is **untimely induction of labor**. The majority of premature deliveries remain undiagnosed.

Conditions associated with improved survival rates among premature foals include delivery associated with **chronic placentitis**, birth via spontaneous vaginal delivery, the absence of systemic disease in the mare and the presence of a suckle reflex in the foal. Laboratory findings in the foal associated with an optimistic prognosis include a white blood cell count ⩾500 cells/μL, a neutrophil–lymphocyte ratio ⩾2:0, the absence of severe metabolic acidosis, and appropriate insulin and cortisol responses. Frequently misleading is the **deceptively robust** appearance of many premature foals immediately post partum. However, within 48 h of birth the foal's inability to maintain homeostasis and signs of multiorgan dysfunction frequently become apparent.

Clinical signs

Physical characteristics of prematurity (Table 14.11) include low birth weight, generalized weakness, diminished suckle reflex, short, silky haircoat, domed forehead, floppy ears and deep red tongue. Periarticular and flexor tendon laxity results in sloped pasterns and increased passive range of limb motion. Premature and dysmature foals have difficulty adapting to the extrauterine environment.

Table 14.11 Characteristics of prematurity in the foal

Parameter	Observation
Gestation length	<320 days
Electrolyte concentrations in pre partum mammary secretions	Calcium <40 mg/dL Sodium >30 mEq/L Potassium <35 mEq/L
Physical characteristics	Small size; fine, silky haircoat; generalized weakness; laxity of periarticular ligaments and flexor tendons; increased passive range of limb motion; floppy, pliant ears; incompletely ossified cuboidal bones
Behavior	Prolonged time to sit sternal, stand, and suckle
Thermoregulation	Increased incidence of hypothermia
Respiration	Increased work of breathing, tachypnea, nostril flare, expiratory grunting, paradoxical breathing, periodic apnea
Digestion	Poor tolerance of oral feeds; gut dysmotility, frequent colic
Hematology	Mean corpuscular volume >39 fL White blood cells = $6 \times 10^3/\mu L$ Neutrophil–lymphocyte <1.0
Blood gases/acid-base status	Arterial pH ⩽7.208 ± 0.034 at birth $PaCO_2$ = 66.2 ± 4.7 mmHg $PaCO_2$= 30.0 ± 4.1 mmHg HCO_3= 23.4 ± 1.7 mmol/L
Endocrine function (within 2 h post partum)	Cortisol <30 ng/mL Poor ACTH response with 28% increase in cortisol No change in neutrophil–lymphocyte ratio Glucose = 41.6 mg/dL Insulin = 8.6 μU/mL Poor insulin response following IV glucose administration More rapid loss of sodium following furosemide administration

Hypothermia is a manifestation of **immature thermoregulation**. Oral feed intolerance accompanied by colic, flatulence, delayed gastric emptying and gastric reflux reflects **gut immaturity**. Incomplete innervation of the gut may contribute to dysmotility patterns and increased incidence of gastrointestinal disturbances observed among premature foals. Reduced collagen content associated with abnormal collagen synthesis and cross-linking contributes to weakened structural support of vessels and lungs, flexor tendon laxity and floppy ears.

Pulmonary insufficiency resulting in hypoventilation and respiratory distress is often multifactorial in origin. Causes include: (1) inefficient gas exchange due to recumbency and dependent lung atelectasis; (2) high compliance of the immature chest wall; (3) ineffectual reflex control of breathing; (4) abnormal paradoxical breathing; (5) pulmonary hypertension and an increase in right to left intrapulmonary shunting; (6) insufficient surfactant production. Many premature foals are born with incompletely ossified cuboidal bones and unrestricted exercise or excessive weight bearing can result in abnormal cuboidal bone calcification producing **severe angular limb deformities** (*q.v.*).

Laboratory findings associated with prematurity (Table 14.11) include leukopenia, neutropenia, hypoglycemia, hypocortisolemia, hypoxemia and hypercapnia. Premature foals delivered because of in utero infection often have a hyperfibrinogenemia.

Table 14.12 Symptomatic treatment of complications associated with prematurity

Condition	Sign or complications	Treatment
Altered behavior	Inability of stand or set sternally	Assist to stand and turn from side to side every 2 h; support in sternal position with pillow
	Inability to nurse from mare; ineffective suckle reflex or swallow reflex	Enteral alimentation via bucket, bottle or nasogastric tube; parenteral nutrition
Abnormal homeostasis	Hypothermia (≤37.2°C)	Raise ambient temperature; hot water bottles, warmed IV fluids in insulated jackets, blankets, hot water pads, radiant heat lamps
	Metabolic acidemia (pH < 7.35)	Fluid replacement if hypovolemic; isotonic bicarbonate (1.3%) once adequate ventilation ensured
	Hemoconcentration; dehydration	IV fluids (maintenance rate = 80–120 mL/kg/day); higher sodium requirements
	Hypoglycemia (glucose ≤ 50 mg/dL)	IV dextrose (5%, 10%), enteral and/or parenteral alimentation
Pulmonary dysfunction	PaO_2 < 65 mmHg; PaO_2 normal	Humidified nasal insufflation of O_2 (3–10 L/min); increase time spent in sternal recumbency
	PaO_2 ≤ 65 mmHg; PaO_2 > 65 mmHg	Mechanical ventilatory support via $PaCO_2$ normal nasotracheal intubation with positive end expiratory pressure; consider intratracheal surfactant administration
Hypogammaglobulinemia	IgG < 400–800 mg/dL	Oral colostrum (1 L minimum) if <18 h old; IV plasma (20–40 mL/kg); broad-spectrum bactericidal antibiotics
Gastrointestinal dysmotility	Gastric reflux, ileus	Decrease frequency and volume of oral feeds; oral or IV metoclopramide
	Constipation, meconium	Gravity and/or retention enemas, retention oral fluids, oral mineral oil, IV fluids, add psyllium to enteral fluids
	Diarrhea	Oral protectants (bismuth subsalicylate), loperamide, *Lactobacillus* intestinal inoculants, active culture yogurt
	Ulceration	Ranitidine, sucralfate, antacids; avoid unnecessary use of NSAIDs
Flexor tendon laxity; periarticular laxity	Inability to stand or walk; increased slope to pasterns	Physical therapy; glue-on shoes with heel extensions; restricted exercise on soft surface
Incomplete cuboidal bone ossification	Angular limb deformities	Restricted exercise; if severe, rigid support with splint or casts

Treatment

Abnormal neuroendocrine and immune functions render the premature foal susceptible to **septicemia** and a variety of metabolic stresses. A certain percentage of premature foals fail to absorb sufficient immunoglobulins despite adequate colostrum ingestion and require **plasma transfusion** (*q.v.*) to correct hypogammaglobulinemia. Blunted insulin responses predispose to hypoglycemia, necessitating frequent enteral feeds and/or continuous glucose infusion. Symptomatic treatments for a variety of the complications associated with prematurity are presented in Table 14.12.

SEPTICEMIA AND SEPTIC SHOCK

Septicemia is the leading cause of neonatal foal morbidity and mortality and is most commonly associated with disseminated, Gram-negative and/or Gram-positive bacterial infection.

Etiology

Septicemia describes the constellation of clinical signs produced by the interaction of microbial toxins and the host immune system. **Over-activation** of the immune system provokes uncontrolled release of endogenous mediators and precipitates a **cascade** of metabolic and hemodynamic changes culminating in **multiple organ system failure**. **Septic shock** is characterized by circulatory failure, perfusion deficits and an inability of the body to use existing metabolic substrate effectively.

One of the most potent mediators of Gram-negative sepsis is **endotoxin** (*q.v.*), the lipopolysaccharide component in the outer cell membrane of Gram-negative bacteria. Endotoxins are released from Gram-negative bacteria whenever their cell membrane integrity is disrupted, as occurs during rapid growth and proliferation or cell death. Some of the local and systemic effects of endotoxin are presented in Table 14.13.

The interaction of endotoxin with neutrophils, mononuclear phagocytes, lymphocytes and vascular endothelial cells results in the release of a **second wave of endogenous mediators** that include tumor necrosis factor, interleukins, prostaglandins, interferons and eicosanoids.

Increased vascular permeability is accompanied by interstitial and pulmonary edema, hypovolemia and decreased cardiac output. Changes in vascular tone are characterized by pulmonary and systemic arterial hypotension and vasoconstriction contributing to a decrease in splanchnic perfusion. Coagulation pathways are activated and capillary microthrombi compromise tissue perfusion even further.

The hypermetabolism and increased catabolism associated with sepsis is mediated by the release of cortisol, catecholamines and glucagon resulting in **peripheral insulin resistance** and increased glycolysis and lipolysis. Sepsis hinders sequentially the utilization of glucose, fat and finally protein as an energy source.

Cardiovascular function is impaired indirectly by endotoxin-stimulated release of myocardial depressant factor. Endotoxin also exerts a direct inotropic depressant effect on the **heart muscle**. During early compensated sepsis,

Table 14.13 Local and systemic effects of endotoxin

Organ system	Response	Net results
Immune system		
Neutrophils	Release of eicosanoids Enhanced chemotaxis and degranulation Enhanced adherence to vascular endothelium Platelet activating factor released (PAF)	Increased inflammation Peripheral neutropenia; release of reactive O_2 species and enzymes; auto-injury Vascular damage, increased vascular permeability Platelet activation, leukocyte chemotaxis, aggregation; macrophage activation; systemic vasodilatation, hypotension; pulmonary, coronary vasoconstriction, negative cardiac inotropy
Macrophages	Release of inflammatory cytokines: tumor necrosis factor (TNF), interleukin-1 (IL-1); neutral proteases; eicosanoids: leukotrienes, prostaglandins; PAF, reactive O_2 species	Potent mediators of sepsis-induced inflammation, auto-injury, changes in systemic vascular tone and permeability, and hemostasis
Lymphocytes T cells B cells	 Decreased suppressor cell activity Cytokines released; antibody production stimulated	 Loss of immune system modulation Inflammation, systemic vascular changes
Vascular endothelial cells	Release of prostacyclins, interleukins, hematopoietic growth factor, PAF, endothelial relaxing factors	Collagen exposed; platelet aggregation, coagulation cascade stimulated; bradykinin released resulting in vasodilatation, hypotension
Platelets	Release of thromboxane, PAF, serotonin	Pulmonary hypertension, vasoconstriction, platelet aggregation, leukocyte chemotaxis
Cardiovascular system	Myocardial depressant factor Direct negative inotropy	Negative inotropy Initially, increased blood pressure; tachycardia, increased O_2 consumption Terminally, decreased vascular tone, low vascular resistance, increased anaerobic metabolism; metabolic acidosis; myocardial failure; hypotension
Pulmonary system	Margination of leukocytes, lymphocytes Intrapulmonary leukocytes, platelets release PAF, eicosanoids	Endothelial damage, increased capillary permeability Initially, increased vascular resistance, pulmonary hypertension Terminally, pulmonary edema, atelectasis, intrapulmonary shunting
Endocrine system		
Pituitary gland	Release of endorphin Release of ACTH Release of antidiuretic hormone	Pain relief, change in mentation, altered vascular permeability Cortisol released Fluid retention
Adrenal gland	Release of cortisol and catecholamine Release of aldosterone	Glycolysis, lipolysis, peripheral insulin release Fluid and sodium retention
Gut	Release of glucagon	Lipolysis, peripheral insulin resistance

a sympathetic response results in an increased heart rate and cardiac index, improved myocardial contractility, and increased oxygen consumption.

As septicemia progresses there is a **decrease in vascular tone** and systemic vascular resistance disproportionate to the increase in cardiac output. Oxygen extraction by peripheral tissues is decreased, metabolic acidosis develops and anaerobic metabolism commences. Terminally, **myocardial failure** develops associated with decreased cardiac output, respiratory decompensation, severe hypotension and profound respiratory/metabolic acidosis.

During sepsis, pulmonary capillary permeability increases and polymorphonuclear leukocytes and lymphocytes marginate and accumulate in the pulmonary microvasculature. Neutrophil degranulation produces endothelial damage, increased capillary permeability and alveolar flooding. Intrapulmonary shunting develops followed by progressive atelectasis and pulmonary edema.

The origin of **neonatal infection** includes opportunistic organisms whose portal of entry includes the gastrointestinal, urogenital and respiratory tracts, the umbilicus and the placenta. Factors predisposing to neonatal septicemia include:

1. Environmental factors: overcrowding, poor ventilation and sanitation, inadequate umbilicus disinfection, iatrogenic stress, excessive use of antibiotics on the farm
2. Disorders of the neonatal immune system: failure of passive transfer, combined immunodeficiency
3. Perinatal stresses: peri partum hypoxia, prematurity, severe musculoskeletal deformities.

Organisms most commonly associated with foal septicemia include *Escherichia coli*, *Actinobacillus* spp., *Pasteurella* spp., *Klebsiella* spp., *Salmonella* spp., *Streptococcus* spp. and *Staphylococcus* spp. (*q.v.*).

Clinical signs

The wide spectrum of clinical signs associated with septicemia depends on the integrity of the **host immune system**, the duration of illness and the severity of the infection. Clinical conditions associated with neonatal sepsis are presented in Box 14.7.

During the early hyperdynamic phase of sepsis, foals display lethargy, loss of suckle, hyperemic mucous membranes due to peripheral vasodilatation, decreased capillary refill time, tachycardia, tachypnea, increased cardiac output, hyperkinetic pulses and variable body temperature. Extremities are still warm. Laboratory data typically reveal leukopenia and neutropenia with a degenerative left shift, and normal or low glucose concentration. Fibrinogen concentration is often normal. **Elevated fibrinogen** levels suggest the infection has been present for a minimum of 48–72 h.

Septic shock (*q.v.*) develops when infection overwhelms the host immune system. Affected foals are usually recumbent, dehydrated and almost moribund with hypotension and decreased cardiac output characterized by tachycardia, cold extremities, thready peripheral pulses, prolonged capillary refill time and oliguria. Hypothermia is common. Gut motility is often decreased and

may be accompanied by gastric reflux, constipation and variable degrees of abdominal distension. Signs of respiratory compromise associated with decreased pulmonary perfusion and increased vascular permeability include tachypnea, dyspnea and hypoxemia (*q.v.*).

Box 14.7 Clinical conditions associated with neonatal septicemia

History: Predisposing factors

- Severe maternal illness
- Premature lactation
- Maternal vaginal discharge, placentitis
- Neonatal hypogammaglobulinemia (FPT)
- Severe neonatal stress
- Prematurity

Physical examination findings

- Early sepsis
  - Loss of suckle reflex
  - Distended udder on dam
  - Lethargy, generalized weakness
  - Variable temperature
  - Injected sclera
  - Hyperemic mucous membranes and coronary bands
  - Variable capillary refill time
  - Tachycardia
  - Tachypnea
  - Hyperkinetic pulses
  - Petechiae on gums, sclera, vulva, pinnae, coronary bands
- Late sepsis
  - Profound weakness and depression
  - Complete anorexia
  - Tachycardia
  - Weak peripheral pulses, hypotension
  - Cold extremities
  - Prolonged capillary refill time
  - Oliguria/anuria
  - Respiratory distress
  - Hypothermia
- Localized sites of infection
  - Pneumonia/pleuritis
  - Meningitis
  - Hepatitis
  - Nephritis
  - Peritonitis, enteritis
  - Synovitis, osteomyelitis
  - Uveitis
  - Omphalitis

Box 14.7 continues on page 831

Box 14.7 Clinical conditions associated with neonatal septicemia [continued]

- Hematology and serum biochemistry
  - Leukopenia, neutropenia, degenerative left shift
  - Thrombocytopenia
  - Hyperfibrinogenemia (variable)
  - Metabolic acidosis
  - Respiratory acidosis
  - Hypoglycemia
  - Lipemia
  - Hypogammaglobulinemia
  - Hyperbilirubinemia
  - Azotemia
  - Disseminated intravascular coagulation

Terminally, **multiorgan system failure** occurs. If the foal does not die of acute septic shock, localized infections develop in one or more body systems (see Box 14.7). During the terminal stages of septicemia, foals frequently display a mixed respiratory/metabolic acidosis, marked hemoconcentration, lipemia, hyperbilirubinemia, azotemia, profound hypoglycemia, and leukopenia with a degenerative left shift. Endotoxin and tumor necrosis factor result in hemostatic dysfunction characterized by disseminated intravascular coagulation.

Hypogammaglobulinemia is common due to inadequate absorption of colostral antibodies and/or increased protein catabolism associated with sepsis. Serial blood cultures obtained prior to antimicrobial therapy increase the likelihood of isolating the offending pathogen(s).

Therapy

Guidelines for the treatment of neonatal septicemia are presented in Table 14.14. Therapy is focused on support of the cardiopulmonary and immune systems and provision of adequate nutrition and intensive nursing care. IV fluid therapy is the mainstay of cardiovascular support and should be administered at the maximal rate tolerated by the foal. Severe septic shock may require flow rates of 20–40 mL/kg/h. Volume expansion should be achieved using a **balanced electrolyte solution** or **plasma**.

The goal of fluid therapy is to reduce peripheral vasoconstriction, restore good peripheral pulse quality, improve renal perfusion and urine output, increase central venous pressure to ⩾5 cm of water and restore arterial systolic blood pressure to ⩾70–80 mmHg. If fluid therapy alone fails to restore acceptable blood pressure and urinary output, β-adrenergic drugs may be indicated (e.g. dopamine, dobutamine). Since most septic foals are hypoglycemic, a **slower, continuous infusion of dextrose-containing solutions** should be included. Rapid administration of concentrated dextrose solutions must be avoided to prevent hyperglycemia and hyperosmolarity.

Minimizing ventilation–perfusion mismatching is the focus of respiratory support. Fluid therapy should proceed cautiously to maintain a high enough left ventricular end diastolic pressure and left atrial pressure to create more

Table 14.14 Guidelines for treatment of neonatal septicemia

Abnormal condition	Cardiovascular support	Parameters to monitor
Dehydration hypotension associated with hypovolemia; oliguria/anuria	IV balanced electrolyte solution, plasma	HR, CVP, BP, pulse quality, urine production, PCV, TP
Anuria/oliguria despite rehydration	Dopamine: low dose (1–4 μg/kg/min): dopaminergic; improves RBF; intermediate dose (5–10 μg/kg/min): β_1-cardiotonic; β_2-systemic vasodilatation (at excessively high doses dopamine acts as an α_1-agonist causing systemic vasoconstriction, decreased RBF)	HR, BP, pulse quality, urine production
Impaired cardiac function; use echocardiography to assess cardiac contractility	Dopamine: intermediate dose for cardiotonic effects Dobutamine (2–15 μg/kg/min); selective β_1-agonist; minimal vasodilatation; increased contractility with little increase in HR	HR, BP, pulse quality, urine production HR, BP, pulse quality
Abnormal condition	**Pulmonary support**	**Parameters to monitor**
Hypoxemia associated with dependent lung atelectasis, pulmonary hypoperfusion	Intranasal oxygen (3–10 L/min) Increase time spent sternal Cautious fluid therapy	Arterial blood gas
Hypoxemia, hypercapnia, pulmonary edema due to capillary leak; atelectasis due to surfactant dysfunction, intrapulmonary shunting	PPV with PEEP Furosemide Correct acidosis Fluid and plasma therapy to maintain BP and CO	Arterial blood gas Capnography and pulse oximetry Thoracic radiographs
Abnormal condition	**Immune system treatment**	**Parameters to monitor**
Gram-negative bacteremia	Broad-spectrum bactericidal antibiotics	Cultures of blood and/or other body fluids (synovia, CSF, peritoneal fluid, urine, TTA); leukogram, fibrinogen concentration
Failure of passive transfer	Oral colostrum if $<$18 h old and gut is functional; plasma transfusion	IgG concentration
Endotoxemia	Low doses of flunixin meglumine; anti-endotoxin serum; hyperimmune plasma	Vital signs, BP, HR pulse quality, mucous membranes
Abnormal condition	**Metabolic treatment**	**Parameters to monitor**
Hypoglycemia	IV glucose Enteral feeds Parenteral alimentation	Glucose concentration (Dextrostix or glucometer)

Table 14.14 (*Continued*)

Abnormal condition	Metabolic treatment	Parameters to monitor
Metabolic acidosis	IV fluids to improve peripheral perfusion Cautious use of IV isotonic bicarbonate	Venous blood gas
Abnormal condition	**Nutritional support**	**Parameters to monitor**
Functional gut and inadequate intake	Enteral feeding via NGT or bottle using mare's milk, goat's milk, or foal milk replacer; goal is 20–25% BW/day divided into frequent feeds every 2–3 h	Body weight, gastrointestinal tolerance: gut motility, reflux, abdominal distension, fecal product
Compromised gut, inadequate intake	Parenteral alimentation using dextrose, amino acids, lipids, multivitamins and trace minerals	Plasma glucose, lipids, electrolytes, osmolarity; urine glucose, PCV/TP
	Miscellaneous	
Abnormal condition	**Treatment**	**Parameters to monitor**
Hemostasis abnormalities; DIC; thrombocytopenia	Heparin, fresh plasma	Clotting parameters; platelet count
Increased capillary and membrane leakiness	Membrane stabilizing drugs: DMSO, steroids, PG inhibitors	Examine for pulmonary and/or generalized edema
Hypothermia	Warm, ambient temperature; warmed IV fluids, blankets, hot water bottles; fluid therapy to correct hypovolemia; radiant heat lamps	Body temperature
Recumbency	Frequent repositioning; chest coupage; bed on soft absorbent fleece mats; keep dry and clean	Examine daily for pressure sores

ABG, arterial blood gas; BP, blood pressure; BW, body weight; CO, cardiac output; CSF, cerebrospinal fluid; CVP, central venous pressure; DIC, disseminated intravascular coagulation; DMSO, dimethyl sulfoxide; HR, heart rate; NGT, nasogastric tube; PCV, packed cell volume; PEEP, positive end expiratory pressure; PG, prostaglandin; PPV, positive pressure ventilation; RBF, renal blood flow; TP, total protein; TTA, transtracheal aspirate.

uniform lung perfusion. Frequent repositioning of the patient's chest helps minimize the development of pulmonary edema. **Intranasal oxygen therapy** is used to treat mild hypoxemia. Mechanical positive pressure ventilation may be required to prevent further alveolar collapse associated with increased tissue pressure due to interstitial edema.

The hypermetabolism and protein catabolism associated with sepsis must be addressed. Parenteral alimentation is often necessary in foals unable or unwilling to consume enough calories orally. When peripheral insulin resistance and glucose intolerance develop, lipids become a valuable source of calories. In severely affected foals, caloric requirements often exceed 120 kcal/kg/day. Specific guidelines for nutritional support are presented elsewhere.

Antimicrobial therapy should be instituted without delay, as soon as sepsis is suspected and before culture results are available. Broad-spectrum, bactericidal antimicrobial agents should be used. If renal function is adequate, **penicillin** and an aminoglycoside (**amikacin** or **gentamicin**) are an effective

drug combination. If renal compromise is present then cephalosporins (**ceftiofur**) or extended spectrum penicillins should be considered.

Plasma from hyperimmunized donors is administered to treat not only failure of passive transfer, but to provide opsonins and to improve foal neutrophil function. Low doses (0.25 mg/kg IV q 8 h) of **flunixin meglumine** may help ameliorate some of the signs of endotoxemia.

Septic foals require **intensive nursing care**. Attention focuses on keeping the recumbent foal dry and clean to prevent decubital ulcers and urine/fecal scalding. Foals should be frequently repositioned to prevent decubital ulcers and dependent lung atelectasis. Vital signs are monitored on a frequent basis to detect subtle changes in the patient's condition. Survival depends on **aggressive supportive care** during the initial stages of acute sepsis to prevent death due to septic shock and to prevent the development of multiple sites of localized infection.

NEONATAL ISOERYTHROLYSIS

Neonatal isoerythrolysis (NI) (*q.v.*) is an important cause of **neonatal icterus** that develops in newborns foals following the ingestion of colostrum from a multiparous mare. The cardinal signs of NI are icterus, anemia and pigmenturia.

Etiology

NI is the result of RBC destruction by alloantibodies produced by the mare as a result of **alloimmunization** (*q.v.*) by foreign erythrocyte antigenic factors of the foal inherited from the stallion and not possessed by the mare. Although there are 32 blood group antigens (*q.v.*) known for horses, Aa and Qa are the antigens most commonly associated with the disease.

Clinical signs

Clinical signs of NI relate to the severity and rapidity of onset of **anemia**. Signs occur only after colostrum has been ingested and sufficient amounts of offending antibody absorbed to result in RBC destruction.

Antibody absorption is usually complete 4–5 h after a meal of colostrum is ingested. In severe cases **profound hemolysis** develops and results in a short, rapidly fatal clinical course that may be only hours in duration. These foals show pallor of mucous membranes, weakness, tachypnea, tachycardia, acute collapse and death. Seizures and other CNS signs may develop as a result of brain hypoxia.

Foals with milder forms of NI exhibit signs of anemia and icterus within hours to days following delivery. As hemolysis progresses, foals develop icterus, lethargy, weakness, loss of nursing vigor, tachypnea, tachycardia and pigmenturia. A low-grade fever may be associated with hemolysis.

Treatment

If clinical signs of NI are detected while the foal is still <24 h old, then further nursing from its dam should be prevented for a minimum of 24–36 h and the

mare stripped of all remaining colostrum. An **alternate source of colostrum** should be obtained. Tachypneic foals may benefit from intranasal oxygen to help fully saturate RBC hemoglobin. Rapidly developing hemolysis may predispose to brain hypoxia and the onset of seizures or other CNS signs (e.g. head tilt). Foals with seizures should receive anticonvulsants (diazepam 5–10 mg IV, or phenobarbital 3–9 mg/kg given slowly IV).

Foals with NI that experience severe, life-threatening hemolysis (PCV $< 15\%$) are in need of an **immediate whole blood transfusion** (*q.v.*) to restore oxygen-carrying capacity. The donor red cells must be compatible with the mare's serum/colostral antibodies since those are the offending antibodies circulating in the foal. **The most unsatisfactory donor is the sire**. The ideal red cell donor is the dam since her red cells will not react with her own antibodies. However, only **washed red cells** from the mare are safe to administer.

Alternate blood sources include an Aa and Qa negative donor or an unmatched gelding or other horse not used for breeding. Oxyglobin (Oxyglobin, Biopure Corp, Cambridge, MA) represents an alternative solution for some valuable NI foals. Oxyglobin is a commercial product containing polymerized ultrapurified bovine hemoglobin. Oxyglobin is a potent colloid. Care must be taken when administering Oxyglobin to normovolemic patients due to its ability as a colloid to rapidly expand the plasma volume and cause circulatory overload and pulmonary edema. The recommended dose is 10–30 mL/kg BW administered at a rate not to exceed 10 mL/kg/h.

Prevention

Prevention of NI should be the focus of future matings. Blood typing can be used to identify mares "at risk" for having a NI foal and to select a "compatible" stallion. Most cases of NI occur when a mare that lacks either the blood group antigen Aa or Qa is bred to a stallion that possesses the corresponding factor, either Aa or Qa. Prevention of NI can be accomplished by identifying a mare at risk to produce an NI foal, identifying a compatible sire, and/or performing a **jaundiced foal agglutination (JFA)** test on the foal's presuckle blood and mare's colostrum. Once a mare has had a NI foal she is at increased risk to have another affected foal.

CLOSTRIDIAL ENTERITIS

Clostridial enteritis (*q.v.*) is increasing in frequency. *Clostridium perfringens* (most commonly type A, less commonly type C) and *Clostridium difficile* have both been identified as causative agents of colic and diarrhea in young foals as young as one day of age.

Etiology

Clostridial enteritis can be sporadic or can affect groups of foals on a farm. Clostridial spores may be ingested from the **environment**. Foals may be more susceptible to infection and overgrowth of the bacteria within the gut due to several factors including: (1) immaturity of the bile, (2) failure of passive transfer, (3) ingestion of diets high in carbohydrates and protein, (4) hypoxic gut damage, (5) concurrent infection with other pathogens such as rotavirus, and (6) concurrent administration of antibiotics.

Clostridial enteritis affects the small intestine more severely than the large intestine and results in **diffuse mucosal edema** with localized damage to the tips of villi or sloughing of the entire villous epithelium. Loss of mucosal integrity contributes to the development of endotoxemia and septicemia (*q.v.*) due to bacterial translocation from the gut lumen into the bloodstream.

Clinical signs

Clinical signs include colic, mild to moderate abdominal distension, and diarrhea. Fever is usually present. Diarrhea associated with *C. perfringens* is usually bloody. Diarrhea due to *C. difficile* may be bloody, but is often brown and fetid. *C. difficile* can also produce a fatal **hemorrhagic and necrotizing enterocolitis**. Blood work often demonstrates leukopenia and neutropenia and varying degrees of hypochloremia, hyponatremia and metabolic acidosis.

Sonographic examination of the abdomen often reveals increased small intestinal peristalsis with the bowel wall appearing more hypoechoic and thicker than normal. Occasionally gas echoes are visualized within the bowel, indicative of pneumatosis intestinalis. Feces should be submitted for **Clostridium cultures** using a Port-a-cul anaerobic tube (Becton Dickinson). Frozen feces should be submitted for toxin assays. A fresh fecal smear can be made to document the presence of Clostridium-like organisms.

Treatment

Therapy includes pain control using **dipyrone** (10–22 mg/kg IV; drug is only available through compounding pharmacies in US) and/or **butorphanol** (2–5 mg IV/IM). Low doses of **flunixin** (0.25 mg/kg IV q 8 h) are used sparingly to ameliorate the effects of endotoxemia. The drug of choice for clostridial enteritis is **metronidazole** (15 mg/kg PO q 8 h). Severe cases also should receive broad-spectrum, bactericidal antimicrobial therapy such as IV **potassium benzylpenicillin** (22 000–44 000 IU/kg IV q 6 h) and **amikacin** (20–30 mg/kg IV q 24 h).

Additional therapy includes **hyperimmune plasma** (containing high levels of Gram-negative core antigen antibodies) and aggressive **IV fluid support** using balanced electrolyte solutions containing added potassium and/or bicarbonate as indicated by serial venous blood gas analysis.

Ulcer prophylaxis should be administered IV in foals with severe colic and bowel distension and orally in foals that are nursing. Drugs and doses include **ranitidine** (1.5 mg/kg IV q 8 h, 8–10 mg/kg PO q 8 h), **cimetidine** (6.6 mg/kg IV q 6–8 h, 15 mg/kg PO q 6 h), and **omeprazole** (4 mg/kg PO q 24 h).

Oral administration of DTO smectite (BioSponge) may prevent binding of *C. difficile* toxins. **Smectite** is an alumino-magnesium silicate clay mixture with tremendous surface area capable of adhering to mucosa to increase barrier protection. Smectite is negatively charged and therefore can attract cations such as bacterial exotoxins and endotoxins. Foals should receive a loading dose of 113–120 g (4–6 oz) in a slurry, followed by 57–113 g (2–4 oz) q 6–8 h until the diarrhea resolves. **Bismuth subsalicylate** (60–120 mL PO q 4–6 h) may help absorb toxins and provide some gastroprotection.

A **Lactobacillus paste** containing *Saccharomyces* spp. should be administered to help re-establish normal gut flora. *Saccharomyces boulardii* has been shown to prevent binding of clostridial toxins.

Neonatal foals that are not nursing should have **blood glucose levels** monitored and should receive **dextrose-containing fluids**. Foals experiencing severe colic with marked abdominal distension and ileus should be prevented from nursing and supported with IV parenteral nutrition. Some foals recovering from clostridial enteritis display varying degrees of **lactose intolerance** (*q.v.*) and benefit from administration of commercially available lactase tablets.

NUTRITIONAL AND RESPIRATORY SUPPORT FOR THE NEONATAL FOAL

A rational feeding program for the sick foal must address the neonate's degree of maturity, high metabolic rate and requirements for rapid growth, and the special nutritional needs created by concurrent illness. Appropriate nutritional supplementation (*q.v.*) requires criteria for assessing nutritional status, guidelines for estimating an individual foal's nutrient requirements, and a thorough understanding of the nutritional formulas and routes of administration available.

EFFECTS OF MALNUTRITION

Malnourishment due to inadequate intake, abnormal absorption or increased utilization results in multiple organ dysfunction and increased morbidity and mortality.

Malnutrition has been associated with weight loss, depressed growth rates, generalized muscle weakness, impaired wound healing, retarded callus formation at fracture sites and decreased collagen production. Protein–calorie undernutrition results in gastrointestinal atrophy, dysmotility and impaired fat and carbohydrate digestion and absorption. Altered hepatic function reduces resistance to a variety of toxic agents including bacterial pathogens.

Nutritionally depleted patients experience **compromised pulmonary function** and reduced ventilatory capacity due to a loss of strength of diaphragmatic, intercostal and abdominal muscles. The most devastating consequence of undernutrition for the neonate is **impaired immune function** resulting in decreased resistance to infection. Malnutrition is associated with depressed bone marrow activity, atrophy of lymphoid tissues, abnormal neutrophil function, impaired antibody production, and depressed secretory, mucosal and cell-mediated immunity (*q.v.*).

NUTRITIONAL ASSESSMENT

Nutritional assessment begins with careful anamnesis and physical examination. Acute weight loss of 5% of BW or chronic weight loss of 10–15% BW is a clear indication for **nutritional supplementation**. However, a foal with a history of restricted oral intake, protracted nutritional losses or increased metabolic demands (Box 14.8) is a candidate for nutritional supplementation even before weight loss occurs or biochemical indices become abnormal.

Physical changes associated with malnourishment include weight loss, reduced growth, muscle atrophy, generalized weakness, lethargy, glossitis and scaly skin with reduced elasticity. Neonatal malnourishment may alter

Box 14.8 Indications for nutritional support in the foal

Restricted oral intake

- Weak or absent suckle reflex due to:
  - Septicemia
  - Peri partum hypoxia
  - Prematurity/dysmaturity
- Dysphagia due to:
  - Botulism
  - Hypoxic brainstem damage
  - Prematurity
  - Congenital anomaly (e.g. cleft palate, subepiglottic cyst)
- Gastrointestinal dysfunction associated with:
  - Peritonitis, enterocolitis
  - Gastroduodenal ulceration
  - Ileus, gastric reflux, delayed gastric emptying
- Orphan foal
  - Loss of dam
  - Rejection by dam

Protracted nutritional losses

- Secretory diarrhea
  - Salmonellosis
- Malabsorption
  - Rotavirus diarrhea
  - Lactose intolerance

Increased metabolic needs

- Sepsis-induced catabolism and disruption of intermediary metabolism
- Increased growth requirements of prematurity
- Fever
- Localized infection (e.g. pneumonia, osteomyelitis)

the foal's long-term growth potential. In neonates, catch-up growth following malnutrition is complete only if the period of undernutrition is relatively brief.

Anthropometric measurements (e.g. triceps skin fold thickness, mid upper arm circumference) and body composition studies (e.g. measurements of body fat, plasma volume, total body water and lean body mass) are helpful in humans but have not been used in clinical veterinary medicine.

Biochemical indices of malnutrition include hypoalbuminemia and hypoproteinemia. Unfortunately, the long 20-day half-life of albumin in the horse renders this parameter unreliable during early stages of malnourishment. Total plasma protein concentrations may be misleading in newborn foals due to the wide range of presuckle protein values and the impact of colostrum ingestion on globulin concentration. Visceral protein markers of nutritional status such as fibronectin, prealbumin, retinal binding protein, transferrin and thyroxin-binding globulin have been helpful in humans, but have not been evaluated in the foal.

Sick, hypophagic adult horses mobilize fat reserves resulting in elevated levels of total lipids, triglycerides and cholesterol. The use of these parameters in foals is complicated by the fact that neonatal hyperlipemia also occurs due to sepsis-induced decreases in lipoprotein lipase activity and impaired lipid clearance.

The most reliable and practical immunologic indices of poor nutrition include **absolute** and **persistent lymphopenia** (≤2000 lymphocytes/μL) and/or **anergy** (depression of delayed hypersensitivity response) following intradermal injection of antigen. Limited intradermal antigen testing has been performed in foals, but results are difficult to interpret since a variety of factors such as prematurity (alone) can result in an abnormal response.

DIGESTION AND ABSORPTION

The β-glycosidase, lactase, reaches maximal levels at birth followed by a steady decline after 4 mo of age. The α-glucosidases, maltase, sucrase and trehalase, are barely detectable in the equine fetus and increase slowly to reach adult levels by 10 mo of age. This pattern of disaccharidase development suggests that neonatal foals would not grow acceptably on a diet relying on sucrose, maltose or polysaccharides as its primary carbohydrate source.

NUTRITIONAL REQUIREMENTS

Since there are no specific nutritional requirements for neonatal foals, guidelines for nutrient intake have been estimated based on the average milk consumption of a healthy foal and the composition of mare's milk.

Healthy full-term foals nurse an average of seven times an hour, consume between 20% and 30% of their BW in mare's milk daily and gain approximately 0.5–1.4 kg/day. On this diet, a 50 kg foal would consume 10–12.5 L milk/day to provide 120–150 kcal/kg/day, 5–6 g protein/kg/day, and 4–5 g fat/kg/day.

Nutrient requirements for premature and growth-retarded foals are poorly defined and can only be extrapolated from guidelines established for infants with similar problems. Premature infants have higher energy and protein requirements and reduced fat absorption due to decreased bile salt synthesis and hepatic immaturity.

A healthy foal ingests approximately 250–290 mg/kg/day of **calcium**. Oral calcium requirements can only be estimated since the calcium retention rate in foals and the intestinal absorption coefficient of calcium in mare's milk are not known. Human milk alone cannot meet the calcium and phosphorus requirements of premature and low birth weight infants. It is likely that **dysmature and premature foals** with incomplete skeletal ossification have higher calcium and phosphorus requirements.

Serum calcium concentration is a poor indicator of the body's calcium needs. Parathyroid hormone (*q.v.*) stimulates calcium mobilization from bone and ensures normal serum calcium concentrations despite inadequate dietary intake. Abnormally elevated serum concentrations of alkaline phosphatase and radiographic decreases in bone density are suggestive of excessive calcium mobilization from bone associated with inadequate calcium intake.

SEPTICEMIA

Septicemia and endotoxin (*q.v.*) precipitate a neurohormonal cascade of events mediated by leukocyte endogenous mediator, catecholamines, glucocorticoids and glucagon resulting in disruption of intermediary metabolism and increased metabolic rate. Sepsis sequentially hinders utilization of carbohydrates, lipids and, finally, protein for energy.

Increased sympathetic activity associated with sepsis results in hepatic gluconeogenesis, glycolysis, lipolysis, proteolysis, water and sodium retention and increased urinary excretion of potassium and nitrogen. Mediators of sepsis inhibit insulin secretion and increase peripheral insulin resistance, thereby contributing to the hyperglycemia and glucose intolerance observed in septic neonates.

Fat utilization is impaired due to decreased lipoprotein lipase activity and a deficiency of the carrier peptide carnitine. Protein degradation, in particular branched chain amino acid catabolism, represents the final fuel source during sepsis. Eventually, excessive amino acid degradation overwhelms the liver's metabolic capacity resulting in uremia, production of false neurotransmitters, and clinical signs of hepatoencephalopathy.

ENTERAL FEEDING

If there is no medical contraindication for oral feeding and the gastrointestinal tract is functional, **enteral alimentation** is the preferred and most effective route of nutrient supplementation. Enteral feeding is more physiological, less expensive, facilitates normal gut maturation, stimulates hepatic and biliary secretions, promotes growth of intestinal villi and production of crypt cells, induces brush border disaccharidase activity and improves nitrogen retention. Oral feeding also stimulates release of enteroinsular hormones such as glucagon, gastrin, cholecystokinin and secretin, which exert a tropic effect on gut maturation.

Enteral feed intolerance is observed frequently among dysmature and growth-retarded foals. In utero malnutrition stunts growth and delays gastrointestinal development characterized by abnormal disaccharidase activity and depressed gut immunity. Foals suffering from hypoxia and septic shock experience **gastrointestinal ischemia** accompanied by varying degrees of mucosal damage, malabsorption and dysmotility. Enteral feeding in these foals must proceed cautiously.

Routes of feeding include nursing from the udder, bottle or bucket, and nasogastric tube intubation. If an effective suckle and swallow reflex is present, bottle feeding can be attempted using infant or lamb nipples.

Udder bumping and teat-seeking behavior can be stimulated by allowing the foal to approach the bottle from behind and under the handler's armpit. This technique also reduces the risk of aspiration by preventing overextension of the head and neck.

Bucket feeding allows the foal to drink with its head and neck in a flexed position and is helpful for foals with a weak swallow reflex or foals destined to be hand raised. Milk should be introduced in a shallow hand-held bowl

and the foal encouraged to drink by wetting the fingers in milk and allowing the foal to suckle from the finger as its head is lowered into the milk. "On demand" feeding is ideal but often impractical and too labor intensive. Foals <7 days of age should be fed a minimum of every 2 h.

Nasogastric intubation is required if ineffectual swallowing and suckling are present. A small-bore, flexible silicone tube (5–7 mm internal diameter) is preferred. Individual choice dictates whether or not the tube is left indwelling or passed with each feeding. Indwelling tubes may be sutured to the nares or taped to the halter with the end positioned in the distal esophagus or stomach. Tubes must be **sealed between feedings** to prevent aerophagia. Recumbent foals should be maintained in sternal recumbency immediately after tube feeding to reduce the risk of gastroesophageal reflux and aspiration.

Popular enteral formulas for foals include mare's milk, goat's milk and artificial milk replacers formulated for foals. **Mare's milk** is preferred since it is the most physiological. **Goat's milk** is an acceptable alternative, and is higher in fat, total solids and gross energy than mare's milk. It is more digestible than cow's milk due to its composition of simpler fatty acids, smaller fat globules, and better buffering capacity. Foals raised on goat's milk occasionally exhibit mild constipation.

Cow's milk can be substituted for mare's milk if **additional sugar** is added and some of the fat is removed. This can be accomplished by using 2% skim milk and adding 20 g dextrose/L milk. A variety of commercially available **mare's milk replacers** are available. The ideal replacer should contain 22% crude protein, 15% fat and less than 0.5% fiber on a dry matter basis. Many of the formulas when reconstituted are more concentrated than mare's milk and may predispose to constipation and dehydration in foals raised solely on milk replacer. Free access to water can ameliorate these problems.

Complications associated with enteral feeding are listed in Box 14.9. Signs of diet intolerance include constipation, diarrhea, gastric reflux, flatulence, abdominal distension and colic. Although healthy foals consume between 20% and 25% BW in milk daily, the provision of 10% BW is a reasonable goal when initiating enteral alimentation in sick foals. At this rate a 50 kg foal requires a minimum of 417 mL of milk every 2 h. Milk should be fed as close to body temperature as possible. Any changes in volume or composition of the enteral diet should be made slowly.

Delayed gastric emptying and **gastroduodenal dysmotility** can be improved in some foals with **metoclopramide** given IV as a slow infusion (0.25 mg/kg/h) or orally (0.6 mg/kg q 4 h). Overdosage is associated with excitement. Metoclopramide is contraindicated if **gastrointestinal obstruction** is suspected.

Diarrhea is treated symptomatically with oral **bismuth subsalicylate** (1–2 mL/kg PO q 4–6 h) and/or **loperamide** (0.1–0.2 mg/kg PO q 6 h). Diarrhea may also respond to administration of a commercial intestinal **probiotic** or **active culture yogurt**.

Nasopharyngeal irritation from repetitive or chronic nasogastric intubation delays the return of a normal suckle reflex. Insufflation of a nasopharyngeal spray containing prednisolone, furacin, glycerin and DMSO helps reduce inflammation.

Box 14.9 Complications associated with nutritional support

Parenteral alimentation

- Metabolic disturbances
  - Hyperglycemia/hypoglycemia
  - Glucosuria/osmotic diuresis
  - Hyperosmolar states
  - Hyperlipemia
  - Hyperchloremic acidosis
  - Uremia/azotemia
  - Electrolyte imbalances
  - Mineral/vitamin imbalances
- Catheter related
  - Thrombosis
  - Phlebitis
  - Sepsis

Enteral alimentation

- Metabolic disturbances
  - Hypoglycemia
  - Electrolyte imbalances
- Gastrointestinal intolerance
  - Colic, ileus
  - Abdominal distension
  - Gastric reflux
  - Diarrhea
  - Constipation
  - Flatulence
- Nasogastric tube-related problems
  - Misplacement of tube
  - Tube occlusion/dislodgement
  - Aerophagia, gastric distension
  - Gastric irritation
  - Rhinitis, pharyngitis, esophagitis
  - Aspiration pneumonia
- Formula problems
  - Poor palatability

PARENTERAL NUTRITION

Parenteral nutrition (PN) involves the IV administration of **hypertonic solutions** containing dextrose, amino acids, lipids, vitamins, electrolytes and trace minerals, and is indicated whenever feeding via the gastrointestinal tract is inadequate, contraindicated or impossible. These PN solutions must be administered **continuously IV** through a large diameter vein to minimize vessel irritation, prevent osmotic diuresis, avoid hyperosmolar states and maximize

Box 14.10 Sample calculations for a 45 kg foal receiving parenteral alimentation

Initial formula

- Glucose 10 g/kg × 45 kg = 450 g = 900 mL 50% dextrose
- Amino acid 2 g/kg × 45 kg = 90 g = 900 mL 10% amino acid
- Lipid 1 g/kg × 45 kg = 45 g = 450 mL 10% lipid
- Total 24 h fluid volume = 2250 mL; flow rate = 94 mL/h

Calories provided

- Glucose 3.4 kcal/g × 450 g = 1530 kcal
- Amino acid 4.0 kcal/g × 90 g = 360 kcal
- Lipids 9.0 kcal/g × 45 g = 405 kcal
- Total caloric intake = 2295; 51 kcal/kg/day

Caloric source

- Glucose = 66% Amino acid = 16% Lipids = 18%
- Non-protein calories = 1935
  6.25 g protein = 1 g nitrogen
- Total nitrogen = 90 g/6.25 = 14.4 g
- Non-protein calories: g nitrogen = 1935/14.4 = 134

substrate utilization. Complications associated with parenteral alimentation are presented in Box 14.9.

Jugular catheterization is the most common access route for PN therapy. Catheters should be of low reactivity and approximately 12–20 cm in length. The Arrow catheter (Arrow International Inc., Reading, PA 19610, USA) is a 16 G, 20 cm polyurethane catheter that is easy to insert using a short introduction trocar and guide wire. These catheters have been used in sick neonates for PN, drug and fluid therapy for as long as 2–3 wk without complications. All catheters should be inserted using aseptic technique. The catheterized vessel should be examined **at least daily** for signs of thrombosis and/or phlebitis. To reduce the risk of catheter-related sepsis and vessel thrombosis blood samples should not be withdrawn from the catheter dedicated to PN therapy. Volumetric infusion pumps, carefully regulated microdrip Buretrols or Solusets, or Dial-a-flow extension sets can be used to ensure accurate PN infusion rates.

Commonly used **stock solutions** for parenteral nutrition include 50% dextrose, 8.5% or 10% amino acids, and 10% or 20% lipid emulsion. Sample calculations for PN are presented in Box 14.10. Other commonly used additives include electrolyte, vitamin and trace mineral mixtures. Parenteral formulas must be compounded aseptically. The use of sterile, empty 3 or 4 L bags with 2 or 3 lead transfer sets (Baxter All-in-One 4 L bag; Baxter Healthcare Corp., Deerfield, IL, USA) facilitates mixing.

To maintain a suitable solution **pH for lipid solubility**, components should be added in the following order: glucose, amino acids and then lipids. Solutions should be refrigerated prior to use and vitamins and trace elements added just prior to administration.

Glucose solutions provide 3.4 kcal/g and are hypertonic at concentrations >5%. Five and 10% glucose solutions alone cannot provide adequate calories for the sick foal and would require infusion rates of 35 and 18 L day, respectively, to provide a 50 kg foal with 120 kcal/kg/day. When initiating parenteral alimentation, glucose infusion begins at 10 g/kg/day and can be increased at a rate of 1 g/kg/day up to 15 g/kg/day.

Lipid emulsions are isotonic, contain primarily long chain triglycerides and provide approximately 9–11 kcal/g. The addition of lipids to PN formulas is associated with a decreased incidence of vessel thrombosis that may be related to the decrease in total osmolality of the PN solution or a protective effect of lipids on vascular endothelium. Lipid infusion rates begin at 1 g/kg/day and can be increased up to 4 g/kg/day.

When insulin-resistant, sepsis-induced hyperglycemia restricts glucose administration in sick neonates, lipids can be used to provide up to 30–60% of non-protein calories. Impaired lipid clearance during sepsis or associated with prematurity may respond to **heparin administration** which augments lipoprotein lipase activity. Heparin can be given as a bolus at 10 units/kg or added to the PN solution at a rate of 1 unit/mL.

Lipid emulsions are not routinely administered to human infants with marked hyperbilirubinemia. Elevated concentrations of free fatty acids associated with lipid administration compete with bilirubin for albumin-binding sites resulting in reduced bilirubin clearance and exacerbation of **kernicterus** (deposition of unconjugated bilirubin in brain cells). Controversy also surrounds the use of lipids in foal neonates with severe pulmonary compromise. There is concern that lipid emulsion interferes with pulmonary microcirculation and gas exchange. Clinical complications associated with lipid administration to foals receiving mechanical ventilatory support, however, are rare. Compared with glucose, lipids are oxidized with a **lower respiratory quotient** (RQ of fat = 0.7; RQ of glucose = 1.0). Use of lipids in the ventilated patient could prove beneficial by reducing metabolic CO_2 production and min ventilation.

The most commonly used **protein solutions** are hypertonic, contain free amino acids with or without electrolytes, and provide approximately 4 kcal/g. Protein solutions are added to the PN formula to provide amino acids and nitrogen for growth and cellular repair. To prevent catabolism of protein for energy the ratio of non-protein calories to nitrogen should be approximately 100 to 200. In neonatal foals protein infusion rates range between 2 and 3 g/kg/day.

Since the daily requirements of **vitamins and trace minerals** are not available for neonatal foals, commercially available human pediatric preparations are commonly used. Potassium supplementation is required by foals not receiving enteral feeds. Foals receiving prolonged, complete PN require calcium and phosphorus supplementation. Only 25–50 mEq/L of calcium gluconate and 5–15 mEq/L of potassium phosphate can be added to PN solution without danger of precipitation. This amount of supplementation is still inadequate to support long-term growth and should be augmented by enteral mineral supplementation.

Parameters listed in Table 14.15 are used to monitor the patient's tolerance of the PN formulation. A foal must be weaned **slowly** onto and off parenteral

Table 14.15 Monitoring procedures for parenteral nutrition

Parameter	Monitoring frequency	
	During initiation of PN	After stabilization
Vital signs	q 4 h	q 8 h
Catheter/vein inspection	q 8 h	q 8 h
Fluid intake/urine output	q 8 h	q 12 h
Body weight	Daily	Daily
Urine glucose	q 6–8 h	q 12 h
Serum glucose	q 6–8 h	q 12–24 h
Serum electrolytes	q 24 h	1–2 × /wk
Creatinine/blood urea nitrogen	q 24 h	2 × /wk
Examine serum for lipemia	q 6–8 h	q 24 h
Triglycerides/cholesterol	Baseline	Weekly
Liver enzymes (GGT, LLDH, SAP)	Baseline	Weekly
Bilirubin	Baseline	Weekly
Hydration status:		
PCV/total protein	q 12–24 h	q 2–3 days
Capillary refill time	q 12 h	q 12 h
Leukogram	Baseline	Weekly
Fibrinogen	Baseline	Weekly

nutrition to allow acclimation of neuroendocrine hormones. Life-threatening **hypoglycemia** may develop if IV nutritional support is stopped suddenly or before adequate enteral nutrition has been initiated. Ideally, a foal should be consuming a minimum of 10% BW in milk daily before discontinuing all PN support.

A foal's daily fluid requirements are not met by the PN solution alone, and **additional balanced electrolyte solutions** are needed. Chronic PN administration has also been associated with an increased incidence of systemic **fungal infections** (*q.v.*) in neonatal foals.

RESPIRATORY SUPPORT

Assessment

Evaluation of the foal's respiratory system begins with physical examination to determine whether respiratory disease is present and, if so, what form of respiratory support is indicated. Signs of **respiratory distress** include tachypnea and increased work of breathing characterized by exaggerated abdominal effort, rib retractions, nostril flaring and expiratory grunting. Foals with severe lung disease display more labored breathing when recumbent and prefer to rest with head and neck extended.

Rapid, shallow respirations are common in foals with **restrictive lung disease** and/or **progressive atelectasis** (*q.v.*). Irregular breathing patterns are associated with prematurity and/or hypoxic damage to the central respiratory center. Unfortunately, thoracic auscultation is not a reliable means of assessing pulmonary disease in the foal and may fail to detect atelectasis and interstitial lung disease. Mucous membrane color is a relatively insensitive indicator of hypoxemia since cyanosis develops only after arterial oxygen (O_2)

concentrations are well below 40 mmHg. Hypercapnia has little effect on mucous membrane pallor.

Lateral radiographs obtained with the foal standing or recumbent help to characterize the nature and extent of pulmonary pathology. Diffuse pulmonary infiltrates occur with bacterial and/or viral pneumonia and atelectasis. Cranioventral and caudoventral pulmonary infiltrates are seen with aspiration pneumonia and bacterial bronchopneumonia. Nodular infiltrates suggest discrete abscessation. Ultrasonography is helpful to detect pleural effusion.

Arterial blood gas analysis

Arterial blood gas analysis determines the type and severity of respiratory dysfunction present and dictates the respiratory therapy indicated. The preferred site for arterial puncture is the **great metatarsal artery**. Other sites include the carotid, brachial, facial and femoral arteries. Arterial puncture requires a small 25 G needle attached to a heparinized 1 or 3 mL Luer slip syringe.

Once the sample is obtained, air bubbles should be removed promptly and the syringe sealed with a cork and kept on ice until analysis is performed. Pressure should be held at the puncture site for 3–5 min. An indwelling arterial catheter eliminates repetitive vessel puncture, but is difficult to maintain in an active foal and requires frequent flushing with heparinized saline or the use of a heparin lock.

The **partial pressure of arterial O_2** is usually between 70 and 100 mmHg in the normal foal. Hypoxemia does not contribute to ventilatory drive until it has fallen to pathologically low levels (<40–50 mmHg). However, tissue anoxia develops below an arterial O_2 tension of 60 mmHg.

Hypoxemia ($PaO_2 \leqslant 60$ mmHg, with a normal or low $PaCO_2$) is caused by ventilation–perfusion mismatching, right-to-left shunting (pulmonary or cardiac shunts), low inspired O_2 concentration, and impaired gas diffusion (*q.v.*). Hypoxemia accompanied by elevated carbon dioxide tensions (PCO_2) is usually the result of hypoventilation due to respiratory muscle fatigue, central depression of the respiratory center or neuromuscular weakness.

The main drive to respiration is the **partial pressure of arterial carbon dioxide**. In normal animals, respiration is controlled to achieve levels of CO_2 tensions of 35–45 mmHg. Any condition that decreases ventilation or increases metabolic rate disproportionately to ventilation results in an increase in $PaCO_2$ concentrations, a decrease in blood pH and respiratory acidosis. Carbon dioxide tensions >65–70 mmHg require mechanical ventilation to correct.

Oxygen therapy

Mild cases of hypoxemia may be improved by repositioning the laterally recumbent foal in **sternal recumbency** to reduce ventilation–perfusion mismatching associated with dependent lung atelectasis. **Persistent hypoxemia** requires oxygen supplementation using an intranasal cannula inserted to the level of the medial canthus. The cannula can be temporarily taped to the foal's muzzle or sutured to the external nares. **Humidified oxygen** is administered using a tank or wall oxygen source or oxygen concentrator and humidifier filled with distilled water.

Oxygen flows between 3 and 10 L/min are regulated using a flow meter attached to the humidifier. The oxygen tubing and cannula should be changed daily and checked frequently for obstruction with nasal secretions. Oxygen flow rates are adjusted to maintain arterial O_2 tensions between 70 and 100 mmHg.

Mechanical ventilation

Persistent hypoxemia that is refractory to nasal insufflation or is accompanied by arterial CO_2 tensions >70 mmHg necessitates **positive pressure ventilatory support**. Mechanical ventilation is time consuming, labor intensive and expensive. Complications associated with mechanical ventilation are presented in Box 14.11. Ideal candidates for mechanical ventilation should have potentially reversible lung disease. Before initiating treatment, the owner should be fully informed of the commitment required.

Short-term manual ventilation can be performed using a self-inflating rebreathing bag (Ambu bag), which can be used with room air or connected to an O_2 source via a reservoir bag to provide oxygen-enriched gases. An oxygen demand valve can also be used to deliver 100% O_2 during brief periods of manual ventilation such as post partum resuscitation. Prolonged periods of positive pressure ventilation require a **mechanical ventilator**.

Effective positive pressure ventilation requires nasotracheal or oral tracheal intubation. The disadvantages of oral intubation include excessive tube mobility and patient discomfort and intolerance. **Nasotracheal intubation** is better tolerated for prolonged periods of time in the conscious foal. Nasotracheal tubes should be a minimum of 50–55 cm long, composed of an inert plastic (preferably silicone) and have high-volume, low-pressure cuffs. Other equipment

Box 14.11 Complications associated with mechanical ventilation

- Air leaks: pneumothorax, pneumomediastinum, pulmonary interstitial emphysema
- Aerophagia, abdominal distension, gastrointestinal dysmotility, ulceration, gastric reflux
- Pneumonia, secondary to introduction of contaminated tracheobronchial secretions
- Asynchronous breathing or "bucking the ventilator", especially when synchronous intermittent mandatory ventilation is not used
- Nasotracheal tube trauma: pharyngitis, laryngitis, rhinitis, chondritis, tracheal stenosis, epistaxis, dysphagia
- Cardiovascular compromise associated with high airway pressures and excessive positive end expiratory pressures
- Bronchopulmonary dysplasia, barotraumas
- Oxygen toxicity
- Inappropriate airway humidification
- Equipment malfunction: delivery of inappropriate tidal volumes, oxygen concentrations, peak airway pressures; nasotracheal tube occlusion

required for mechanical ventilation includes a pressure-cycled or volume-cycled ventilator, an oxygen blender to deliver variable inspired oxygen concentrations, an oxygen analyzer to monitor blender accuracy, an in-line humidifier, and source of oxygen and compressed gas.

Guidelines for initial ventilator settings are as follows: tidal volume = 10–15 mL/kg, respiratory rate = 15–25 breaths/min, F_IO_2= 0.4–1.0, proximal airway pressure = 18–25 cmH_2O, end expiratory pressure = 0–8 cmH_2O, I:E ratio = 1:2. Additional programming changes are made according to arterial blood gas analysis.

Foals that continue to resist attempts at positive pressure ventilation require sedation. Low doses of **phenobarbital** (2–5 mg/kg given as a slow IV infusion) are usually quite effective.

Ventilators that allow foals to breathe spontaneously between pre-set ventilator breaths employ a synchronous, intermittent mandatory ventilatory (SIMV) mode. This ability to synchronize mandatory breaths with spontaneous breathing efforts eliminates a great deal of patient anxiety. Foals rarely require sedation when ventilated using SIMV.

To reduce the risk of oxygen toxicity the F_IO_2 should be reduced to 40 mmHg as soon as possible. The nasotracheal tube should be changed every 24–36 h, or more frequently if secretion accumulation is a problem. Sterile suctioning is performed as needed, but prolonged suctioning is avoided to prevent hypoxia. Arterial blood gases are monitored as needed to evaluate pulmonary function and adjust ventilator settings. A capnograph may be used to measure end tidal CO_2 concentration to reduce the number of invasive arterial punctures required.

Weaning from the ventilator is done slowly by decreasing the F_IO_2, peak airway pressure, positive end expiratory pressure, and number of ventilator delivered breaths. It is helpful to wean the foal onto continuous positive airway pressure (CPAP) or intranasal oxygen therapy and re-evaluate pulmonary function prior to discontinuing all forms of respiratory support.

Other forms of respiratory therapy

Foals have a **poorly developed cough reflex** and removal of tracheobronchial secretions may be difficult. **Chest coupage** using a cupped hand or electric percussor helps stimulate the natural cough reflex. **Ultrasonic or hydrosphere nebulizers** are used to administer a variety of agents such as saline to help moisten secretions, bicarbonate to act as a mucolytic agent, and bronchodilators to help relieve bronchospasm. **Nebulization followed by percussion** is often quite effective in mobilizing secretions.

Respiratory stimulants are used to treat **periodic apnea** (*q.v.*) and abnormally slow breathing patterns associated with central depression of the respiratory center. Chemical respiratory stimulants should be used **cautiously** in the foal since overdosing leads to excessive CNS, myocardial and gastrointestinal stimulation resulting in agitation, seizures, tachycardia, hypertension, colic and diarrhea. **Doxapram** is a general CNS stimulant with direct effects on the medullary respiratory centers. Although it produces transient increases in respiratory rate and tidal volume, these changes are accompanied by increases in work of breathing and myocardial oxygen consumption, resulting in little

change in oxygen tensions. Doxapram will stimulate ventilation when CNS depression is present, but will not reverse secondary apnea during cardiopulmonary arrest. Doxapram (0.2 mg/kg IV) should not be used in patients suffering from seizures, head trauma, cerebral edema or respiratory failure secondary to neuromuscular weakness.

Caffeine is used most frequently to stimulate the respiratory neuronal activity and increase receptor responsiveness to elevated carbon dioxide concentrations. Caffeine is the safest of the methylxanthines to use. The caffeine loading dose is 10 mg/kg administered orally followed by a maintenance dose of 2.5–3.0 mg/kg PO q 24 h.

Theophylline and **aminophylline**, both xanthine derivatives, are commonly used **bronchodilators** in foals but can also be used to improve diaphragmatic contractility and to treat **periodic apnea** associated with prematurity. Oral dosages and IV infusion rates are not available for the foal and must be extrapolated from the human literature. When calculating doses, 1.0 mg aminophylline equals approximately 0.8 mg theophylline. Adverse drug effects include excessive stimulation of the CNS and myocardium, and diuresis. The therapeutic range of theophylline in humans is 10–20 μg/mL. Therapeutic and toxic concentrations of theophylline have not been established for foals. Drug clearance is decreased and the potential for toxicity increased when these bronchodilators are administered concurrently with erythromycin or cimetidine. Terbutaline and albuterol have also been used for bronchodilation in the foal.

NEONATAL RESUSCITATION

INTRODUCTION

Cardiopulmonary emergencies in foals are the result of respiratory and/or circulatory failure that is usually secondary to systemic disease or failure to adapt during the immediate post partum period. Cardiopulmonary failure results in **hypoxic acidosis** that causes respiratory arrest followed by severe **bradycardia** and eventually asystole.

Cardiopulmonary failure may arise from:

1. Peri partum hypoxia leading to central respiratory center depression and/or myocardial damage resulting in hypoventilation and cardiac failure
2. Primary lung disease leading to hypoventilation and hypoxia
3. Circulatory failure due to septic or endotoxic shock
4. Hypovolemic or hemorrhagic shock
5. Severe metabolic acidosis
6. Hyperkalemia (e.g. uroperitoneum)
7. Vasovagal reflex
8. Hypothermia
9. Congenital cardiac defects.

Both **acute and chronic asphyxia** in the prenatal period may induce damage to multiple body systems. The compromised neonate suffering from the effects

of hypoxia may have **profound central nervous depression**, leading to respiratory center dysfunction and lack of stimulus to breathe, and respiratory acidosis. Metabolic acidosis occurs simultaneously, following the onset of anaerobic metabolism due to poor tissue perfusion. This further exacerbates both the respiratory failure and circulatory failure due to the effects on the hemoglobin–oxygen dissociation curve, the respiratory center and the myocardium.

Resuscitation of the neonate at birth may require no more than stimulation of breathing by methods such as palpation of the nasal mucous membranes, insertion of a finger in the ear, brisk rubbing of the thorax and extension of the limbs. The airways should be cleared manually, and with suction if necessary. **Coupage of the chest** will also help clear the airways. However, **cardiopulmonary resuscitation (CPR)** may be required at any time during the neonatal period, most frequently for severely depressed neonates immediately after birth, but also in foals that develop either respiratory or cardiac failure as a consequence of other diseases.

CPR refers to emergency treatment and initial stabilization. Its goal is to sustain life by providing an oxygenated blood supply to vital organs, in particular the brain and myocardium. The principles of CPR in foals are similar to those applied to other species.

A flow chart for CPR is given in Figure 14.1. The protocol and priorities for CPR can be memorized as **ABC**: **A**irway, **B**reathing, **C**irculation. In addition, emergency measures to address specific problems may also be required. For example, the airways may have to be suctioned to remove meconium, or the

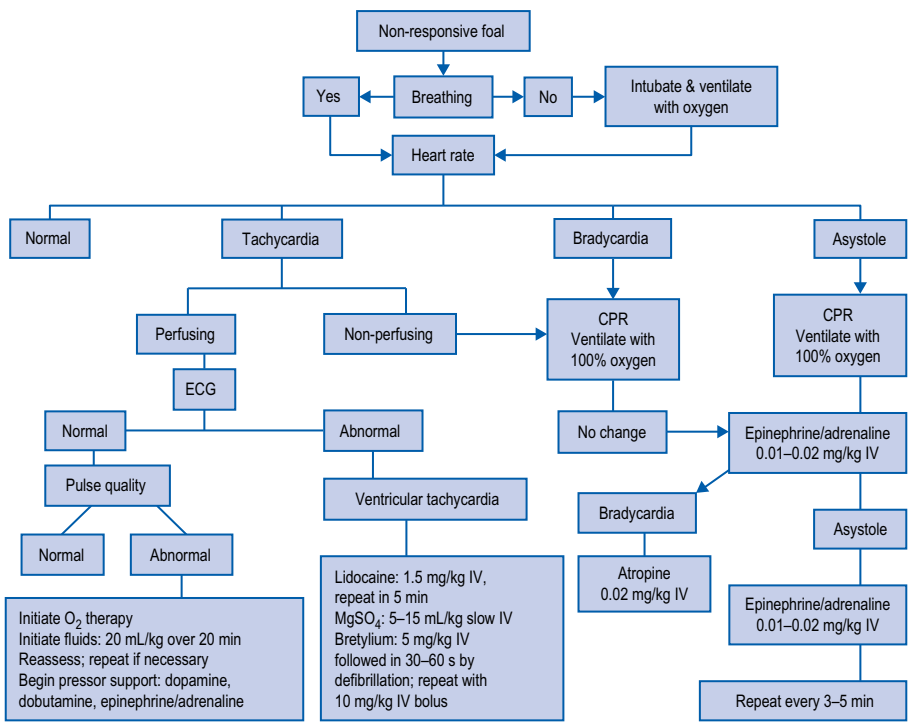

Figure 14.1 Flow chart for cardiopulmonary resuscitation.

stomach may have to be decompressed in foals with gastrointestinal obstruction. Nevertheless, a standardized protocol is most likely to be successful, and support of the respiratory and the circulatory systems must be given priority.

CPR is most likely to have a favorable outcome if a team of trained personnel work together and appropriate equipment is assembled and kept **ready in advance**. Table 14.16 lists the components of a **crash cart** and Table 14.17 details drugs required for CPR.

AIRWAY

Foals may be **intubated** via the nose or the mouth. The nose is preferred if the foal is likely to recover consciousness while intubated. Silicone tracheal tubes of 7–12 mm in diameter and 45–55 mm in length are preferred. Cuffed tubes allow positive pressure ventilation.

To insert the endotracheal tube, the foal should be positioned with its head in extension, and the curve of the tube directed ventrally. Once the tube reaches the level of the arytenoid cartilages it should be rotated to allow the bevelled end to spread the arytenoids. Correct placement is ascertained by compressing the chest and detecting air movement out of the tube. Palpation of the proximal esophagus during intubation also helps ensure proper placement of the tube.

Table 14.16 Equipment required for a neonatal crash cart

Airway	Cuffed silicone nasotracheal tubes (selection of sizes: 7–12 mm diameter, 45–55 mm in length) Suction device and catheters Nasal insufflation catheter and tubing Tracheostomy tube (7–10 mm diameter) Laryngoscope Tapes and suture Air syringe and sterile lubricating jelly
Breathing	Demand valve Ambu resuscitation bag Oxygen supply and equipment Tidal volume meter Heparinized syringes for blood gas samples
Circulation	Electrocardiograph, leads, alcohol spray Indirect blood pressure monitor Board to provide firm support for external cardiac massage Electrical defibrillator Intravenous catheters (selection of sizes: 14–18 G) Syringes, needles and fluid administration sets
Miscellaneous	Surgical gloves Surgical packs, suture and scalpels Floor padding or mattress Heat lamps, hot water bottles and blankets Thermometer Penlight Watch Record sheets and pen Stomach tube

Table 14.17 Dosages for emergency drugs in foals

Drug	Indications	Dosage	Complications
Epinephrine (adrenaline)	Asystole, pulseless electrical activity, bradycardia	Initial: 0.01–0.2 mg/kg IV Subsequent: 0.1 mg/kg IV IT; repeat q 3–5 min	Hypertension, tachyarrhythmias, increased cardiac O_2 demand
Atropine	Bradycardia not responsive to hyperventilation	0.02 mg/kg IV 0.04–0.06 mg/kg IT Repeat once in 5 min	Tachycardia; increased myocardial O_2 consumption, exacerbate hypoxia
Bretylium	Ventricular fibrillation, ventricular tachycardia	5 mg/kg IV undiluted followed in 30–60 s by defibrillation; repeat with 10 mg/kg IV bolus	Hypotension, hypertension, tachycardia
Calcium gluconate/chloride	Hyperkalemia, hypocalcemia, hypermagnesemia	10% Ca Gluconate: 0.6–0.75 mL/kg 10% Ca chloride: 0.2–0.25 mL/kg	Rapid infusion produces bradycardia; can result in rapid cell death in presence of hypoxia
Dexamethasone	Shock	5–10 mg/kg IV	Suppress immune function
Dextrose solution: 5–10%	Hypoglycemia, hyperkalemia	4–8 mg/kg/min CRI	Hyperglycemia, hyperosmolality
Dimethyl sulfoxide (DMSO)	Cerebral edema, reperfusion injury	0.5–1.0 g/kg as 10–20% solution given IV over 1–2 h	Concentrated solutions or rapid administration can cause hemolysis
Dobutamine	Hypotension	CRI: 1–20 μg/kg/min	Tachycardia, arrhythmias, hypertension
Dopamine	Hypotension, anuric/oliguric renal disease	CRI: 1–15 μg/kg/min; α-effect (pressor) at low doses; β-effect (inotrope) at higher doses	Tachycardia
Doxapram	Primary apnea, only if ventilation is not available	0.5–1.0 mg/kg IV, sublingual	Ineffective for secondary apnea; increases myocardial O_2 consumption; overdose can produce seizures
Furosemide	Diuretic: pulmonary edema/oliguric renal disease	1 mg/kg IV/IM CRI: 0.25–2.0 mg/kg/h	Dehydration, hypokalemia, enhances aminoglycoside toxicity
Hypertonic saline (7%)	Hypovolemic hypotension	4 mL/kg IV	Hypernatremia; use in conjunction with polyionic crystalloids
Insulin	Use with glucose to treat hyperkalemia associated with ruptured bladder	0.1 U/kg regular insulin IV with 0.5–1.0 g/kg dextrose IV	Hypoglycemia

Table 14.17 (*Continued*)

Drug	Indications	Dosage	Complications
Lidocaine	Ventricular fibrillation, ventricular tachycardia	Initial: 1.5 mg/kg IV, repeat in 5 min CRI: loading dose: 1.0 mg/kg IV followed by 20–50 μg/kg/min	Seizures, paresthesia, myocardial depression, circulatory depression
Magnesium sulfate (50%)	Refractory ventricular fibrillation	14–28 mg/kg, diluted to 10 mL in 5% dextrose in water, slow IV push	Hypotension
Plasma	Septic shock; improve oncotic pressure; support immune function	5–15 mL/kg IV over 1–3 h	
Polyionic fluids (non-glucose-containing fluids)	Hypovolemic/septic/hemorrhagic shock	20 mL/kg IV bolus; reassess, repeat if necessary	Fluid overloading exacerbates cardiac failure and may decrease coronary perfusion
Sodium bicarbonate	Hyperkalemia (ruptured bladder), severe metabolic acidosis	0.5–1.0 mEq/kg IV over 1–2 min; repeat once in 5–10 min if indicated	Hypernatremia and hyperosmolality with secondary cerebral hemorrhages, cardiac depression, left shift of oxyhemoglobin saturation curve

CRI, constant rate infusion; IT, intratracheal—via a catheter inserted in an endotracheal tube; IV, intravenous.

Once inserted, the cuff should be inflated until no airflow is detected from either nostril.

Tracheostomy is indicated if there is upper airway obstruction: a longitudinal incision is made on the ventral aspect of the neck, the tracheal ligament is incised, and a small (7–10 mm) tracheostomy tube is inserted between the tracheal rings.

Vacuum suction should be used to clear the airways of secretions, particularly if meconium has been aspirated. This should be performed prior to commencing ventilation, and periodically thereafter. However, excessive suction exacerbates hypoxemia and should be avoided. Suctioning should be followed by oxygen administration.

BREATHING

Mechanical ventilation may be achieved using a self-inflating resuscitation (Ambu) bag or an oxygen demand valve. **Oxygen** is preferred over room air for initial resuscitation. A respiratory rate of 15–25 breaths/min is required. The inspiration phase is continued until a complete chest excursion is achieved, avoiding excessive pressure (20–40 cmH_2O). The passive expiration phase should be two to four times the duration of inspiration. If **external cardiac**

massage is being conducted simultaneously, the rates should be coordinated to give 5–6 breaths per chest compression.

In foals that are breathing spontaneously but inefficiently (e.g. due to respiratory distress syndrome and atelectasis), arterial blood gas analysis is used to identify **hypercapnia**. Alternatively, it may be helpful to assess the spontaneous tidal volume with an appropriate tidal volume meter to determine the need for mechanical ventilation (normal tidal volume = 10–12 mL/kg). Careful evaluation of chest excursion and breathing pattern may be equally informative, and allow prompt identification of foals which will benefit from assisted ventilation.

The respiratory stimulant doxapram is not recommended in respiratory failure unless no form of positive ventilation is available. Doxapram is a CNS stimulant used to stimulate the respiratory center during primary apnea. In secondary (terminal) apnea, the respiratory center is no longer responsive to chemical stimuli, thus doxapram is not efficacious. In those foals in which it is effective in stimulating respiration, doxapram may be counterproductive in that it increases the oxygen demand of the myocardium in the face of prolonged hypoxia.

CIRCULATION

Support of the circulation is aimed at both maintenance of blood pressure and treatment of asystole or specific cardiac arrhythmias. Palpation of **peripheral pulses** and inspection of the **mucous membranes** are the initial means of evaluating perfusion.

An IV catheter should be inserted aseptically and **polyionic fluids** (e.g. Normosol-R, Plasmalyte, 0.9% saline) administered at a modest rate (e.g. 4–6 mL/kg/h) while evaluation of the patient proceeds. Overzealous fluid administration is contraindicated during asystole or non-perfusing rhythm. If volume replacement is necessary to treat severe dehydration, bolus administration is preferred rather than continuous high flow rates.

An **ECG** (*q.v.*) should be obtained. A lead II or base-apex strip is adequate to assess rhythm. Indirect arterial blood pressure is measured from the middle coccygeal artery, using an oscillometric or a Doppler sphygmomanometer.

Cardiac massage

Cardiac arrest is assumed if no palpable pulse is present; **external cardiac massage** should be instituted immediately. It is now known that the effects of external cardiac massage are not on the heart alone, but rather it acts as a **thoracic pump**. Increasing intrathoracic pressure, by compression of the chest, leads to the evacuation of the arteries and veins. Forward flow in the arteries is unimpeded, whereas retrograde flow in the veins is limited by the IV valves.

The primary aim of external cardiac massage is to generate **cerebral blood flow**. Chest compression is unlikely to support oxygenation for extended periods but it is effective in increasing blood flow in the short term. Re-establishing **coronary blood flow** is essential for return to a normal cardiac rhythm. During cardiac compression, coronary blood flow is restricted to the diastolic period. Diastolic aortic pressure determines coronary perfusion.

The foal is placed in **right lateral recumbency**, on a firm surface. External cardiac massage is performed by placing one palm on top of the other hand, and applying pressure **immediately behind the elbow**, in the fourth or fifth intercostal space. The pressure should be applied evenly, with a compression rate of 60–80/min. Approximately 35 kg of pressure is necessary for a 50 kg foal. Excessive pressure may result in rib fractures, visceral damage or pneumothorax.

The administration of **epinephrine/adrenaline** (initial dose 0.01–0.02 mg/kg IV or intratracheally [IT]; subsequent doses: 0.1 mg/kg IV/IT), a strong α-adrenergic agonist, increases arterial wall stiffness and total peripheral vascular resistance. This improves intrathoracic arterial blood flow by reducing the arteries' tendency to collapse. Other α-adrenergic effects include elevating systolic and diastolic pressures while decreasing splanchnic, renal, mucosal and dermal circulation. Epinephrine also has β-adrenergic effects that include increasing myocardial contractility and heart rate and relaxing bronchial smooth muscle. Epinephrine is the drug of choice during asystole because of its ability to improve coronary perfusion pressure. This is achieved by increasing diastolic aortic pressure and by increasing aortic tone.

Internal cardiac massage has been shown to be more effective than external methods in other species. Its use in horses has been described, however it has yet to be widely adopted in the equine neonatal intensive care unit.

Cardiac asystole and arrhythmias

Five **electrophysiologic abnormalities** are associated with cardiopulmonary failure: (1) asystole; (2) ventricular fibrillation; (3) electrical–mechanical dissociation; (4) ventricular tachycardia; and (5) profound bradycardia. An ECG (*q.v.*) must be obtained promptly so that the precise abnormality can be documented, and based on this, rational therapy instituted. The ECG features of these arrhythmias and appropriate pharmacologic agents for their treatment are listed in Table 14.18. Drug dosages are listed in Table 14.17.

Ventricular fibrillation is seen most commonly. **Electrical defibrillation** is the method of choice for treatment. However, this requires specialist equipment and trained personnel. Defibrillation is performed with an initial series of up to three rapid charges: 2 J/kg, 4 J/kg, 4 J/kg. Subsequent defibrillations of 4 J/kg can be performed 30–60 s after administration of epinephrine/adrenaline, lidocaine or bretylium. Large paddles are placed on either side of the heart, ensuring good chest contact.

Lidocaine is an effective pharmacologic agent for the treatment of ventricular fibrillation and ventricular tachycardia. Lidocaine suppresses ventricular arrhythmias by decreasing automaticity and decreasing conduction of re-entrant pathways. The drug prevents recurrence of ventricular fibrillation following conversion. It may be administered in **IV boluses** (1.0–1.5 mg/kg) or injected into the **trachea** via a catheter inserted in an endotracheal tube. This dose may be repeated at 3–5 min intervals. Use in conjunction with defibrillation.

Bretylium prevents recurrence of ventricular fibrillation or ventricular tachycardia (*q.v.*). Bretylium is an adrenergic neuronal blocker and is **synergistic with lidocaine**. Bretylium administered at 5 mg/kg IV can be followed in 30–60 s by defibrillation. If fibrillation persists, repeat with 10 mg/kg boluses. Do not administer more than a total dose of 35 mg/kg. Bretylium alone will

Table 14.18 Cardiac emergencies in foals

	ECG findings	Treatment
Asystole	Flat line	Epinephrine/adrenaline
Ventricular fibrillation	Chaotic (saw-tooth) undulations	Electrical defibrillation Lidocaine Bretylium Magnesium sulfate
Electrical–mechanical dissociation	Normal	Adrenaline
Ventricular tachycardia	Rapid ventricular complexes	Lidocaine Quinidine
Sinus bradycardia advanced 2nd degree and 3rd degree AV block	Infrequent complexes	Ventilate with oxygen Epinephrine/adrenaline Atropine Dopamine

not reverse ventricular fibrillation, but it may be beneficial in that the fibrillation pattern is made coarser and more amenable to correction. Similarly, epinephrine/adrenaline is used to convert asystole to ventricular fibrillation, which is then treated with electrical defibrillation or lidocaine.

Magnesium sulfate can be used for refractory ventricular fibrillation when counter shock, epinephrine/adrenaline, lidocaine and bretylium have been unsuccessful. Administer 14–28 mg/kg diluted to 10 mL in 5% dextrose in water as an IV push.

In **electrical–mechanical dissociation**, cardiac electrical activity is normal but no contraction occurs. Electrical–mechanical dissociation is recognized by a normal ECG accompanied by a blood pressure of less than 50 mmHg.

Epinephrine/adrenaline is administered to attempt to restore cardiac contractility. In the past, calcium was included in CPR protocols for its inotropic action. However, studies in humans have indicated that survival is not improved by calcium administration and it may be detrimental, as calcium influx is an end-stage process in myocardial necrosis. It should be reserved for use in cases with hypocalcemia, and for the treatment of hyperkalemia (e.g. uroperitoneum).

Vagally mediated, profound bradycardia is treated with **epinephrine/adrenaline** (0.01–0.02 mg/kg IV) or **dopamine** (sympathetic atropine: 0.02 mg/kg IV) stimulation; 1–10 μg/kg CRI) or with parasympatholytic agents such as glycopyrrolate or atropine (0.02 mg/kg IV). Most cases of neonatal bradycardia are caused by hypoxia and are treated by hyperventilation with 100% oxygen and epinephrine/adrenaline. Hypoxemia and hypercapnia stimulate the carotid body to increase vagal tone and produce secondary bradycardia. Hyperventilation results in lung inflation and stimulates pulmonary receptors that override the carotid body stimulus.

Occasionally, extreme intestinal distension may be associated with high vagal tone. **Atropine therapy** is indicated when hyperventilation and epinephrine/adrenaline are ineffective. Atropine is administered at a dose of 0.02 mg/kg IV

or 0.04–0.06 mg/kg intratracheally. Concurrent ventilation with oxygen is important since atropine may exacerbate the hypoxic insult by increasing the oxygen demand of the myocardium.

Ventricular tachycardia may occasionally be seen. In these foals, lidocaine is the drug of choice. Quinidine gluconate and bretylium may also be effective.

Cardiac arrhythmias are common in foals with **uroperitoneum** (*q.v.*), associated with hyperkalemia. Ventricular premature contractures, ventricular tachycardia and ventricular fibrillation are seen, but third degree atrioventricular block has been documented most frequently.

In foals in which **electrolyte disorders** are the underlying cause of cardiac arrhythmias, attempts should be made to correct these. Specific measures to reduce serum potassium include the administration of **insulin** (0.5 IU/kg), **dextrose** (2–4 g/unit of insulin used) and **sodium bicarbonate** (2 mEq/kg). Hypocalcemia may enhance potassium's arrhythmogenic effects, and calcium administration may be cardioprotective during hyperkalemia.

Pressure support

The restoration of **effective circulating volume** is essential to maintain blood pressure. Crystalloid (polyionic) or colloidal solutions, plasma or whole blood are all suitable alternatives. **Polyionic solutions** are most widely used, however colloidal solutions and plasma have the advantage that they are maintained in the intravascular space for longer. Fluids should be administered IV at up to 20 mL/kg/h. Hypertonic (7%) saline can be used to increase rapidly the effective circulating volume (see Table 14.17), but it is contraindicated in **renal failure** (*q.v.*), a common problem in asphyxiated and septicemic neonates.

The adrenergic agents **dopamine** and **dobutamine** are indicated if fluid administration alone does not increase blood pressure. Dopamine has dose-dependent effects. At low doses (1–3 μg/kg/min), it produces vasodilatation in the renal vascular beds, mediated through dopaminergic receptors. β_1-Adrenergic effects are induced by moderate doses (3–5 μg/kg/min), and these are responsible for dopamine's positive inotropic action. At high doses (greater than 5 μg/kg/min), α-adrenergic stimulation produces vasoconstriction. This may be detrimental and should be avoided.

Information on dopamine dose rates for foals has largely been extrapolated from other species and further research is required. Human neonates are less responsive to dopamine than adults, and, clinically, it appears that this may be true in foals. Therefore, dopamine administration must be **titrated to effect** in each individual foal.

Dobutamine is a synthetic adrenergic agent that produces strong β_1- and weak α-adrenergic effects. Consequently, it has strong inotropic effects. It is used alone, or in combination with dopamine, to provide pressor support (see Table 14.17).

Epinephrine/adrenaline CRI can also be used. Begin epinephrine/adrenaline administration at 0.1 μg/kg/min and titrate to effect up to 1 μg/kg/min or higher. Monitor for tachycardia.

If there is no response to traditional pressor therapy, **methylthioninium chloride** therapy (0.5–2 mg/kg IV) may be beneficial. Methylthioninium chloride blocks the action of **nitric oxide**, which is a potent vasodilator. **Naloxone**

has also been used to block endorphin-mediated hypotension as occurs during hemorrhagic and septic shock.

SUPPORTIVE THERAPY

The foal's respiratory and cardiovascular problems should be addressed first, but supportive therapy is also important. For example, **furosemide** (1.0 mg/kg IV) is indicated if **pulmonary edema** is present; antibiotic therapy should be instituted as appropriate; and plasma containing antibodies to endotoxin, or drugs such as **flunixin** may be useful.

Metabolic acidosis

In the presence of hypoxia and circulatory failure, **lactic acidosis** develops rapidly as anaerobic metabolism ensues. Administration of **sodium bicarbonate** may be indicated in profound metabolic acidosis. A severe base deficit (≥10 mEq/L) must be documented by blood gas analysis prior to administration of bicarbonate.

Acidosis depresses myocardial function, and correction with bicarbonate will improve the effectiveness of epinephrine. However, the use of bicarbonate in CPR protocols is becoming increasingly less popular as a growing body of evidence suggests that it may not be beneficial overall. Complications include metabolic alkalosis, hyperosmolarity, hypernatremia and intracranial hemorrhage. Bicarbonate is metabolized to carbon dioxide; therefore adequate ventilation must be established prior to the administration of bicarbonate in order to prevent the development of respiratory acidosis.

Hypoglycemia

The severely compromised neonate is frequently **profoundly hypoglycemic**. In septic and hypovolemic shock, increased catecholamine secretion and hypothermia may increase glucose utilization, and glucose production decreases in association with hepatic and endocrine dysfunction.

Neonates, particularly premature foals, may have insufficient glycogen stores. In utero, hypoxemia may deplete cardiac glycogen stores, impairing cardiac function during subsequent periods of hypoxemia. Dextrose should be administered IV at 4–8 mg/kg/min in a 5–10% solution for initial stabilization. Serum glucose concentrations can be monitored using a dextrometer, and should be frequently evaluated to guide replacement therapy and prevent post asphyxia hypoglycemia. Hyperglycemia should be avoided as this may exacerbate brain injury.

Body temperature

Neonates have limited ability to regulate temperature. Human neonates will lose 4°C in skin temperature in 5 min, and 2°C in core temperature in 20 min if left naked and wet in ambient temperatures. Similarly, **the wet newborn foal loses a large amount of heat by evaporation**. Newborn foals should be dried with towels.

Radiant heat is the most effective means of maintaining body temperature, and heated pads, hot water bottles (not hotter than can be comfortably held in the hand) and blankets are also useful. Rectal temperature should be monitored frequently (every 10–15 min during initial stabilization) to ensure that the foal does not become hyperthermic under radiant heat.

Cerebral edema and reperfusion injury

Reperfusion injury plays a central role in the pathogenesis of myocardial and cerebral damage induced by cardiopulmonary failure (*q.v.*). Free radical scavenging drugs such as **dimethyl sulfoxide (DMSO)** may help to minimize this process (see Table 14.17).

In foals, the use of mannitol to reduce cerebral edema is controversial. There is concern that it may exacerbate cerebral hemorrhage, which is associated with neonatal maladjustment syndrome. Consequently, mannitol should be avoided.

SURVIVAL FOLLOWING CARDIOPULMONARY ARREST

In human medicine, precise details are known of the prognosis following cardiopulmonary failure, particularly the neurologic outcome and long-term survival and their relationship to the duration of the period of arrest and the **APGAR score** (a clinical assessment used to identify hypoxic babies—see Table 14.9). Unfortunately, such information on long-term outcome is lacking for foals and there are no firm guidelines on the point at which CPR should be abandoned. In other species, neonates are more resistant to the effects of hypoxia than adults, and can survive longer periods of cerebral hypoxia.

In foals, the most useful clinical parameter on which to base termination of CPR is the absence of the **corneal reflex** as this reflects profound CNS dysfunction. It may also be helpful to decide the precise duration for which CPR will be continued in advance (for example 15 or 20 min) as this will ease the final decision to stop resuscitation.

DEVELOPMENT OF A NEONATAL INTENSIVE CARE SERVICE

The four essential ingredients for neonatal intensive care are: (1) facility; (2) laboratory support and equipment; (3) trained personnel; (4) knowledge of foal diseases and intensive care techniques.

THE FACILITY

The level of care can vary from basic supportive nursing care provided in a stall environment to round the clock monitoring in a specially designed facility.

Critically ill foals should be kept in a warm, quiet, well-ventilated but draught-free area, separate from any transient adult horse population. Whenever possible the **mare** should be kept within sight and smell of her foal to reduce neonatal stress and foster good maternal bonding.

Intensive care delivery is facilitated by a few **stall renovations**. Working on a recumbent foal in the presence of the dam requires a large stall (average size 3.7 × 5.5 m [12 × 18 ft]) with a sturdy, removable stall partition (approximately 1.2 m [4 ft]) in height. Fenestrated partitions constructed of stainless steel or aluminum are easily disinfected and allow the mare to see and smell her foal without obstructing ventilation.

Although clay and dirt floors provide the best footing for young foals, an easily disinfected surface is preferred. Heavy rubber textured mats are an ideal alternative. Lightweight wrestling mats provide additional padding for recumbent neonates. The ability to pad the walls and floor of a 1.2 × 1.8 m (4 × 6 ft) area in a stall corner allows confinement of foals at increased risk for self-trauma.

A centrally placed **swivel hook** in the ceiling above the foal side of the stall facilitates fluid administration, especially when used in conjunction with a coiled IV fluid administration set. Ceiling hooks can be used to suspend heat lamps and oxygen lines entering from either wall outlets or oxygen tanks or oxygen concentrators positioned outside the stall.

Good lighting is essential for reliable evaluation of mucous membranes, sclera and other physical examination parameters as well as for performing a variety of procedures including catheter placement. Easily accessible electrical outlets are mandatory for the wide array of equipment frequently employed during the work-up and care of a sick foal. A small refrigerator is an invaluable storage area for antibiotics and milk. Although a warm water bath can be used to rewarm cold milk and heat fluids, a microwave is more efficient.

Simple **hand washing** remains the most important means of infectious disease control among sick neonates. Therefore, a sink and mild antiseptic soap should be in close proximity of the mare and foal stall(s). Traffic into the foal care area should be limited.

LABORATORY SUPPORT

Foals sick with a variety of problems frequently **stop nursing** and experience varying degrees of hypoglycemia, dehydration and hypogammaglobulinemia (*q.v.*). Rapid evaluation of these parameters is essential to provide basic supportive care. A pocket size, battery-operated **glucometer** provides fast, stall-side glucose determination. A countertop microhematocrit centrifuge and a handheld refractometer will measure PCV and total protein concentration, respectively. Serum IgG concentration can be readily determined using a variety of easily performed assays that include zinc sulfate turbidity, latex agglutination and ELISA technology.

Critically ill foals are **metabolically unstable** and experience a variety of biochemical disturbances that are not apparent from physical examination alone. If serum biochemistries cannot be performed in the clinic, then arrangements should be made with an independent laboratory service capable of providing results within 6–12 h.

Sudden changes in the leukogram, such as leukopenia with a degenerative left shift signaling the onset of septicemia, may require **aggressive changes** in case management. **Same-day hematology** results are desirable. Changes in plasma fibrinogen concentration reflect more chronic trends in a patient's condition and same-day results are not mandatory.

Systemic and localized bacterial infections remain the most common problems of the newborn. The ability to perform bacteriologic cultures and cytology on blood and other body fluids is essential. Identification of offending pathogens and their antibiotic susceptibility patterns helps guide rational microbial therapy.

Hypoxemia and hypercapnia are difficult conditions to identify clinically. Although tissue damage begins once arterial O_2 concentrations decrease <60 mmHg, **cyanotic mucous membranes** only develop at arterial O_2 tensions <40 mmHg. Hypercapnia does not produce any appreciable change in mucous membrane color. Respiratory support is often initiated based on signs of respiratory distress. Arterial blood gas analysis characterizes the type and severity of pulmonary dysfunction and is essential if aggressive mechanical ventilatory support or prolonged respiratory therapy is anticipated.

EQUIPMENT

Equipment needs are dictated by the level of intensive care to be provided. A detailed list of supplies is presented in Table 14.19. Deep straw bedding is satisfactory for weak but ambulatory foals. Recumbent neonates require softer, more absorbent bedding to reduce the risk of **decubital sores**.

The ideal foal bed should be easily moved and cleaned. Options include a heavy-duty inflatable air mattress or twin bed mattress encased in a removable vinyl cover. **Water beds** can be used: they have the advantage of providing a temperature-controlled environment and the disadvantage of being cumbersome and difficult to move. Washable, synthetic fleece pads, available from most hospital supply companies, provide the ideal bedding to prevent pressure sores and can be used on any of the foal beds described. Towels, soft brushes and cornstarch containing baby powder assist in keeping foals dry and clean.

Foals unwilling or unable to nurse from the mare must be fed enterally by bottle, bucket or nasogastric tube, or parenterally using a variety of IV catheters and infusion devices. The mare can be **milked by hand** or with a human breast pump or udder pump. If artificial powdered milk replacer is used, a blender facilitates the mixing process. Foals with an effective suckle and swallow reflex can be fed using a baby bottle and selection of nipples.

Wide, shallow containers are ideal for bucket feeding. Nasogastric tubes should be soft and approximately 50–55 cm in length. Stallion urinary catheters or human enteral feeding tubes can be used as substitutes for commercially available, foal nasogastric tubes. Some form of flow regulating device (e.g. Dial-A-Flow extension set, Soluset, Buretrol, infusion pump) is needed to control delivery of parenteral alimentation.

Weak foals unable to nurse require **fluid therapy** in addition to nutritional support. Catheters should be available in a variety of gauges and lengths and made of low reactivity material such as polyurethane or polyvinyl chloride. In the dehydrated foal, catheters that use a short introduction trocar and guide wire are easier to insert than over-the-needle catheters with long stylets. Fluids commonly used for foals include 5% dextrose, 0.9% sodium chloride, 5% or 2.5% dextrose and 0.45% sodium chloride and a balanced electrolyte solution. Additives frequently required include concentrated bicarbonate, calcium,

Table 14.19 Equipment for neonatal intensive care

Bedding/stall supplies	Potential source
Mattress or equivalent with removable vinyl covering	Local department store
Synthetic fleece pads to reduce risk of decubital sores	Hospital supply companies
Pillows (with vinyl covers) to support foals in sternal recumbency	Local department stores
Wall mats to reduce risk of self-trauma	Dandy Products, Goshen, Ohio, USA www.dandyproductsinc.com
Soft flooring: Wrestling mats SoftStall	Stable Marketing, RR#1 Rockwood, Ontario NOB 2KP, Canada www.softstall.com
Assortment of towels, sheets and blankets	Local department stores
Baby powder with corn starch to keep intertriginous areas dry	Local pharmacy
Fluid and parenteral nutrition supplies	**Potential source**
Long-term polyurethane catheters	Arrow Catheter, Product ES-04301 16 G, 20 cm catheter with extension set Arrow International, Inc., Reading, PA, USA MILA catheter, Cat 1410 or 1610 14 or 16 G 20 cm catheter with extension set MILA International, Inc., Florence, KY, USA Milaint@worldnet.att.net
Coiled fluid administration set and extension sets	International WIN, Ltd., Kennett Square, PA 19348, USA Cook Veterinary Products, 127 South Main Street, PO Box 266, Spencer, IN, 47460, USA
Dial-A-Flow extension set	Abbott Labs, Inc., North Chicago, IL 60064, USA
Buretrol fluid regulator with 150 mL reservoir chamber	Travenol Labs, 1 Parkway North, Suite 430, Deerfield, IL, 60015, USA
Soluset fluid regulator with 150 mL reservoir chamber	Abbott Labs, Inc., North Chicago, IL 60064, USA
IV Backpack and 500 mL administration pump	MILA International, Inc., 7604 Dixie Highway, Florence, KY 41042, USA Milaint@worldnet.att.net
Infusion pumps, IV fluid poles	IMED Corporation, 9775 Business Park Avenue, San Diego, CA 92131, USA Baxter Healthcare Corporation, Deerfield, IL 60015, USA
Enteral feeding tube with Y-site proximal connector, tungsten weighted	Abbott Labs, Inc., North Chicago, IL 60064, USA
Parenteral nutrition supplies: 3-in-1 3 L TPN bags 8.5–10% Aminosyn 10–20% Liposyn 50% dextrose 5% dextrose 0.9% sodium chloride 5% dextrose/0.45% sodium chloride Balanced electrolyte solution Concentrated bicarbonate solution (8.4%) Sterile water 50% dextrose 23% calcium gluconate Potassium chloride (20 mEq/L)	Abbott Labs, Inc., North Chicago, IL 60064, USA

Table 14.19 (*Continued*)

Monitoring and diagnostic equipment	Potential source
Electrocardiograph	
Capnograph—end-tidal CO_2 monitor	Datascope Corp, Paramus, NJ 07652, USA
Indirect blood pressure monitor:	
Sphygmomanometer, blood pressure cuffs	Tyco Life Sciences, 95 Glenn Bridge Road, Arden, NC 28704, USA
Ultrasonic stethoscope with Doppler	Medasonics, Mountain View, A 94039, USA
Non-invasive oscillometric blood pressure monitor	Datascope Corporation, 580 Winters Avenue, Paramus, NJ 077632, USA Critikon Inc., 5820 West Cypress, Suite B, Tampa, FL 33634, USA Johnson and Johnson Medical, Arlington, TX 76004, USA
Ultrasound machine—sector scanner optimal with 3.0, 5.0, 7.5 MHz transducers	
Pulse oximeter	
Central venous pressure manometer	

Supplies to prevent/treat hypogammaglobulinemia	Potential sources
Methods to measure colostral IgG:	
Colostrometer	Lane Inc., Denver, CO 80222, USA
Eclipse colostrum refractometer	Bellingham and Stanley Inc., Lawrenceville, GA 30043, USA www.bs-rfm.com
Gamma-Check C	Veterinary Dynamics, Inc., Templeton, CA 93465, USA
Tests to determine IgG in foal serum:	
Midland Quick Test Kit	Midland BioProducts Corp, Boone, Iowa 50036, USA
Gamma-Check E	Veterinary Dynamics, Templeton, CA 93465, USA
Snap Foal Test	IDEXX, Blue Ridge Pharmaceutical, Westbrook, ME 04092, USA IDEXX Europe BV, Luchthaven Schipol, The Netherlands
Colostrum bank	
Hyperimmune equine plasma	Veterinary Dynamics, Templeton, CA 93465, USA Lake Immunogenics, Ontario, NY 14519, USA www.lakeimmunogenics.com
Seramune Oral (oral IgG supplement)	Sera Inc., Shawnee Mission, KS 66285, USA

Heating supplies	Potential sources
Micro-Temp circulating water blankets and pump	Jorgensen Labs, 1450 N. Van Buren Ave, Loveland, CO 80538, USA info@jorvet.com
Infrared heat lamps with thermostat	Kalglo Electronics Co., Inc., Bethlehem, PA 18017, USA www.kalglo.com
Hot water bottles	
Insulated blankets	Camping supply stores
Fluid and blanket warmer	

Respiratory support	Potential sources
Intranasal oxygen catheters	Jorgensen Labs, 1450 N. Van Buren Ave, Loveland, CO 80538, USA www.jorvet.com, info@jorvet.com
Oxygen tubing	
Oxygen humidifier	
Oxygen flow meter (1–15 L/min)	

(*Continued*)

Table 14.19 (*Continued*)

Respiratory support	Potential source
Oxygen source:	
Oxygen concentrator: 1–5 L/min or 1–10 L/min models	Jorgensen Labs, 1450 N. Van Buren Ave, Loveland, CO 80538, USA www.jorvet.com Respironics, www.respironics.com
Portable oxygen tanks or central supply using liquid oxygen	Home health care pharmacies
Cuffed silicone nasotracheal tubes: 50–55 cm long, selection of sizes (8, 9, 10, 11, 12 mm internal diameter)	Bivona Inc., Gary, IN 46406, USA Cook Veterinary Products, Bloomington, IN 47404, USA
Resuscitator with reservoir bag	Laerdal Medical, 1 Labriola Ct., Armonk, NY 10504, USA
McCullough Constant Delivery Foal Resuscitator with oxygen adaptor	McCullough Medical, McCullough Products Ltd., NSMC Auckland 1330, New Zealand SurgiVet (USA distributor) www.surgivet.com
Portable suction pump and suction tubing Nebulizer	Laerdal Medical, Armonk, NY 10504, USA
Compact portable suction pump	Laerdal Medical, Armonk, NY 10504, USA

Additional supplies for mechanical ventilation	Potential source
Pressure or volume cycled ventilator Selection of ventilation modes: control, assist control, SIMV[1], CPAP[2] Wide range of tidal volumes Peak flow range: 10–102 L/min PEEP[3]: 0–30 cmH_2O Audible and visible alarms for high/low pressures, apnea, low inspired tidal volume, variety of ventilator inoperative conditions In-line humidifier Oxygen analyzer Tidal volume monitor Source of compressed air in addition to oxygen Oxygen blender	

Laboratory supplies	Potential sources
Glucometer:	
ACCU-Check III	Boehringer-Mannheim Diagnostics, Indianapolis, IN 46250, USA
One Touch Glucometer	Johnson and Johnson, Arlington, TX 76004, USA
IRMA Blood Analysis System Series 2000	Diametrics Medical, St. Paul, MN 55113, USA
i-STAT Portable Clinical Analyzer	IDEXX, Blue Ridge Pharmaceutical, Westbrook, ME 04092, USA

Miscellaneous
Soft foal halters Selection of splints and bandage material Urinary catheters Enema bucket and tubing Refrigerator, freezer, microwave Clippers Scale Washer and dryer

[1] *SIMV, synchronized intermittent mandatory ventilation.*
[2] *CPAP, continuous positive airway pressure.*
[3] *PEEP, positive end expiratory pressure.*

potassium chloride and dextrose solutions. A coiled IV fluid administration set and fleece-lined fluid surcingle facilitate fluid administration in even a barn situation. Plasma and blood transfusions (*q.v.*) require special administration sets with appropriate filters.

Respiratory support covers a wide spectrum of techniques including post partum resuscitation, intranasal oxygen therapy, nebulization therapy, with percussion and mechanical positive pressure ventilation. Effective resuscitation can be performed using a nasotracheal tube and self-inflating resuscitator bag with or without oxygen enrichment or an oxygen demand valve. Intranasal oxygen therapy requires an intranasal or intratracheal cannula, oxygen tubing, and humidifier with flow meter and oxygen source.

An **oxygen concentrator** capable of delivering 5–10 L/min may be an attractive and affordable alternative to having compressed gas or liquid oxygen tanks in a clinic or farm setting. The concentrator requires only an electrical outlet. A variety of nebulizers are available that can be used to deliver solutions containing bronchodilators, mucolytic agents and wetting solutions. Foals in respiratory failure require positive pressure mechanical ventilation using a volume- or pressure-cycled ventilator, oxygen blender, oxygen analyzer, on-line humidification system and continuous supply of compressed air and oxygen.

Hypothermia plagues many sick foals. Correction of hypothermia complicated by severe dehydration and/or septic shock (*q.v.*) requires **volume repletion** in addition to any external warming aids. Ideally, the external environment itself should be warmed and draughts eliminated. To reduce environmental hazards and overheating of the patient, radiant heat lamps should be hung securely and equipped with a thermostat control. IV fluids can be warmed in either a microwave or commercially available insulated fluid jacket. Additional aids include warm water bottles and hot water pads strategically placed under an insulated blanket or blankets warmed in a dryer or commercial blanket warmer.

If **chronic intensive care** is anticipated, an electrocardiograph and indirect blood pressure monitor are recommended. Additional diagnostic aids include an ultrasound machine, preferably a sector scanner with 3, 5 and 7.5 MHz transducers. Ultrasonography is useful to diagnose a variety of problems including cardiac defects, ruptured bladder, umbilical remnant infection and intussusception. Radiography is helpful in evaluating thoracic and abdominal disease and a variety of musculoskeletal disorders including incomplete cuboidal bone ossification, angular limb deformities, and septic arthritis and/or osteomyelitis.

The equipment listed in Table 14.19 represents a comprehensive inventory required by an intensive care facility. If an **ambulatory foal service** is anticipated, the supply list can be reduced to those items required to provide resuscitation, intermittent intranasal oxygen and fluid therapy, plasma administration and enteral nutrition. A suggested pharmacy inventory is presented in Box 14.12.

PERSONNEL

The nucleus of any foal care program is the **support staff**. To maximize the chance of survival, the sick foal must be identified as soon as possible and its

Box 14.12 Suggested pharmacy inventory

Antibiotics, antifungal agents
- Procaine benzylpenicillin, benzylpenicillin in aqueous solution, or ampicillin
- Amikacin, gentamicin (potentially nephrotoxic)
- Trimethoprim–sulfamethoxazole
- Ceftiofur
- Oxytetracycline (for treatment of contracted tendons)
- Erythromycin
- Clarithromycin (for treatment of *Rhodococcus equi* infections)
- Rifampicin
- Fluconazole (antifungal agent)
- Metronidazole

Gastrointestinal drugs
- Acetylcysteine powder (6 g in 150 mL water as a retention enema)
- Sucralfate
- Ranitidine, cimetidine or famotidine
- Omeprazole
- Antacids
- Bismuth subsalicylate
- DTO Smectite: Biosponge (Platinum Performance Inc.)
- Metoclopramide
- Bethanechol
- Loperamide
- Probiotics
- Lactase tablets

Analgesics, sedatives, anti-inflammatory drugs
- Phenylbutazone
- Flunixin meglumine
- Ketoprofen
- Xylazine
- Detomidine (use with caution in sick neonatal foals)
- Butorphanol
- Dipyrone
- Acepromazine (for mare sedation)
- Dimethyl sulfoxide (DMSO)

Anticonvulsives and other CNS drugs
- Diazepam
- Phenobarbital
- Magnesium sulfate solution
- Thiamine
- Ascorbic acid
- Alpha tocopherol

Box 14.12 continues on page 867

Box 14.12 Suggested pharmacy inventory [continued]

Cardiac and renal drugs
- Lidocaine
- Epinephrine/adrenaline
- Bretylium
- Dopamine
- Dobutamine
- Mannitol
- Furosemide

Miscellaneous
- Oxytocin
- Domperidone
- Bronchodilators: albuterol, clenbuterol
- Caffeine
- Ophthalmic ointments/solutions
- Antibiotic preparation without steroids
- Steroid preparation: prednisolone acetate or dexamethasone
- Atropine
- Acetylcysteine
- Artificial tears
- Fluorescein strips (to detect corneal ulcers)

progress monitored frequently by **trained observers**. Continuing education programs offering information on mare/foal husbandry and foal diseases serve to educate stud farm personnel and hospital attendants and to attract the additional workers required during the foaling season.

The level of care required by even a few critically ill foals can be extremely labor intensive, and a pool of trained, temporary "foal sitters" is essential. Eager volunteers can often be found among preprofessional students in search of veterinary experience. In the academic setting, veterinary students provide invaluable assistance in the neonatal ICU. Additional nursing support can be found in the local community among interested horsemen and women, but reliability and commitment are usually improved if the seasonal positions are offered at wages considered competitive within the horse community.

KNOWLEDGE OF NEONATOLOGY AND INTENSIVE CARE TECHNIQUES

Veterinarians and their attendants interested in providing critical foal care must remain current in their knowledge of foal diseases and critical care methodologies. Veterinarians usually have little difficulty meeting this obligation; however, many practices overlook the tremendous advantage of having one or more well-trained **veterinary nurses**. These individuals should be encouraged to enhance their skills and experience by attending formal veterinary programs and by establishing a close working relationship with their counterparts in the human neonatal nursing field.

Chapter 15

The musculoskeletal system

M. H. MacDonald (Consultant Editor), N. Kannegieter, J. F. Peroni and Wm. E. Merfy

Chapter contents

INTRODUCTION

Most horses are produced and kept for athletic purposes although ambitions range from intermittent use for pleasure riding to the extreme demands placed on the elite racing Thoroughbred. Whatever the requirements, **lameness** is the greatest contributor to loss of performance, missed training and attrition of horses, and consequently is the **single most common problem** of equine practice.

Disturbances of the locomotor system have attracted research funds and initiatives such that the equine veterinary literature abounds with advances in diagnostic and treatment modalities. Understanding in this field exceeds that of other domestic species and therefore the services available to horses are similar to those provided for human athletes.

The conditions encountered daily in general veterinary practice range from ill-fitting shoes through developmental conditions to long bone fractures. Accurate diagnosis and understanding of pathophysiology are vital for appropriate early case management. These areas are therefore highlighted in this section. Emphasis is also placed on the management of common problems; more esoteric considerations can be made after additional investigation of the literature or at a referral center.

Despite advances in imaging modalities, diagnostic **local analgesia** remains pivotal in the investigation of equine lameness. Understanding of basic local analgesic techniques is therefore necessary for all who evaluate lame horses.

DIAGNOSTIC LOCAL ANALGESIA

The importance of diagnostic local analgesia in the investigation of equine lameness has been well documented. Typically this involves perineural or

regional analgesia and intrasynovial analgesia although epidural analgesic techniques (*q.v.*) are frequently used for treatment of orthopedic pain.

The judicious use of local analgesia in the investigation of equine lameness should be deferred until a **thorough clinical appraisal**, including assessment of the gait abnormality, limb palpation, etc., has been completed. This is particularly true when the history or performance level suggests that there may be a nondisplaced fracture or serious soft tissue injury.

Fortunately, aberrant distribution of the appendicular nervous system is uncommon in horses. There are few indications for the use of ring blocks or field blocks as diagnostic techniques because they usually produce little more than cutaneous desensitization. However, when aberrant nerve routes are suspected they may be a useful adjunct to perineural analgesia.

When possible, **intrasynovial analgesia** should precede perineural infiltration when involvement of a specific joint, bursa or tendon sheath is suspected, since this will not interfere adversely with the interpretation of subsequent regional blockade. The reverse is, however, not true. Moreover it is acceptable to "leapfrog" with intrasynovial techniques whereas perineural analgesia should be performed in a **sequential manner** beginning distally. Intrasynovial analgesia is usually specific, and periarticular structures such as ligaments and tendons usually retain sensation. There are a few notable exceptions to this generalization, including intra-articular (IA) anesthesia of the distal interphalangeal joint.

Local analgesics are salts of weak bases in aqueous solution. Penetration and diffusion in tissues is determined by their lipid solubility. These salts dissociate in neutral or alkaline areas, and are therefore not as active in acid media, e.g. **infected sites**. The local analgesic cation binds to anionic receptors on the nerve fiber blocking the sodium channels. As a result, sodium entry and depolarization are prevented. This is referred to as a non-depolarizing block. Since the myelin sheath of nerves is both an electrical and pharmacologic insulator, access of local analgesic to myelinated fibers is limited to the nodes of Ranvier and so a higher concentration of agent is necessary to induce anesthesia of myelinated compared with non-myelinated nerves.

Although transmission in all nerve fibers can be blocked by local anesthetics, there is generally a **difference in susceptibility** of various types of nerves. Sensations disappear in order from pain, cold, warmth, light touch, joint proprioception to deep pressure, and return in the reverse order. As a result, when desensitizing a peripheral nerve, **differential blockade** may be produced—pain may be overcome completely (i.e. type A-δ and C fibers are blocked) but motor function and touch (type A-α and A-β fibers) can remain unaffected.

Once the local anesthetic agent has been deposited around a nerve it diffuses from outside toward the center. Small diameter nerve trunks are therefore more susceptible to blockade than large nerves. In addition, since the most distal limb elements supplied by a particular nerve are the core fibers, and therefore blocked last, the most pertinent tests of efficacy are performed as far distal to the site of infusion as possible.

Following vascular removal from a site, agents are detoxified by liver and plasma pseudocholinesterases (principally the former) and metabolites are excreted by the kidneys.

The three most suitable local analgesic agents are:

1. Mepivacaine hydrochloride 2%
2. Lidocaine hydrochloride 2%
3. Bupivacaine hydrochloride 0.5% and 0.75%.

Two per cent mepivacaine hydrochloride is widely used and demonstrates reduced local tissue reaction in equines, particularly with IA infusion. Systemic toxicity is unlikely to be a problem at dose rates up to 10 mg/kg in local infiltration. However, both systemic and local reactions can occur with repeated doses, and inadvertent rapid IV injections can produce initial excitement followed by CNS depression. **Intravenous barbiturate** is the treatment of choice if an **overdose** is suspected.

All local anesthetic agents (with the exception of cocaine) cause **peripheral vasodilatation**, thereby enhancing vascular absorption, although the intensity of response varies with the site of injection, dosage and between individual agents. The duration of action of mepivacaine and lidocaine is reported to be as short as 45–60 min. However, clinical experience suggests that these times are frequently exceeded and there are reports that effects persist for up to 3 h. **Bupivacaine** has a duration of action of up to 6 h and is therefore a useful agent when sedation is required for administration of a diagnostic block.

The **duration of action** of all agents is prolonged by the addition of a vasoconstrictor, e.g. epinephrine/adrenaline hydrochloride. Systemic toxicity is also reduced but at a price, since prolonged local exposure will increase the effects of tissue irritation at the site of injection. Epinephrine/adrenaline at 1 in 50 000 dilution results in **local tissue ischemia** and necrosis. Generally 1 in 100 000 or 1 in 200 000 is adequate and will almost double the duration of local anesthetic action, but even at these concentrations the subsequent production of white hairs at nerve block sites can be a problem, and epinephrine/adrenaline is generally avoided.

Clean injection techniques are essential when performing perineural local analgesia, and aseptic technique is mandatory for IA procedures or for performing regional nerve blocks that can inadvertently enter a synovial cavity. Appropriate aseptic technique requires **full surgical skin preparation**, and wearing sterile surgical gloves. Studies have shown that it is not necessary to clip the hair over the injection site, but with a heavy haircoat or gross contamination of the area it may be advisable to do so. Many experienced practitioners still routinely clip before synovial injection.

A **new vial** of local anesthetic should be used for intrasynovial analgesic administration.

Many of the inflammatory reactions that occur following local analgesic techniques are probably due to poor technique including **iatrogenic contamination**. While antibiotics are not usually necessary when intrasynovial analgesia is undertaken, if conditions are less than ideal or repeated injections are required, they can be added. It is important to select antibiotics that **do not precipitate** when mixed with the local anesthetic agent (i.e. 2% lidocaine mixed with penicillin or ampicillin). The aminoglycosides **gentamicin** (300 mg) and **amikacin** (250 mg) can be mixed with local anesthetics without precipitating and they maintain their antibiotic efficacy in the mixture. Consequently, they are used regularly, particularly when there is a concern about potential contamination or when sepsis is already present.

PRACTICAL ASPECTS OF DIAGNOSTIC LOCAL ANESTHESIA

General

The minimal amount of **restraint** conducive to good technique and personal safety is recommended. When the technique in question is most easily performed with the limb weight bearing then an assistant lifting another leg is often the most effective option. A twitch can be employed when necessary and in some circumstances sedation may be required.

There are obvious difficulties in interpretation of local analgesia of a sedated animal, and a sedative with a shorter duration of action than the local anesthetic should be utilized. **Intravenous xylazine** (*q.v.*) is often the drug of choice, although almost any sedative or sedative combination can be employed if bupivacaine is used. When xylazine or another α_2-agnoist is used, the sedation can also be reversed with an appropriate antagonist such as **atipamezole** or yohimbine to allow for earlier re-evaluation. Nervous horses can be sedated with low doses of acetylpromazine (0.02 mg/kg IV or 0.04 mg/kg IM). The drug should be administered before evaluating the horse's baseline lameness, as the sedation can actually facilitate the examination and augment lameness.

For injection around **deep nerve trunks**, e.g. median nerve or tibial nerve, and for difficult intrasynovial infusions or fractious horses, a small SC bleb of local anesthetic greatly facilitates the procedure. Eliminating patient movement increases the accuracy of placement and reduces iatrogenic damage.

During intrasynovial techniques, accuracy of placement can be ensured by aspirating synovial fluid before infusion although this is not possible in all locations. It is **not necessary** to withdraw the same volume of synovial fluid as of the local analgesic agent to be infused. When synovial fluid cannot be aspirated, careful movement of the needle can also be used to confirm IA or intrasynovial placement. This can usually be supported by observation of the site as injection proceeds. **Ultrasound** can also be invaluable in guiding difficult intrasynovial injections, e.g. the coxofemoral joint.

There is general agreement that approximately 5–10 min should be allowed for regional blockade to be effective and 15–30 min for intrasynovial analgesia. However, there is significant variation in these times between sites and between individual patients, e.g. some intrasynovial techniques have shown responses in <5 min and some proximal (large) perineural blocks may take >30 min for full effect. During this time the horse is usually walked quietly to become accustomed to the desensitized area and to provide diffusion of intrasynovial anesthetic agents before reassessing the animal's gait and, where appropriate, the quality of the block.

Evaluation of the efficacy of perineural local analgesia requires knowledge of the zones of cutaneous innervation provided by individual nerves together with the deeper structures supplied. Whenever possible both should be evaluated.

Individual techniques

Details of forelimb and hindlimb regional and intrasynovial analgesia are given in Table 15.1.

Table 15.1 Techniques for diagnostic local anesthesia

Site	Needle	Volume[1]
FORELIMB REGIONAL ANALGESIA		
Palmar digital nerves		
SC between the mid-pastern and the proximal border of the cartilages of the distal phalanx, immediately palmar to the medial and lateral palmar digital arteries *or* SC just distal to the proximal border of the cartilages of the distal phalanx, immediately palmar to the medial and lateral palmar digital arteries	0.5 × 16 mm (25 G × 5/8")	1–1.5 mL (avoid larger volumes to prevent spread through fascial planes to the dorsal branches of the palmar nerves)
Site	**Structures desensitized**	
SC between the mid-pastern and the proximal border of the cartilages of the distal phalanx, immediately palmar to the medial and lateral palmar digital arteries *or* SC just distal to the proximal border of the cartilages of the distal phalanx, immediately palmar to the medial and lateral palmar digital arteries	Navicular bone, navicular bursa, collateral sesamoidean and distal sesamoidean impar ligaments, insertion of the distal sesamoidean ligaments, distal DDFT and associated digital synovial sheath, insertion of the SDFT, digital cushion, palmar laminar corium and corium of sole and frog, palmar solar and variable amounts of dorsal distal phalanx, collateral cartilages, most of the distal interphalangeal joint, collateral ligaments of the distal interphalangeal joint, palmar aspect of the proximal interphalangeal joint, skin over the heel bulbs	
Site	**Needle**	**Volume[1]**
Palmar nerves at the level of the proximal sesamoids (abaxial sesamoid block)		
SC immediately palmar to the medial and lateral palmar arteries over the abaxial surfaces of the proximal sesamoid bones *or* SC immediately palmar to the medial and lateral palmar arteries at the base of the proximal sesamoid bones	0.5 × 16 mm (25 G × 5/8")	2–3 mL
Site	**Structures desensitized**	
SC immediately palmar to the medial and lateral palmar arteries over the abaxial surfaces of the proximal sesamoid bones *or* SC immediately palmar to the medial and lateral palmar arteries at the base of the proximal sesamoid bones	As noted for palmar digital nerves plus remaining content of the hoof, middle phalanx and associated soft tissues, proximal and distal interphalangeal joints, distal and palmar aspects of proximal phalanx and associated soft tissues, distal sesamoidean ligaments, occasionally portions of the metacarpophalangeal joint, skin over medial lateral and palmar aspects of the pastern and variable areas of skin dorsally from coronary band to proximal phalanx	

DDFT, deep digital flexor tendon; SDFT, superficial digital flexor tendon. (*Continued*)

[1] *All volumes of local anesthetic agent are for 2% mepivacaine hydrochloride.*

Table 15.1 (*Continued*)

Site	Needle	Volume[1]
Low palmar (a) and palmar metacarpal (b) nerves (low four-point block, low volar block)		
(a) Just dorsal to the DDFT and palmar to the suspensory ligament at the level of the button of the second and fourth metacarpal bones (or slightly higher if the digital sheath is distended) medially and laterally in the subcutaneous space	0.7 × 25 mm (22 G × 1")	2–3 mL
(b) Immediately distal to and at the depth of the buttons of the second and fourth metacarpal bones	0.5 × 16 mm (25 G × 5/8")	1–2 mL
Site	**Structures desensitized**	
(a) Just dorsal to the DDFT and palmar to the suspensory ligament at the level of the button of the second and fourth metacarpal bones (or slightly higher if the digital sheath is distended) medially and laterally in the subcutaneous space (b) Immediately distal to and at the depth of the buttons of the second and fourth metacarpal bones	As noted for abaxial sesamoid block plus the entire metacarpophalangeal joint and associated tendons and ligaments, proximal sesamoid bones and associated soft tissues, distal third metacarpal bone, digital synovial sheath and enclosed flexor tendons, branches of the suspensory ligament and their insertions, skin over the dorsal aspect of the proximal phalanx and skin over most of the fetlock, but some skin sensation may be present over the dorsal surface of the fetlock	
Site	**Needle**	**Volume[1]**
High palmar (a) and palmar metacarpal (b) nerves (high four-point block, subcarpal block)		
(a) Medially and laterally adjacent to the DDFT palmar to the suspensory ligament in the proximal metacarpus beneath a heavy fascial layer	0.5 × 16 mm (25 G × 5/8")	2–3 mL
(b) Axial to the heads of the second and fourth metacarpal bones and adjacent to the suspensory ligament	0.7 × 25 mm (22 G × 1")	3–5 mL
Site	**Structures desensitized**	
(a) Medially and laterally adjacent to the DDFT palmar to the suspensory ligament in the proximal metacarpus beneath a heavy fascial layer (b) Axial to the heads of the second and fourth metacarpal bones and adjacent to the suspensory ligament	As noted for the low four-point block plus the DDFT and SDFT, accessory ligament of the DDFT, suspensory ligament, metacarpal bones and associated interosseous ligaments, skin over the palmar metacarpus. The carpometacarpal and middle carpal joints may be blocked inadvertently	
Site	**Needle**	**Volume[1]**
Lateral palmar nerve block (high two-point block)		
Laterally at a point midway between the accessory carpal bone and the head of the fourth metacarpal bone through the palmar border of the accessoriometacarpal ligament. Anesthetic must be injected beneath the flexor retinaculum	0.7 × 25 mm (22 G × 1")	5–6 mL

Table 15.1 (*Continued*)

Site	Structures desensitized	
Laterally at a point midway between the accessory carpal bone and the head of the fourth metacarpal bone through the palmar border of the accessoriometacarpal ligament. Anesthetic must be injected beneath the flexor retinaculum	Can be used in conjunction with the high medial palmar nerve block (high two-point block) to block the structures noted for the high four-point block with a lower risk of inadvertently blocking the middle carpal and carpometacarpal joints. The carpal canal may be blocked unintentionally.	
Site	**Needle**	**Volume[1]**
Median (a) and ulnar (b) nerves		
(a) Medially, 5 cm below the elbow joint, in dense fascia at a depth of 2–3.5 cm, adjacent to the caudomedial border of the radius and the median artery in the angle between the superficial pectoral and flexor carpi radialis muscles	1.1 × 38.1 mm (19 G × 1.5")	10–15 mL
(b) Beneath the antebrachial fascia, at a depth of 1–1.5 cm in the groove between the flexor carpi ulnaris and ulnaris lateralis, approximately 10 cm (one hand's breadth) proximal to the accessory carpal bone on the caudal aspect of the forelimb	0.9 × 38.1 mm (20 G × 1.5")	10–12 mL (as withdrawn an additional 2 mL is injected)
Site	**Structures desensitized**	
(a) Medially, 5 cm below the elbow joint, in dense fascia at a depth of 2–3.5 cm, adjacent to the caudomedial border of the radius and the median artery in the angle between the superficial pectoral and flexor carpi radialis muscles (b) Beneath the antebrachial fascia, at a depth of 1–1.5 cm in the groove between the flexor carpi ulnaris and ulnaris lateralis, approximately 10 cm (one hand's breadth) proximal to the accessory carpal bone on the caudal aspect of the forelimb	In addition to structures blocked with a high four-point block, the radiocarpal, middle carpal and carpometacarpal joints and associated carpal ligaments, carpal canals and enclosed tendons, and distal radius	
Site	**Needle**	**Volume[1]**
FORELIMB INTRASYNOVIAL ANESTHESIA[2]		
Navicular bursa[3]		
Palmar midline through the digital fossa between the bulbs of the heels, parallel to the bearing surface until contact is made with the navicular bone. Radiographic control or ultrasound guidance is required to confirm location	1.2 × 89 mm (18 G × 3.5")	2–4 mL
Site	**Needle**	**Volume[1]**
Distal interphalangeal (coffin) joint[4]		
Either adjacent to the common digital extensor tendon or through the tendon on dorsal midline, and 1.5 cm proximal to the coronary band; direct the needle distally and toward the mid-sagittal plane	1.1 × 38.1 mm (19 G × 1.5")	3–6 mL

[2] Alternative methods of intrasynovial anesthesia of the forelimb and hindlimb have been described in the literature for many of these sites.
[3] More than five different approaches to the navicular bursa have been described and compared in the literature.
[4] Lateral and palmar approaches to the distal interphalangeal joint have also been described.

(*Continued*)

Table 15.1 (*Continued*)

Site	Structures desensitized	
Distal interphalangeal (coffin) joint[4]		
Either adjacent to the common digital extensor tendon or through the tendon on dorsal midline, and 1.5 cm proximal to the coronary band; direct the needle distally and toward the mid-sagittal plane	Analgesia of the distal interphalangeal joint is not specific for IA pain and can eliminate pain associated with many conditions of the foot including navicular syndrome and sole pain	
Site	**Needle**	**Volume[1]**
Proximal interphalangeal (pastern) joint[5]		
1.5 cm from the midline and below the palpable palmar condylar eminence of the first phalanx; insert the needle underneath the extensor tendon directed distally and toward the mid-sagittal plane	0.9 × 38.1 mm (20 G × 1.5″)	4–5 mL
Site	**Needle**	**Volume[1]**
Metacarpophalangeal (fetlock) joint[6]		
Into the palmar pouch through or adjacent (proximal or distal) to the collateral sesamoidean ligament	0.9 × 25 mm (20 G × 1″)	5–7 mL
Site	**Needle**	**Volume[1]**
Digital flexor tendon sheath[7]		
Proximal to the proximal sesamoids and palmar annular ligament, and adjacent to the DDFT *or* On the palmar aspect of the pastern distal to the palmar annular ligament at the level of the proximal interphalangeal joint	0.9 × 25 mm (20 G × 1″)	5–7 mL
Site	**Needle**	**Volume[1]**
Middle carpal and carpometacarpal joint		
Medial or lateral to the extensor carpi radialis tendon and sheath with the limb flexed *or* Adjacent to the ulnar/fourth carpal articular palmarolaterally with the limb extended	1.1 × 38.1 mm (19 G × 1.5″) 0.9 × 25 mm (20 G × 1″)	5–8 mL

[5] *Dorsal midline and palmaroproximal injection sites have also been described.*

[6] *A dorsal approach to the metacarpophalangeal joint is often utilized to distend the joint prior to arthroscopic surgery, and can be used diagnostically as well.*

[7] *An alternative approach made axial to the midbody of the proximal sesamoid bone through the annular ligament with the fetlock joint flexed is particularly valuable when the sheath is not distended and is difficult to palpate proximal or distal to the annular ligament.*

Table 15.1 (*Continued*)

Site	Structures desensitized
Medial or lateral to the extensor carpi radialis tendon and sheath with the limb flexed *or* Adjacent to the ulnar/fourth carpal articular palmarolaterally with the limb extended	The carpometacarpal and middle carpal joints reliably communicate. Palmar pouches of the carpometacarpal joint can desensitize the origin of the suspensory ligament and the proximal palmar metacarpal region

Site	Needle	Volume[1]
Antebrachiocarpal joint		
Medial or lateral to the extensor carpi radialis tendon and sheath with the limb flexed, *or* Adjacent to the radius proximal to the accessory carpal/ulnar carpal bone articulation palmarolaterally with the limb extended	1.1 × 38.1 mm (19 G × 1.5″) 0.9 × 25 mm (20 G × 1″)	5–8 mL

Site	Needle	Volume[1]
Carpal sheath		
Palmarolaterally just proximal to the accessory carpal bone between the lateral digital extensor and the ulnaris lateralis tendons *or* On the palmaromedial aspect of the proximal metacarpus between the DDFT and accessory ligament of the DDFT	0.9 × 38.1 mm (20 G × 1.5″)	5–7 mL

Site	Needle	Volume[1]
Cubital (elbow) joint[8]		
Immediately cranial or caudal to the lateral collateral ligament distal to the lateral epicondyle of the humerus *or* Caudolateral approach cranial and distal to the olecranon process directing needle craniomedially into the caudolateral joint pouch	0.9 × 38.1 mm (20 G × 1.5″) 1.1 × 38.1 mm (19 G × 1.5″)	10–15 mL

Site	Structures desensitized
Immediately cranial or caudal to the lateral collateral ligament distal to the lateral epicondyle of the humerus *or* Caudolateral approach cranial and distal to the olecranon process directing needle craniomedially into the caudolateral joint pouch	A needle placed just caudal to the lateral collateral ligament enters the bursa of the ulnaris lateralis muscle and this bursa does not always communicate with the joint

[8] *A number of modifications of these approaches to the cubital joint have been reported.* (*Continued*)

Table 15.1 (*Continued*)

Site	Needle	Volume[1]
Scapulohumeral (shoulder) joint		
Through the notch between the cranial and caudal eminences of the greater tubercle of the humerus, needle directed caudomedially	1.2 × 89 mm (18 G × 3.5")	15–25 mL
Site	**Structures desensitized**	
Through the notch between the cranial and caudal eminences of the greater tubercle of the humerus, needle directed caudomedially	Occasionally a communication exists between the joint and the intertubercular bursa	
Site	**Needle**	**Volume[1]**
Intertubercular (bicipital) bursa		
Needle directed proximomedially from a distal position just cranial to the humerus and proximal to the deltoid tuberosity Ultrasound guidance is valuable	1.2 × 89 mm (18 G × 3.5")	7–8 mL
Site	**Structures desensitized**	
HINDLIMB REGIONAL ANALGESIA		
Plantar digital nerves		
As for the forelimbs	As for the forelimbs	
Site	**Needle**	**Volume[1]**
Plantar nerves		
As for the forelimbs, performed in abaxial or basisesamoid positions with additional anesthetic solution injected dorsally lateral and medial to the long digital extensor tendon to anesthetize the dorsal metatarsal nerves	0.5 × 16 mm (25 G × 5/8")	1–2 mL
Site	**Structures desensitized**	
As for the forelimbs, performed in abaxial or basisesamoid positions with additional anesthetic solution injected dorsally lateral and medial to the long digital extensor tendon to anesthetize the dorsal metatarsal nerves	As for the forelimbs	
Site	**Needle**	**Volume[1]**
Low plantar (a), plantar metatarsal (b) and dorsal metatarsal (c) nerves		
As for the forelimbs (a, b) with additional anesthetic solution injected dorsally lateral and medial to the long digital extensor tendon to anesthetize the dorsal metatarsal nerves (c)	0.5 × 16 mm (25 G × 5/8")	1–2 mL

Table 15.1 (*Continued*)

Site	Structures desensitized
As for the forelimbs (a, b) with additional anesthetic solution injected dorsally lateral and medial to the long digital extensor tendon to anesthetize the dorsal metatarsal nerves (c)	As for the forelimbs

Site	Needle	Volume[1]
High plantar (a), plantar metatarsal (b) and dorsal metatarsal (c) nerves (subtarsal block)		
(a, b) Distal to the tarsometatarsal joint and axial to the second or fourth metatarsal bone; inject as withdrawing	1.1 × 38.1 mm (19 G × 1.5")	10 mL
(c) Dorsally lateral and medial to the long digital extensor tendon or a dorsal ring block performed	0.7 × 25 mm (22 G × 1")	2–3 mL

Site	Structures desensitized
(a, b) Distal to the tarsometatarsal joint and axial to the second or fourth metatarsal bone; inject as withdrawing (c) Dorsally lateral and medial to the long digital extensor tendon or a dorsal ring block performed	Can be associated with unintended penetration of the tarsometatarsal joint and tarsal sheath. Infiltration of the origin of the suspensory ligament is often substituted for this nerve block, but is also associated with inadvertent penetration of the tarsometatarsal joint

Site	Needle	Volume[1]
Tibial (a) and peroneal (b) nerves		
(a) Medially or laterally, 10 cm proximal to the calcaneal tuber, cranial to the calcaneal tendon, caudal to the DDFT beneath the crural fascia at a depth of 1–1.5 cm	0.9 × 38.1 mm (20 G × 1.5")	10–15 mL
(b) Laterally, 10 cm proximal to the point of the hock, 2–3 cm deep to the crural fascia in the groove between the long and lateral digital extensor muscles	1.1 × 38.1 mm (19 G × 1.5")	8–10 mL deep and an additional 4–6 mL as withdrawn to anesthetize the superficial branch

Site	Structures desensitized
(a) Medially or laterally, 10 cm proximal to the calcaneal tuber, cranial to the calcaneal tendon, caudal to the DDFT beneath the crural fascia at a depth of 1–1.5 cm (b) Laterally, 10 cm proximal to the point of the hock, 2–3 cm deep to the crural fascia in the groove between the long and lateral digital extensor muscles	Deep structures distal to the tarsus, tarsal joints and associated tendons and ligaments, and tarsal sheath, calcaneal tendon. Skin sensation is lost over the plantar pastern and heels, but may persist medially and caudally

(*Continued*)

Table 15.1 (*Continued*)

Site		
HINDLIMB INTRASYNOVIAL ANALGESIA[2]		
Distal to the tarsus		
As described for the forelimb		
Site	**Needle**	**Volume[1]**
Tarsometatarsal joint		
Laterally, proximal to the head of the fourth metatarsal bone; needle directed dorsally and distomedially	1.1 × 38.1 mm (19 G × 1.5")	4–6 mL
Site	**Structures desensitized**	
Laterally, proximal to the head of the fourth metatarsal bone; needle directed dorsally and distomedially	The tarsometatarsal joint occasionally communicates with the distal and proximal intertarsal joints and the tarsocrural joint, and anesthetic may also enter the tarsal sheath. In addition, distal outpouchings may anesthetize the origin of the suspensory and plantar proximal metatarsal regions	
Site	**Needle**	**Volume[1]**
Distal intertarsal joint		
Medially, in the depression between the central, second and third tarsal bones and below or through the palpable edge of the cunean tendon	0.7 × 25 mm (22 G × 1")	3–4 mL
Site	**Needle**	**Volume[1]**
Tarsocrural and proximal intertarsal joint		
Craniomedial aspect of the tarsocrural joint immediately medial or lateral to the saphenous vein *or* Plantarolateral approach between the tibia and the calcaneus	0.9 × 38.1 mm (20 G × 1.5")	10–20 mL
Site	**Structures desensitized**	
Craniomedial aspect of the tarsocrural joint immediately medial or lateral to the saphenous vein *or* Plantarolateral approach between the tibia and the calcaneus	The tarsocrural and proximal intertarsal joints reliably communicate	
Site	**Needle**	**Volume[1]**
Cunean bursa		
Medially from the distal edge of the cunean tendon proximally under the tendon	0.7 × 25 mm (22 G × 1")	4 mL

Table 15.1 (*Continued*)

Site	Needle	Volume[1]
Tarsal sheath		
Medially or laterally over the deep digital flexor, proximal to the calcaneal tuber and cranial to the calcaneal tendon	1.1 × 38.1 mm (19 G × 1.5")	7–8 mL
Site	**Needle**	**Volume[1]**
Femoropatellar joint[9]		
Below the apex of the patella, between the middle and lateral (or medial) patellar ligaments, needle directed caudally or caudoproximally	1.1 × 38.1 mm (19 G × 1.5")	20–30 mL
Site	**Structures desensitized**	
Below the apex of the patella, between the middle and lateral (or medial) patellar ligaments, needle directed caudally or caudoproximally	The femoropatellar joint can communicate with the medial, and less often the lateral femorotibial joints. These communications are not reliable	
Site	**Needle**	**Volume[1]**
Medial femorotibial joint[10]		
Between the medial patellar and medial collateral ligaments, 1–2 cm proximal to the tibia	1.1 × 38.1 mm (19 G × 1.5")	10–20 mL
Site	**Needle**	**Volume[1]**
Lateral femorotibial joint[10]		
Just proximal to the tibia, between the lateral patellar ligament and the lateral collateral ligaments cranial, through or caudal to the tendon of origin of the long digital extensor tendon	1.1 × 38.1 mm (19 G × 1.5")	10–20 mL
Site	**Needle**	**Volume[1]**
Coxofemoral (hip) joint		
The notch between the cranial and caudal eminences of the greater trochanter of the femur, needle directed cranially, distally and medially. Ultrasound guidance facilitates this difficult block	1.2 × 152 mm with stylet (18 G × 6")	15–25 mL

[9] *The femoropatellar joint can also be approached laterally.*
[10] *Alternative approaches to the medial and lateral femorotibial joints have been described.*

OSTEOLOGY

STRUCTURE AND FUNCTION OF BONE

Four major functions of bone can be identified. The tissue provides:

1. The supportive and protective framework of the body
2. The levers by which muscles effect locomotion
3. Reservoirs of inorganic elements and fat
4. Red blood cells and many types of white blood cells.

To function as a skeleton, the bones must be stiff, and bone is one of the hardest substances in the body.

Bone derives from the embryonic mesenchyme, developing either by endochondral ossification or by intramembranous ossification. Long bones have specialized sites of endochondral ossification—the growth plates. In both types of ossification the method of bone deposition is the same. Under the influence of increased vascularity, mesenchymal cells differentiate and become **osteoblasts**. These cells line the surfaces on which bone matrix is being deposited. **Osteoid** is the organic portion of bone that is laid down first and later becomes mineralized. Both the production and mineralization of osteoid seams are functions of the osteoblast. The matrix of mature bone is approximately one third organic (mainly osteocollagenous fibers) and two thirds inorganic (hydroxyapatite crystals of calcium phosphate).

Early in its formation bone is described as woven because the collagen fibers are entwined in a haphazard fashion. Fetal bone and the first bone produced at sites of fracture repair have a high woven component. In certain specialized localities, such as dental alveoli or osseous labyrinths, woven bone persists into maturity. However, woven bone is usually gradually replaced by lamellar bone in which the collagen fibers are organized into layers.

According to the density of lamellae, bone may be classified as compact (**cortical**, dense) or spongy (**cancellous**, trabecular). Lamellae may be piled in one plane, but more typically they are ordered according to the Haversian system in which between 4 and 20 layers of bone describe concentric rings around a central canal containing blood vessels. Each Haversian unit is called an osteon. The principal cell of mature bone is the **osteocyte**. Osteocytes function to preserve the integrity of bone matrix. They respond to certain stimuli to release calcium and are also capable of bone destruction. The specialized cell for bone destruction is, however, the **osteoclast**.

The external, non-articular surfaces of bones are covered by **periosteum** consisting of an outer fibrous layer permeated by blood vessels and nerves and an inner osteogenic layer. Periosteum derives from the periosteal bone collar, which supplies osteoblasts to the periphery of developing bones. At that stage it is a highly vascular structure, but in adulthood it is a relatively loose covering of connective tissue containing mostly venules and capillaries. Nonetheless the periosteum retains osteogenic potential if injured. At certain sites, e.g. ligament, tendon or capsular insertions, modified periosteal fibers called **Sharpey's fibers** penetrate cortices providing firm anchorage. Endosteum is similar to periosteum, but is thinner and lines the medullary cavity of the bone.

Vascularity of bone is maintained through a medullary and periosteal blood supply, and the blood supply to bone differs between mature and immature states. Generally the blood supply to immature bone is more extensive. In developing bones with active growth plates the epiphysis and metaphysis have separate supplies because most vessels do not traverse the cartilaginous plate. There are transphyseal vessels in large epiphyses. The epiphysis is supplied by a network of vessels entering at articular margins circumferentially—an arrangement particularly vulnerable to trauma. The metaphyseal side of the growth plate is supplied by a similar arborization of vessels entering via numerous foramina. These anastomose with branches of the nutrient artery before coursing perpendicular to the active growth plate. Periosteal vessels supply the outer third of forming cortical bone of the diaphysis. In mature bone significant periosteal supply persists only at sites of firm fibrous attachments.

The principal supply to long bones is via a main nutrient artery which enters the diaphyseal cortex at a fascial attachment, passes through the cortex to the medulla and then divides into ascending and descending branches. These subdivide to supply intramedullary bone, sites of hematopoietic marrow plus the inner two thirds of all cortical bone. The metaphyseal ends of long bones are supplied by the proximal and distal metaphyseal arteries that persist from the immature state. Blood flow through cortical bone is mainly centrifugal, i.e. from medullary cavity to periosteum, with an intravascular pressure gradient between vessels at the two sites. Blood supply to flat and irregular bones is much more diverse than that to long bones, with multiple afferent and efferent points.

Marrow is the term used to describe the soft substance occupying the intertrabecular spaces of spongy bone. Marrow in the fetus and neonate is primarily hematopoietic (red). In the adult the marrow of long bones becomes primarily fatty (yellow) but does contain primordial stem cells. In the midshaft of some long bones the medulla has no spongy bone present and is termed the medullary cavity.

MODELING AND REMODELING OF BONE

Bone is a unique material that can change shape as it grows in a process called **modeling**. It can also regenerate itself through **remodeling**, in which the bone is activated and areas are resorbed and reformed. Bone responds readily to the complex forces on the skeletal system that cause small deformation of the bone, but superimposed on the mechanical requirements of bone is the need for it to fulfill its metabolic role, specifically in calcium homeostasis. Bone is therefore subject to adaptive activity in response to a wide range of biochemical influences, principally hormonally mediated. There are three major hormones (*q.v.*) that affect the activity of bone cells:

1. **Parathyroid hormone** (PTH) is secreted by the parathyroid glands from cells highly sensitive to the calcium concentration in blood. PTH (*q.v.*) is the principal hormone regulating plasma calcium levels. Its action on bone is to increase resorption thus elevating blood calcium.
2. **Calcitonin** is secreted by C cells of the thyroid gland, which are also sensitive to plasma calcium concentration. Calcitonin (*q.v.*) is inhibitory to

PTH and disables osteoclasts, therefore acting to decrease blood calcium levels.

3. **Cholecalciferol** (vitamin D_3) is both ingested and, catalyzed by ultraviolet radiation, synthesized in the epidermis. The principal purpose of vitamin D_3 (*q.v.*) is to provide sufficient extracellular calcium and phosphorus for mineralization to take place, and its chief role is increasing intestinal absorption of these.

The interactions of these three hormones are complex. In addition, their effects on bone cells can be modified or overridden by many other factors including the effects of other hormones, age, nutritional status, pathologic processes and biomechanical influences.

Although the basic blueprint for their overall structure is genetically predetermined, bones will **model** and **remodel** according to the use to which they are put or as a result of disease processes. In the course of normal activity a bone is intermittently loaded causing intermittent deformations of its structure. This physical property is at least part of the stimulus enabling bones to maintain mechanical competence. Excessive strains, either absolute or relative to the state of the bone under load, can be the cause of structural deterioration and ultimate failure.

The end stage of the modeling/remodeling adaptation is a function of antagonistic processes: resorption of existing bone and formation of new. In normal bone, equilibrated with its environment, there is still a constant need to replace damaged tissue. In compact bone, osteoclasts bore through existing **Haversian systems**, which become filled in by secondary osteons. In cancellous bone, the same occurs in large trabeculae but the smaller ones ossify by appositional deposition on their surfaces. With a decrease in customary strain levels, osteonal replacement rate increases but more bone is resorbed than is laid down. Consequently, cortices become porotic and can also become progressively thinner due to endosteal resorption.

Excessive strain levels cause damage to bone matrix, which stimulates replacement. The first phase of this involves bone resorption, further weakening the structure. If activity levels persistently outstrip the ability of a bone, or area of a bone, to remodel then defects in structure may progress to failure. This is the phenomenon sometimes referred to as exercise/stress adaptation mismatch or **stress fracture**. Candidates for such injuries are **immature animals** subjected to physiologically abnormal levels of exercise, perhaps with inappropriate training, or **high performance athletes** that undergo a change in training regimen for which they were unprepared. A series of studies at the University of Pennsylvania has provided an excellent example of the failure of bone remodeling to keep pace with athletic training.

Young Thoroughbred racehorses exercising at speed often develop a syndrome of **bucked shins** (*q.v.*) due to repetitive motion injury associated with high-strain cyclic fatigue of the third metacarpal bone, and can develop a **stress fracture** up to a year after the original injury. **Adaptive exercise programs** (*q.v.*) involving high-speed exercise in small doses can change the geometric properties of the bone and reduce the incidence of fatigue failure by changing the shape and substance of the bone.

Grooves and prominences on the outer surfaces of bones develop in adaptation to the pressure from overlying muscle bellies or tendons and the pull from soft tissue attachments, respectively. Mature periosteum can be reactivated by increased vascularity to form new bone at, or close to, sites of injury. Subchondral bone is also subject to remodeling in the face of repetitive functional overloading. This reduces its compressibility, undermining its ability to absorb shock, and so contributes to the vicious circle of **osteoarthritis** (*q.v.*).

The ultimate mechanical failure of bone is exemplified by **fracture**. The immediate response at a fracture site is an **acute inflammatory reaction** (*q.v.*) to soft tissue disruption and periosteal tearing, and to the necrosis caused by vascular compromise of the fracture ends. The **inflammatory phase** is succeeded by the **reparative phase** during which the initial hematoma is invaded by capillary buds (the process of granulation) that deliver mesenchymal cells enabling organization to occur. A **callus** is formed comprising fibrous tissue, cartilage and immature woven bone. The proportion of bone increases steadily, and with it the stability of the fracture site improves. The final step in healing of bone is the **remodeling phase** during which, through osteoclastic and osteoblastic activity, mature lamellar bone is produced. On occasion, fracture ends can be rigidly stabilized, permitting primary bone formation in which cutting cones of osteoclasts traverse the fracture gap and filling takes place via Haversian remodeling, bypassing the fibrocartilaginous callus stage.

BONE INFECTION (OSTEOMYELITIS, OSTEITIS)

Bone infection can cause **periosteitis**, **osteitis** or **osteomyelitis**, depending on the depth of involvement. When the infection is initiated in the **periosteum** and outer cortex the term **osteitis** or osteoperiostitis is used, and when the infection begins in or extends into the **medullary cavity** the term **osteomyelitis** is more appropriate. An acute inflammatory process is provoked leading to edema, thrombosis and ischemic bone necrosis. Infective material travels through the Haversian and Volkmann's canals, spreading the process. Extension into epiphyses and joints is possible because of the communication between metaphyseal and epiphyseal vessels.

As the disease progresses, **scar tissue** forms. Necrotic bone is sequestrated by osteoclastic activity and becomes encapsulated by dense sclerotic bone (**involucrum**). Inflamed periosteum lays down new bone. If the process is not arrested then **pathologic fractures** may result from physiologic loads applied to bone with a compromised infrastructure.

Etiology

Infection occurs by **hematogenous spread** of organisms, via direct local trauma to bone or by extension of infection into bone from an adjacent septic focus. Osteomyelitis following bacteremia is most common in foals. The physeal regions in the long bones of foals are predilection sites for bacterial localization, probably because of the slowing of blood flow in metaphyseal end vessels. Traumatic wounds (*q.v.*) are common in horses and are frequently complicated by infection and bony injury. Such conditions favor the development of sequestra, which occur at various sites, particularly in the lower limbs. Sequestrum formation requires both avascularity and infection.

Clinical signs

Particularly in the early stages, lameness and pain on palpation of the affected site are evident. Associated soft tissue swelling may subside with time or with antibiotic therapy, or may become fluctuant. In cases of open wounds, chronic, purulent discharge is an indication of sequestration or the presence of a foreign body. In cases of extensive osteomyelitis or in those that are secondary to bacteremia, there may be signs of systemic response such as general malaise, pyrexia, neutrophilia and hyperfibrinogenemia.

Diagnosis

Clinical signs can be highly suggestive but **radiography** is the definitive diagnostic procedure. Osteomyelitis may however be radiographically **silent** in the early stages and optimal radiographic definition is necessary to maximize diagnostic sensitivity. The first signs are typically **mottling** within the trabecular pattern, which progresses to areas of distinct radiolucency within the bone. Lesions are frequently discrete and with chronicity become surrounded by the radiodense involucrum. **Sequestra** are separated from the parent bone by radiolucent halos and they may increase in radiodensity. Periosteum adjacent to a site of bone infection may lift off the surface and produce palisading new bone.

Ultrasonography can also be valuable in identifying osteomyelitis and sequestrum formation. Ultrasound is particularly valuable for early identification of periosteal inflammation and subperiosteal fluid accumulation associated with infection or for evaluating areas that are difficult to evaluate radiographically such as the scapula.

Osteomyelitis has an intense uptake pattern with standard nuclear **scintigraphy**, and specialized nuclear imaging techniques including white blood cell labeling and radiolabeled ciprofloxacin can also be used to identify bone infection in difficult cases such a vertebral osteomyelitis. **Computed tomography** (CT) can also provide improved localization of osteitis lesions by eliminating superimposition in cross-sectional images. **Magnetic resonance imaging** has been found to be more sensitive for osteomyelitis than CT or radiography.

Treatment

The objectives of treatment are to **remove necrotic bone fragments**, to debride remaining tissue surfaces and to eliminate infection. Sequestra generally require surgical removal because elimination of infection at such sites is often impossible by medical means alone. Pathology resulting from direct trauma tends to be superficial and in accessible locations. These cases generally carry a good prognosis and often require minimal parenteral antibiotic therapy. Osteomyelitis resulting from hematogenous seeding of bacteria frequently involves less accessible and/or more vulnerable sites. Surgical debridement of septic physeal lesions is indicated but carries the risk of long-term **physeal dysplasia** (*q.v.*).

Parenteral antibiotics are recommended in these cases are mandatory and should preferably be selected according to the results of blood culture or culture of needle aspirates from lesions. Prolonged courses of bactericidal drugs are necessary. Regional antibiotic administration using intramedullary, IV or IA techniques can also be used effectively to eliminate the infection.

THE DISTAL (THIRD) PHALANX (P3, COFFIN BONE)

See Diseases of the foot (*q.v.*) (Table 15.2).

THE MIDDLE PHALANX (SECOND PHALANX, SHORT PASTERN BONE, P2)

Fractures

Etiology

Fractures of the middle phalanx (P2) are usually **comminuted**, occur most frequently in the hindlimbs and are most common in athletic Quarter Horses. Calks and rims to augment traction may predispose to P2 fractures.

Simple fractures usually involve one or both plantar/palmar eminences, but longitudinal fractures can occur, most often in the frontal plane. Fractures are thought to be the result of compression, bending and torsional forces associated with abrupt stops and turns. **Palmar/plantar eminence fractures** presumably occur due to hyperextension of the proximal interphalangeal joint and tensile forces transmitted from soft tissue insertions. Comminuted fractures probably occur due to the complex forces generated with the digit moving relative to a fixed hoof position.

Clinical signs

Sudden onset of severe lameness at exercise is usual. Quite often the rider will report hearing a crack. In instances where the fracture occurs at apparently low-level exercise it is presumed that a stress fracture had previously weakened the bone. Limited swelling above the coronary band develops quickly. Pain, crepitus and instability can be elicited by palpating and manipulating the lower pastern. Simple fractures are generally less obvious. Palmar/plantar process fractures may be detectable by applying pressure directly over the site.

Diagnosis

Dorsopalmar, lateromedial and several oblique radiographs are required to effectively evaluate the fracture configuration.

Treatment

Simple fractures are best treated by a **lag screw technique** with or without arthrodesis of the proximal interphalangeal joint and the prognosis is favorable if repair is performed without delay. Most cases require a proximal interphalangeal **joint arthrodesis** and numerous effective arthrodesis techniques have been described.

Comminuted fractures are often amenable to internal fixation with a proximal interphalangeal joint arthrodesis. When the distal interphalangeal joint is not involved the prognosis is better than with biarticular fractures because of the ability of horses to perform with an arthrodesed proximal interphalangeal

Table 15.2 Fracture stabilization for transport to treatment facility

Limb involved	Fracture location	Stabilization method recommended
Forelimb or hindlimb	Distal phalanx	None
Forelimb	Middle phalanx Proximal phalanx Proximal sesamoids and distal metacarpus	Light bandage up to carpus. Dorsal splint from carpus to toe. Align dorsal surfaces of the cannon bone and phalanges with toe extended *or* **Kimsey Leg Saver Splint**
Forelimb	Mid to proximal metacarpus Carpus Distal radius	Robert-Jones bandage (*q.v.*) extending to the axilla Rigid splints from elbow to the ground secured with duct tape or other non-elastic tape
Forelimb	Ulna Humerus Neck of scapula	Padded bandage extending to the elbow Rigid splint from elbow to the ground to fix the carpus in extension
Forelimb	Mid to proximal radius	Robert-Jones bandage extending to the axilla Rigid splints to prevent abduction of the limb
Forelimb	Body of scapula	None
Hindlimb	Middle phalanx Proximal phalanx Proximal sesamoids and distal metatarsus	Light bandage up to hock. Plantar splint from tarsus to toe. Align sole surface, plantar fetlock and flexor tendons *or* Kimsey Hindlimb Leg Saver Splint
Hindlimb	Mid to proximal metatarsus	Lighter version of Robert-Jones bandage extending to point of hock. Rigid splints using the calcaneal tuber as a functional extension of the metatarsus
Hindlimb	Tarsus Tibia	Thick Robert-Jones bandage extending up to stifle. Rigid splint to prevent abduction and provide rotational stability
Hindlimb	Femur	None
Hindlimb	Pelvis	None
Limb involved	**Splint placement**	
Forelimb or hindlimb	NA	
Forelimb	Single dorsal splint. Use minimal padding and secure splint with duct tape and/or cast material	
Forelimb	Two splints placed caudally and laterally from the elbow to the ground	
Forelimb	Single splint caudally from the elbow to the ground	
Forelimb	Two splints. One placed caudally from the elbow to the ground. One placed laterally extending up the lateral aspect of the chest and taped securely around the forelimb and chest	
Forelimb	NA	
Hindlimb	Single plantar splint with sole flat against the splint and the fetlock flexed. Secure splint with duct tape and/or cast material. Can wire splint to the toe for longer applications	
Hindlimb	Two splints placed caudally and laterally from the calcaneal tuber to the ground	
Hindlimb	Single lateral splint extending from the ilium to the ground (preferably angled to match angle of the hock and stifle, or a straight 15–20 cm board splint)	
Hindlimb	NA	
Hindlimb	NA	

NA, not applicable.
Information derived from Bramlage, L.R. (1996) First aid and transportation of fracture patients, in Nixon, A.J. (ed) Equine Fracture Repair, *W.B. Saunders, Philadelphia, pp. 36–42.*

joint. In severely comminuted cases internal fixation may not be an option and if healing can be achieved it is invariably accompanied by osteoarthritis. Long-term casting with transfixation pins or the use of an external fixation device will be required to salvage a horse for pasture or breeding soundness.

Euthanasia (*q.v.*) is often elected in severe cases when both articular surfaces are involved and the horse does not have value for breeding. If the blood supply has been compromised, salvage may not be feasible. Blood supply can be evaluated using standard radiography, computed tomography (CT) or fluoroscopy in conjunction with vascular contrast injections.

Palmar/plantar process fractures can be stabilized by lag screw fixation, but osteoarthritis often develops and arthrodesis of the proximal interphalangeal joint is usually recommended. Casting is necessary regardless of the treatment selected, but duration of casting should be kept as short as possible to avoid associated complications.

Periarticular new bone formation (high ringbone)

Periosteal new bone formation on the dorsal, medial and lateral surfaces of the second phalanx is one manifestation of the condition known as **phalangeal exostosis** or ringbone. Where this involves distal second and proximal third phalanges it is called **low ringbone** (*q.v.*), and where proximal second and distal first phalanges are involved, **high ringbone** (*q.v.*). Depending on whether the interphalangeal joints are involved or not the ringbone may be articular or non-articular. Articular ringbone is dealt with in the subsection on arthrology (*q.v.*).

Etiology

Non-articular (or periarticular) ringbone affects both front and hind limbs. The periosteitis is presumably triggered by **tearing of fibers** of soft tissue attachments, e.g. common digital extensor tendon or collateral ligaments, or by direct external trauma. Depending on the time and nature of the insult, cases may present with acute or chronic lameness or with no associated lameness.

Clinical signs

In **acute cases**, sudden onset, moderate to severe lameness develops. There is increased digital pulse amplitude and often a discrete area around the pastern that is sensitive to pressure. Absence of solar pain is a useful aid to locating the site of pain. In **chronic cases** lameness is usually low grade and may be gradually progressive. If considerable exostosis has developed this will be palpable.

Diagnosis

Lameness is alleviated by palmar/plantar perineural analgesia at the basilar sesamoid or abaxial sesamoid level. Some cases will improve following a palmar/plantar digital nerve block. Intra-articular analgesia (of P1/P2 and P2/P3 joints) should differentiate articular and non-articular cases. Radiography is necessary for diagnosis and periosteal new bone should be assessed for signs

of activity. Acute cases may not show radiologic changes for 3–4 wk following injury. Nuclear scintigraphy will identify active bone involvement. Ultrasound should be considered to evaluate soft tissue structures and joint stability.

Treatment

In **non-articular** cases, rest is the only appropriate therapy available. Immobilization of the lower limb is advisable, and if there is associated joint instability cast immobilization may be required. Box confinement is necessary for 4 wk, followed by a further 2 or 3 mo of controlled exercise depending on the age and activity of the lesion. The prognosis for non-articular cases is generally favorable.

THE PROXIMAL PHALANX (FIRST PHALANX, LONG PASTERN BONE, P1)

Fractures

Simple proximal phalanx (P1) fractures include fractures involving one fracture plane in which the fragment is too large to be classified as a chip fracture. Proximodorsal and proximal palmar/plantar P1 IA fractures are addressed in the subsection on arthrology (*q.v.*).

A variety of configurations of simple P1 fractures occur routinely including **sagittal** fractures and **dorsofrontal** fractures. Comminuted fractures of the proximal phalanx are also common racehorse injuries, but can also occur as accidents during other activities. These range in complexity and are classified as having mild, moderate or severe comminution.

Etiology

Depending on the configuration, the cause of fracture may be combined compressive/torque forces, hyperextension of the fetlock or ligamentous avulsions. Comminuted fractures can result from either internal compressive/torque forces or external trauma.

Clinical signs

Most fractures involve the **proximal articular surface** and therefore sudden onset joint pain is likely. However, if articular surface involvement is marginal the lameness may not be severe and may abate quickly. Some fetlock **joint effusion** can usually be detected and pain on palpation might be elicited if pressure is applied across the fracture plane.

Short dorsofrontal fractures are usually identified in the chronic stages because these horses can train reasonably well with the injury and only display an intermittent low-grade lameness. Similarly, palmar/plantar process fractures and incomplete sagittal fractures that extend only a short distance from the articular facet (and perhaps involve only the dorsal cortex) can be missed in their acute phase and identified later as the cause of a chronic lameness. Larger frontal and complete sagittal fractures (emerging at the P1/P2 articulation or at the lateral or medial cortex) usually present with more severe signs and are therefore easier to diagnose quickly.

Extreme lameness, crepitus, massive distension of the fetlock joint and rapid development of soft tissue swelling are hallmarks of **comminuted fractures**.

Diagnosis

Radiography is the definitive diagnostic procedure and several projections are required to adequately map out the fracture plane or even to find the fracture line if there is minimal displacement. On the standing dorsopalmar projection, proximal to distal obliquity removes superimposition of the proximal sesamoid bones on the proximal P1 articulation. Two radiolucent lines are often seen. These should not be confused as two fractures; they are often the **deficits in each cortex** caused by the same fracture.

Non-displaced incomplete fractures will sometimes require full lameness work-up before they are diagnosed. Occasionally, cases of lameness caused by P1 fractures will be alleviated by regional analgesia of the palmar/plantar nerves at abaxial sesamoid level, but most will only be obliterated by analgesia of the palmar/plantar plus palmar metacarpal/plantar metatarsal nerves at distal splint bone level (**low four-point block**) (*q.v.*). In the hindlimb the pastern and fetlock may receive additional innervation from the dorsal metatarsal nerves, which can be blocked either side of the long digital extensor tendon at the same level (**low six-point block**).

There is significant risk of developing a **catastrophic fracture** when horses with incomplete fractures are evaluated for lameness following a regional nerve block. If there is a history or there are clinical signs consistent with fracture, radiographs should be taken prior to performing regional nerve blocks. In addition, nuclear scintigraphy can be helpful in detecting fractures that are not apparent radiographically.

Treatment

Short, simple, incomplete sagittal fractures will usually heal with rest, but lag screw repair is often elected to facilitate rapid return to work. Longer incomplete fractures and simple complete sagittal fractures require internal fixation, usually with compression using lag screw techniques. Incomplete fractures have been reported to heal well when immobilized with external support. However, if an articular surface is involved, the risk of displacement and/or subsequent osteoarthritis will be reduced by rigid internal fixation. The prognosis for simple fractures is good, especially if fixation can be performed in the acute stage.

Dorsofrontal P1 fractures are relatively uncommon and are almost exclusively seen in the hindlimbs. Incomplete fractures are managed conservatively with controlled exercise. Displaced or complete non-displaced fractures are managed surgically using lag screws.

In cases with **moderate comminution** in which the number and position of fragments is known, reconstruction with several appropriately directed screws is recommended. A buttress plate may be necessary if cortical deficits persist. Surgical repair using internal fixation is generally feasible if there is at least one intact strut spanning the length of the bone. Combined with protracted casting, such cases carry a reasonable prognosis. If it is not possible to

reconstruct the distal articular surface it may be feasible to perform a proximal interphalangeal joint arthrodesis during the same surgery.

On occasion the comminution and/or soft tissue disruption (e.g. sesamoidean ligament attachments) will be so severe that surgical repair cannot be contemplated. In these cases, **prolonged immobilization** in a transfixation cast or the use of an external skeletal fixator may permit salvage as a breeding animal but provide only a fair prognosis for survival. Otherwise euthanasia is indicated.

Periarticular new bone formation

Distal P1 can be involved in high ringbone as described above (*q.v.*). The distal limbs, and P1 in particular, are predilection sites for periosteal reactions that occur as part of the hypertrophic osteopathy syndrome (Marie's disease) (*q.v.*). In addition, palmar/plantar periosteitis sometimes develops secondary to injury to the distal sesamoidean ligaments. Rest is required for this reaction to resolve and the long-term consequences relate more to soft tissue pathology than that of bone.

THE PROXIMAL SESAMOID BONES

The proximal sesamoid bones are an integral part of the suspensory apparatus and of the metacarpophalangeal joint itself. Injuries are **common**, particularly in racehorses.

Sesamoiditis

Sesamoiditis is an imprecise term used to describe a variety of **remodeling** changes of the proximal sesamoid bones, which are usually, if not invariably, secondary to inflammation of associated soft tissues. It remains debatable whether sesamoiditis exists as a clinically definable disease of bone or whether it is a bony manifestation of what is essentially a disease of soft tissue.

Etiology

All components of the fetlock are subject to high strains during extreme extension, which occurs during load at exercise. Tearing of the fibrous attachments to the sesamoid bones can produce **bony pathology (enthesopathy)** at those sites. This may result from a single severe episode of **desmitis** or from repetitive smaller injuries.

Clinical signs

By the time sesamoid pathology develops, lameness has frequently become chronic, although the process may have been initiated by an acute desmitis causing sudden onset lameness. Pain can sometimes be elicited by pressure applied over the sesamoid bones, and large bony proliferations (enthesophytes) may be palpable. Associated ligamentous damage may also be apparent grossly or ultrasonographically.

Diagnosis

Lameness is localized to the fetlock area by regional analgesia (*q.v.*). Although palmar/plantar nerve blockade at abaxial sesamoid level would not be expected to desensitize the region, an effect from local infiltration is possible. Similarly, it is possible for local anesthetic injected into the fetlock joint to diffuse extra-articularly and desensitize adjacent tissues. Most cases however require a low four-point nerve block to relieve the lameness. **Standard radiographic views** of the fetlock are needed but the most informative are the dorsolateral—palmaromedial and dorsomedial—palmarolateral oblique projections profiling the two bones individually.

Changes include new bone formation on the abaxial and basilar surfaces of the bone, changing its contour, and poor/disorganized trabeculation. An increase in the size and number of the vascular channels is another reported abnormality, but its significance is questioned. **Vascular channels** can usually be differentiated from fractures based on their radial orientation. Changes are often confined to single sesamoid bones but may affect both bones in the same limb or bones of more than one limb. **Dystrophic mineralization** in adjacent soft tissue may be an additional finding.

A thorough **ultrasound evaluation** of the fetlock and pastern regions is indicated to determine the extent of the associated soft tissue injuries. Nuclear scintigraphy may be required to differentiate chronic changes from active bone remodeling.

Treatment

Changes in the sesamoid bones detected on radiographs are **permanent** once formed. Treatment centers on suppressing the inciting inflammatory process. Confined rest is indicated at first, possibly with the administration of a non-steroidal anti-inflammatory drug (NSAID), e.g. **phenylbutazone**, and **cryotherapy**. Complete healing (in as far as this is achieved) requires a prolonged period of inactivity reflecting the primary role of ligamentous injury. Once chronic lameness is accompanied by radiographic changes, the prognosis for a return to full athletic performance is guarded.

Osteopenia

Although technically not a disease, the **demineralization of bone**, which is consequent to **protracted disuse** (e.g. when a limb is immobilized in a cast) can be detected earlier in the proximal sesamoid bones than at other sites. The process is reversible but the vulnerability to pathologic fracture should be considered when planning the rehabilitation of long-term orthopedic patients.

Fractures

Sesamoid fractures occur commonly in racehorses due to excessive tensile forces and direct trauma.

Fractures—general

Etiology

The proximal sesamoid bones are subjected to bending and marked tensile forces by virtue of their role in the suspensory apparatus. Asynchrony of these

forces, as might occur following abnormal foot placement or in a fatigued horse, can lead to failure of the bone's infrastructure. Predisposing weakness in the bone due, for example, to osteopenia (*q.v.*), sesamoiditis (*q.v.*) or juvenile bone in foals, may lead to a fracture under physiologic loading. Interference with a thoracic limb from a hind foot is also thought to be the cause of some forelimb fractures.

Sesamoid fractures also occur in young foals when they are turned out in pasture, especially following a prolonged period of stall confinement. The signs are often remarkably subtle. In foals, these fractures frequently form a bony union, and displaced fractures result in the appearance of an elongated sesamoid. Minimally displaced fractures will heal with rest alone.

Clinical signs

With **complete fractures**, sudden onset lameness is accompanied by rapid development of local soft tissue inflammation and usually distension of the fetlock joint. If the animal is weight bearing there will be a marked reduction in extension of the affected fetlock. Flexion of the fetlock joint and pressure applied over the injured bone elicit pronounced withdrawal reactions. Many cases are not diagnosed in the acute phase and therefore present with chronic, low-grade lameness. Horses with **small apical fractures** are typically only mildly to moderately lame unless there is a concurrent suspensory ligament injury.

Diagnosis

Diagnosis is based on results of a complete lameness examination and radiographs. Lameness is localized to the fetlock by regional and/or IA anesthesia. Dorsopalmar, standing and flexed lateromedial and oblique radiographic projections are required for full evaluation. Lateromedial projections taken with proximodistal obliquity may assist in the imaging of some lesions. For example, with abaxial fractures **special views** (lateral proximal–medial distal or medial proximal–lateral distal oblique projections) may be necessary to identify the lesions and determine whether the fracture has an **articular component**. A thorough **ultrasound evaluation** is indicted to evaluate the integrity of the suspensory apparatus.

Fractures—apical and abaxial

Apical fractures are the most common proximal sesamoid bone fractures, and are frequently articular. If they involve less than a third of the bone they respond well to **surgical removal**, performed arthroscopically or via a small arthrotomy. Ultrasound evaluation of the suspensory branch is required to determine the length of postoperative convalescence.

Abaxial fractures are avulsion fractures involving the insertion of the suspensory ligament and can be articular or non-articular. Smaller abaxial fragments that involve the dorsal articular surface are amenable to arthroscopic removal. Others may be extra-articular avulsions within suspensory ligament insertions and both conservative treatment (i.e. rest for up to 6 mo) and removal have been described, but most horses perform successfully without surgery. Only extremely large fragments require internal fixation.

Fractures—axial

Axial fractures along the longitudinal axis of the proximal sesamoid bone have been described in association with condylar fractures of the cannon bone. They are generally non-displaced and can heal with conservative treatment. Diagnosis requires high quality dorsopalmar radiographic images.

Fractures—mid-body, basal and comminuted

Transverse fractures through the body of the proximal sesamoid bone may be apical, mid-body or basal. They occur in a horizontal plane across the bone, involving the dorsal articular surface.

Treatment of transverse sesamoid fractures

For apical fractures in which the proximal fragment is less than one third of the size of the whole bone, early surgical removal offers a reasonable chance of success. Careful dissection from the attachment to the suspensory ligament is imperative. Mid-body fractures involve disruption of the suspensory apparatus but can be repaired by lag screw fixation or a self-compressing cannulated screw technique using a combined clamp and drill guide placed across the fracture. Cerclage, transfixed-cerclage and suture techniques using wire or polyethylene cable are also reported, and may provide similar or even improved repair strength. Surgical repairs may be supplemented by the use of cancellous bone grafts (*q.v.*). Alternatively the latter may be employed alone in conjunction with external fixation. Fractures repaired with internal fixation benefit from the support of a cast. As an ultimate salvage procedure, fetlock arthrodesis is also possible.

Articular basal fragments can be removed arthroscopically. Horses with basilar fractures have a fair prognosis for return to racing following arthroscopic fragment removal when a portion of the base is involved. Small non-articular basilar fractures typically require conservative management because removal involves excessive soft tissue damage. Large basal fractures, particularly those involving the entire base of the sesamoid, comminuted fractures and those with marked displacement have been reported to have a guarded prognosis due to associated soft tissue damage and difficulties associated with removal or repair. The severity of distal sesamoidean ligament desmitis (*q.v.*) observed with large fractures may also be associated with a poor outcome.

Osteomyelitis

Osteomyelitis of the axial border of the proximal sesamoid bones can occur associated with a septic desmitis (*q.v.*) of the intersesamoidean ligament. Patients usually present with a chronic, moderate to severe lameness localized to the fetlock area by regional analgesia. Destructive lesions at the attachment of the intersesamoidean ligaments are evident on dorsopalmar and palmar proximal–palmar distal oblique (skyline projection) radiographs and increased bone turnover can be demonstrated by nuclear scintigraphy. The intersesamoidean ligament can be evaluated with ultrasound and/or via

palmar/plantar fetlock arthroscopy and digital sheath tenoscopy. Treatment with long-term systemic and regional antibiotic administration in conjunction with surgical curettage is recommended, but the prognosis is guarded to poor.

THE THIRD METACARPAL/METATARSAL (CANNON) BONE

Condylar fractures

Condylar fractures are parasagittal fractures of the distal end of the third metacarpal or metatarsal bone.

Etiology

Fractures through the distal condyles of the third metacarpus (MC3) and metatarsus (MT3) are relatively common in racehorses. There are a number of theories regarding the pathophysiology of these injuries including accumulated subchondral bone damage, fatigue failure with the accumulation and coalescence of small parasagittal microcracks, asynchronous rotation of the cannon bone, and pre-existing articular or suspensory ligament injuries. Thoroughbreds wearing toe grabs are more likely to develop fatal condylar fractures.

The **lateral condyle** is much more commonly involved than the medial. Fractures are classified as complete or incomplete and displaced or non-displaced. Most fractures emerge at the ipsilateral cortex a variable distance up the bone. However **spiraling fissures** as far as the proximal articular surface do occur, particularly with medial condylar fractures and/or in the hindlimb. Medial condylar fractures are also associated with an occult Y-shaped configuration in the mid-diaphysis.

Clinical signs

Because of the weight-bearing location, most horses with condylar fractures are moderately to severely lame. However, non-displaced, incomplete fractures of the cannon bone may not be detected as acute conditions and are sometimes found only after a full investigation including nuclear scintigraphy. Fetlock joint effusion is expected with condylar fractures, as is exacerbation of the lameness by fetlock flexion. Most cases however become **acutely lame** during or immediately after exercise, rapidly develop a fetlock joint effusion and have an obviously painful distal cannon bone. With displaced fractures crepitus can be palpated and may be accompanied by fetlock instability.

Diagnosis

Incomplete fractures of the cannon give rise to a lameness that will improve with IA fetlock analgesia, or four/six-point (low or mid cannon) nerve blocks (*q.v.*). Nuclear scintigraphy may also be of use in detecting lesions. If there is any suspicion that a fracture may exist, radiography should precede regional analgesia techniques. Trotting horses with incomplete fractures under the effect of local anesthetic runs a significant risk of worsening the injury.

Standard radiographic views are required using cassettes long enough to include the full length of the cannon bone and the fetlock joint. Fractures that

do not clearly emerge at lateral or medial cortices should be further investigated with differing angles of obliquity to determine the presence or absence of a proximally spiraling fissure. Small Y comminutions at the palmaro/plantarodistal extremities of condylar fractures frequently go unrecognized in conventional projections. These can adversely affect the prognosis and can be highlighted with a 125° dorsodistal–palmaroproximal oblique view. This view can be obtained by flexing the fetlock, or by elevating the extended limb.

Radiographs, ultrasound and even arthroscopy should be used to look for other associated injuries including axial sesamoid fractures, osteoarthritis, palmar and plantar erosive lesions of the condyles and suspensory ligament desmitis. Computed tomography can be used to precisely define three-dimensional fracture configuration prior to repair to allow accurate implant placement when proximal spiraling is suspected.

Treatment

Most condylar fractures should be reduced and stabilized by lag screw fixation or using a self-compressing cannulated screw system. Simultaneous arthroscopic evaluation can improve articular alignment. Some clinicians recommend conservative treatment of incomplete non-displaced fractures, but residual defects in the distal articular surface of the cannon bone are likely to result in osteoarthritis. With prompt and accurate repair the prognosis for complete non-displaced condylar fractures is good.

The prognosis for horses with **displaced condylar fractures**, regardless of treatment, is much poorer for return to athletic performance. Prognosis is also adversely affected by associated articular comminution or with subchondral erosive lesions in the palmar/plantar cannon bone. Spiral fractures often require plate fixation, and a minimally invasive technique of plate application has been described.

Diaphyseal fractures

Etiology

Almost invariably, significant external trauma is necessary for the strong diaphysis of third metacarpal/metatarsal bones to break. In **foals** the cause is often **trampling by the dam** while adult horses often present with a history of being kicked. The fractures are frequently open because the lack of soft tissue protection over the bone allows external objects or internal fragments to penetrate the skin easily. For the same reason the fractures are often complicated by **damage to vital structures**, in particular the palmar/plantar vessels and nerves. Fractures can assume a variety of configurations from simple fissures to severely comminuted fractures.

Clinical signs

Horses are usually non-weight-bearing and the fracture readily palpable, if not visible. Caution should be exercised in the examination of patients since **self-inflicted trauma** in a fractious animal can easily render a previously repairable fracture hopeless. Complete but non-displaced fractures may be more difficult to identify.

Diagnosis

Clinical signs enable the diagnosis to be made in the majority of cases. If treatment is an option, radiographs are required to delineate fracture planes. However it is often most sensible to transport the horse to a center capable of performing the necessary surgery rather than taking preliminary radiographs. A **full-limb splint** (see Table 15.2) should be immediately secured to the limb before moving the horse.

Treatment

There may be good cause to recommend euthanasia: gross contamination, severe comminution, volatile patient temperament and prohibitive costs are all valid reasons. If treatment is attempted, internal fixation is required in most cases. Non-displaced fractures in foals have been reported to heal in casts but the risks (and expense) of protracted full limb casting usually do not justify such an approach. Some comminuted proximal fractures in foals can be managed with transfixation casting.

Double plating is usually necessary in front limbs whereas single dorsolateral plating may be sufficient in MT3, which has a more obvious tension side. **Autologous bone grafting** (*q.v.*) is indicated if there are cortical deficits. Even after fixation numerous complications can prevent a successful outcome, e.g. contamination leading to osteomyelitis, implant failure or poor quality bone production at the repair site.

Dorsal cortical disease (bucked shins and dorsal cortical fractures)

A number of clinicopathologic entities comprise the syndrome variously referred to as **dorsal cortex disease**, **dorsal metacarpal disease**, **bucked shins**, **sore shins** and **shin splints**.

Etiology

Juvenile horses subjected to rigorous race training are at particular risk of developing the disease, which is one manifestation of an exercise/stress adaptation mismatch. It has been reported that up to 70% of young Thoroughbreds in race training will experience **bucked shins**, but the condition also appears to be more common among horses training on harder surfaces in North America.

This is a **fatigue injury** of bone and usually occurs in **2-year-olds in early training**. Failure occurs as a result of repetitive motion injury associated with high-strain cyclic fatigue when the required adaptive bone modeling and remodeling cannot keep pace with the level of work the horse is undertaking. Classical training schedules induce bone formation on the dorsomedial surface of MC3 due to high strain events of bending of MC3. The new bone formation is an appropriate response to repetitive motion injury of MC3, and it is the underlying injury that needs to be prevented.

In 3 and 4 yr olds there appears to be a specific manifestation of cortical stress fractures occurring obliquely, dorsolaterally and at the junction of middle and distal thirds of the bone. The location suggests that these injuries happen secondary to earlier remodeling of the dorsomedial cortex, which may

then leave the dorsolateral cortex vulnerable to fracture propagation. Dorsal cortical fractures are seen in horses that previously experienced bucked shins. Catastrophic complete midshaft MC3 fractures can occur when horses with pre-existing dorsal cortical fractures are exercised at speed.

Clinical signs

Acute cases will have **increased skin temperature** over the dorsal cannon and be **sensitive to palpation** there, particularly following exercise. Swelling can also occur. Lameness is often minimal and may show only as a bilateral shortening of stride or simply as poor performance. The condition is much more common in MC3 than in MT3. Signs typically predominate in the limb that is on the **inside of the horse's usual running direction**. Chronic cases develop visible and palpable callus and a lameness that waxes and wanes with work and rest.

Diagnosis

In early cases, clinical signs precede radiographic changes and a tentative diagnosis can be made from the clinical findings and the appropriate age–training relationship. It is usually not possible to be site specific in desensitizing the area with **regional analgesia** (*q.v.*). Lesions can be subtle and require high definition radiography to be detected. Zones of cortical osteolysis appear on dorsopalmar and oblique projections, succeeded by periosteal new bone formation. Dorsolateral cortical fractures typically run distoproximally, but proximodistal and complete saucer fractures are also seen regularly. Nuclear scintigraphy may assist in detecting changes earlier than radiography.

Treatment

Mild cases respond to rest until signs of acute inflammation have subsided. More severe cases may need longer periods of rest and some horses reportedly never return to previous performance levels. Horses that buck their shins and stop training may **re-buck** when reintroduced to training, and **modifications in training** are preferable to complete rest when horses can be maintained in work.

Cortical stress fractures that show no tendency to heal by second intention are amenable to fixation with a unicortical screw and/or to surgical osteostixis (where small holes are drilled through the bone). Although **osteostixis** alone can lead to healing, a combination of screw fixation and osteostixis is probably the most reliable surgical treatment. However, surgical treatment of dorsal cortical stress fractures is not always indicated. Stress fractures that involve the distal or proximal ends of the bone typically develop much more callus and require less intervention than the indolent fractures in the middle of the bone. The optimal candidate for surgical treatment is a horse with an obvious fracture line with minimal healing response and distinct associated clinical signs.

Extracorporeal **acoustic shock wave treatment** using a single 2000 pulse dose at high energy has also been used to facilitate fracture repair (*q.v.*), but should be used with caution due to resulting analgesic affects that could allow a horse to return to work before the fracture has healed, possibly predisposing to catastrophic MC3 fractures.

Prevention involves **modifications in training** (*q.v.*) that allow the bone to model and remodel, changing the inertial properties of MC3 to resist bending in the dorsopalmar direction. Research has shown that **high-speed exercise** in small doses is highly protective against bucked shins, while long galloping exercise increases the risk for bucked shins. Horses that do not develop bucked shins in their early training also do not develop stress or saucer fractures or midshaft MC3 fractures.

Palmar/plantar cortical disease (incomplete palmar cortical fractures and avulsion fractures at the origin of the suspensory ligament)

Trabecular disruption and palmar/plantar cortical deficits are sometimes found in conjunction with injury to the **origin of the suspensory ligament**. **Avulsion fractures** are the extreme example. Generally confined rest followed by controlled exercise for a total of 3–6 mo offers a good prognosis, but refractory cases may respond to **acoustic shock wave treatments** (*q.v.*) or **surgical forage (osteostixis)** of the affected cortex. It is essential to perform an ultrasound evaluation in conjunction with radiographic imaging to determine the severity of injury to the suspensory ligament itself (*q.v.*).

Surgical treatments reported for unresponsive cases of **desmitis** at the origin of the suspensory ligament that may be considered with associated avulsion fractures include: ultrasound guided suspensory desmoplasty (surgical fasciotomy and splitting), tibial neurectomy (hindlimb), or plantar metatarsal neurectomy and fasciotomy (hindlimb) (*q.v.*). Similarly, injections of bone marrow, extracellular matrix (ACell Vet™ Powder), stem cells or growth factors have also been advocated for proximal suspensory desmitis with or without associated avulsion fractures (*q.v.*).

Incomplete longitudinal palmar cortical fatigue fractures of the third metacarpus are relatively common and can extend proximally to involve the joint. They are usually associated with radiographically visible sclerosis of the palmar cortex and are therefore thought to be stress fractures. They occur most often in young horses in race training. Lameness can be mild to severe, and diagnosis is based on response to local analgesia, dorsopalmar radiographic projections revealing sclerosis and a longitudinal fracture line on the palmar medial cortex. Some cases are initially detected with nuclear scintigraphy. Ultrasound should be performed to rule out an associated soft tissue injury. Most horses respond to rest for 3–6 mo.

THE SECOND AND FOURTH METACARPAL/METATARSAL (SPLINT) BONES

Exostosis (splints)

A **true splint** forms as a result of tearing of the **interosseous ligament** between the second or fourth and third metacarpal/metatarsal bones and is therefore centered over the groove between the splint bone and the cannon bone. In addition, a large number of exostoses occur in response to direct trauma to the periosteum, usually on the abaxial aspect of a splint bone, and

these are referred to as **false splints**. The term **blind splint** refers to interosseous ligament inflammation and swelling on the axial surface of the splint that is difficult to detect on physical examination.

Etiology

Splints occur more frequently **medially** and in the **forelimbs**, reflecting preferential loading at these sites. The splint bones articulate with the carpometacarpal and tarsometatarsal joints and are load bearing bones (the fourth metatarsal bone has only a small articulation). Excessive intrinsic stresses cause **tearing of fibrous attachments** between the splint bones and the cannon bone, provoking an inflammatory process (desmitis, periostitis) that can progress to ossification. The new bone production will ultimately fuse the splint to the cannon bone and eliminate the source of irritation.

Direct external trauma that injures periosteum also initiates new bone formation. Such exostoses occur more frequently laterally and in hindlimbs, reflecting their traumatic etiology. Some of these "false splints" are calluses at the site of splint bone fracture. Encroachment by the associated new bone growth onto the adjacent suspensory ligament or into the carpometacarpal/tarsometatarsal is a potential complication.

The condition is most common in **young horses**, particularly those that have recently started **vigorous training**. **Hard ground** predisposes to the condition in any age of horse. **Poor conformation** also contributes to development of metacarpal exostoses, either by elevating strain on the interosseous ligament (medial splints are common in horses with offset carpi or bench knees) or by predisposing to interference (toe-out conformation predisposes horses to wing-in and interfere). With age, metacarpal fusion occurs in most horses without clinical evidence of inflammation, and active true splints are uncommon in older horses.

Clinical signs

Splints often occur suddenly with a **primary soft tissue swelling** that is typically much larger than the underlying bony enlargement. The area is painful and often warm in the early stages. The degree of lameness varies from none to moderate.

Diagnosis

Clinical signs are usually diagnostic. Sometimes there is doubt over the contribution of a splint to lameness, in which case the innervation to the site can be blocked with reasonable specificity by injecting local anesthetic (*q.v.*) around the palmar metacarpal/plantar metatarsal nerve, axial to the head of the affected splint bone. Radiographically, oblique views are the most useful to detect the true size of the splint and its degree of activity. Dorsopalmar projections can give an idea of axial encroachment. Radiographic examination is necessary if joint involvement is a concern. Ultrasonography is indicated to investigate associated soft tissue pathology, particularly when new bone production appears to be interfering with suspensory function. Scintigraphy is a sensitive indicator of splint bone remodeling.

Treatment

Rest is the most important component of the treatment regimen for acute splints and this often requires stall confinement for 6 wk. This lay-up period is almost always sufficient to allow clinical resolution although a small bony lump often persists permanently. Many cases are not strictly rested because it is well known that some splints arise, remodel and settle without causing appreciable lameness. However, failure to impose a strict regimen is a common reason for some splints becoming chronically troublesome or unusually large.

The inflamed area should be treated aggressively with **topical cold therapy** applying ice (or an effective alternative cryotherapy technique) at least two times daily for 30 min. Anti-inflammatory medication, administered parenterally (e.g. **phenylbutazone**) or topically (e.g. dimethyl sulfoxide [DMSO] plus a corticosteroid), along with pressure wraps can also be of benefit. **Intralesional corticosteroid** or hyaluronan (hyaluronic acid/sodium hyaluronate, *q.v.*) administration can also reduce inflammation and prevent excessive new bone production.

Occasionally there is justification to excise the splint surgically along with the distal extent of the metacarpal/metatarsal bone, because of a refractory inflammatory process, for cosmetic reasons or because it is impinging on the suspensory ligament. Counter-irritation, in particular the use of pin-firing, has enjoyed considerable popularity as a therapy for splints but evidence of its efficacy remains anecdotal. In cases of traumatically induced splints, protective splint boots or wraps should be used during future exercise.

Fractures

Etiology

Splint bone fractures can be divided into two types: fractures of the distal third and fractures of the proximal and middle thirds of the bone. **Distal third fractures** are typically caused by intrinsic forces, and are usually thought to be the result of abnormal tension on the bone as a result of hyperextension of the fetlock, pre-existing changes in the elasticity of the interosseous ligament and/or suspensory desmitis (*q.v.*). There are strong fascial attachments from the distal end of the splint bones to the suspensory apparatus. The resulting fractures are simple and closed, are more common in the forelimbs and usually occur medially. They usually occur in older racehorses. **Fractures of the middle and proximal thirds** are usually the result of external trauma, e.g. kicks from other horses. These fractures are frequently open, comminuted and lateral.

Clinical signs

Instability of the distal third fracture fragments may sometimes be palpable in the acute phase but more often the presenting signs are those of the associated suspensory desmitis (the majority of these patients do have suspensory desmitis). Lameness is usually low grade. A periosteal reaction occurs relatively quickly and can be felt as a discrete area of hard swelling separate from the suspensory ligament. The more proximal fractures present with acute lameness, with heat, swelling and pain over the fracture site. Often there is an

associated wound that develops serosanguineous, then purulent, discharge. Probing the wound may reveal the presence of small fragments. Sometimes fractures are not presented acutely, but only after failure of the wound to heal because of sequestration. By this time a significant callus may have formed.

Diagnosis

Standard radiographic views are necessary for full evaluation but the appropriate oblique projection is usually the most informative.

Treatment

For distal fractures, when there is considerable displacement or infection, surgical removal of the distal fragment is recommended (amputation or segmental ostectomy). Conservative management is otherwise usually effective, especially considering the fact that any active soft tissue injury will require an extended period of rest. Bony or fibrous union will usually occur during a 2–4 mo rest period, and the length of convalescence is dictated by the degree of suspensory desmitis.

Non- or minimally displaced fractures of the middle third of the splint bone can be managed conservatively, but fracture displacement or sequestration of bone fragments often dictates surgical removal. Surgery can involve removal of the fracture and the entire distal splint (amputation) or of the fracture fragments only (segmental ostectomy). Efforts should be made to resolve any associated infection prior to surgery to avoid spreading the infection. Up to two thirds of the length of the splint can be removed.

Several considerations apply to the management of **proximal fractures**. Conservative management may result in a satisfactory outcome, but the repair is slow and often impeded by infection, sequestration and instability of fragments such that non-unions with massive fibrous callus formation can occur. **Surgery** is therefore often indicated to expedite healing.

Unfortunately, removal of proximal splint bones can result in **carpal/tarsal instability** (the exception being the fourth metatarsal bone which can be completely removed without creating instability). As a result, fractures involving the proximal one third of the bone may require surgical stabilization. However, fixation of an unstable proximal fragment to the cannon bone has the disadvantage of removing the normal independent movement of small and large metacarpal/metatarsal bones and should be avoided when possible.

The most biomechanically desirable repair is achieved by application of a small plate across the fracture line without engaging the third metacarpus, after removal of sequestra and contaminated debris. If removal of the distal splint is necessitated, a small reconstruction plate can be contoured from the remaining splint bone onto the cannon bone to restore the length of the lever arm of the splint bone and prevent avulsion of the head of the splint bone. Such an approach is especially important for the most proximal fractures in which disruption of the articulations of the splint bones has occurred. If the proximal segment of bone is stable, segmental ostectomy has also been reported to be effective. That technique has the advantage of avoiding the extensive incision and dissection associated with amputation, or the risks of infection associated with implants.

THE CARPAL BONES

See Carpus, (*q.v.*).

THE ACCESSORY CARPAL BONE

Fractures

Etiology

The etiology of carpal fractures remains unclear. Although direct external trauma cannot be ruled out, many **accessory carpal fractures** are thought to be the result of forces exerted by soft tissue attachments to the bone. **Ligamentous avulsions**, usually from the dorsoproximal border, can develop if the carpus is hyperextended. Larger fractures are generally thought to occur when the limb is weight bearing and in slight flexion, such as may happen during a fall after a jump. In addition to the biomechanical forces associated with ligamentous attachments, these fractures may occur as a result of the bone being crushed between the cannon bone and the radius during the fall.

Clinical signs

Small avulsion fractures often show few acute signs. There may be localized inflammation proximal to the bone associated with low-grade lameness.

Dorsoproximal fractures that involve the **articular surface** can result in radiocarpal joint effusion. Larger fractures can occur horizontally across the proximal third of the bone, but by far the most common configuration is a frontal plane (vertical) fracture through the proximal and distal borders, usually along a line palmar to the line of the groove for the ulnaris lateralis tendon. **Sudden onset** of moderate to severe lameness is associated with localized swelling and severe pain on flexion of the carpus. Before distraction of the fragments occurs, crepitus may be detected. **Synovial distension** of the carpal sheath/canal characteristically develops (*q.v.*). Compartment syndrome affecting this canal (*q.v.*) is frequently noted as a potential sequel to fracture of the accessory carpal bone, but many horses do not develop this complication.

Diagnosis

Radiography is required to confirm the diagnosis. Lateromedial projections of the carpus are the most useful for detecting and defining the fracture. Flexed views are useful for assessing instability.

Treatment

While surgical procedures have been described for fixation of frontal plane fractures, surgery probably does not improve the prognosis beyond that obtained with conservative treatment. Attempts to reduce and compress the fracture frequently result only in a fibrocartilaginous repair, and this will occur with confined rest for an average of 6 mo. As a result, conservative management is generally recommended.

The initial phase of rehabilitation should be complemented by a full limb **Robert Jones bandage** (consisting of a heavy, multilayered bandage with each

layer about 2.5 cm (1 inch) thick and secured with gauze and the final diameter approximately three times the diameter of the limb) to **minimize motion at the fracture site**. Many cases return to athletic performance, but others are complicated by residual radiocarpal osteoarthritis or carpal canal syndrome. Surgical resection of a portion of the flexor retinaculum may be required to return the horse to athletic performance. Ulnar neurectomy has also been reported but the benefits are not well documented. Avulsion fractures require similar periods of rest. Intra-articular **fracture fragments** (avulsion chip fragments off the proximodorsal aspect of the bone) should be removed arthroscopically.

THE RADIUS

Osteochondroma

The caudomedial metaphysis of the distal radius is a predilection site for **solitary osteochondroma** formation. An osteochondroma is an **exostosis** (*q.v.*) that is continuous with the cortex of the bone and covered by cartilage. Osteochondromas typically develop immediately proximal to the caudal distal radial physis, often medial to midline.

Etiology

Osteochondromas are thought to develop due to separation of a portion of a border of the physis during development. They can occur in a number of long bones and have even been reported in intramembranous bones, but the **radius** is the most common location. The separated chondrogenic tissue establishes a separate focus of endochondral ossification that forms the bony protrusion. Osteochondromas possess a cortex and medullary cavity and are covered by a cartilage cap. Unlike the condition of hereditary multiple exostosis, single osteochondromas do not appear to have a hereditary factor.

Clinical signs

Presenting signs tend to be those of compartment syndrome of the carpal flexor canal (*q.v.*), i.e. effusion of the carpal sheath, pain on carpal flexion and a mild to moderate intermittent lameness that increases with exercise. Despite the presence of lesions in juveniles, most growths are identified in adult horses. The onset of lameness may be insidious, reflecting a gradual increase in pressure within the canal and impingement on the deep digital flexor tendon (DDFT). Large exostoses are palpable and are usually medial on the caudal radius surface.

Diagnosis

Lameness should be responsive to median and ulnar nerve blocks or, more specifically, to intrasynovial analgesia of the carpal canal. The diagnosis is generally confirmed by radiography, revealing an exostosis from the cortical surface 2–4 cm proximal to the residual physeal scar. Lateromedial and/or slightly oblique radiographic projections of the distal radius project the lesions best. Ultrasound evaluation of the carpal canal is indicated as DDFT

tendinitis is commonly responsible for much of the observed lameness, and the irregular bone contour will also be visible.

Treatment

Although rest or intrasynovial **corticosteroid treatment** will provide a respite in the lameness, resumption of exercise is likely to result in recurrence. Therefore, surgical relief of the compressed carpal canal is indicated. Flexor retinaculum release should be complemented by removal of the osteochondroma and debridement of any torn fibers of the DDFT. Most lesions can be identified and removed endoscopically. Periosteal reaction does not usually complicate recovery and recurrence of the lesion is rare. Prognosis for return to performance is good.

Exostosis of the caudal perimeter of the radial physis (physeal remnant spikes)

Recently, endoscopic evaluation of the carpal canal has identified a syndrome very similar to osteochondroma involving **tenosynovitis** of the carpal synovial sheath (*q.v.*) caused by small physeal remnants or physeal spikes from the caudal distal radius. These exostoses can cause traumatic injury to the DDFT.

Etiology

Exostoses of the caudal perimeter of the radial physis are structurally different from radial osteochondromas (*q.v.*), lacking the distinctive cartilage cap, and are located directly at the level of the physis. They are essentially the sharp edges of an irregular bone remodeling process of the caudal surface of the distal physis that developed at the time of physeal closure.

Clinical signs

Patients typically present with a history of intermittent mild to moderate effusion of the carpal synovial sheath associated with exercise and there may be moderate lameness with exercise. The effusion may resolve rapidly after exercise.

Diagnosis

Regional perineural (median and ulnar) and intrathecal anesthesia of the carpal sheath should be used to confirm that lameness is associated with the sheath.

Radiographs will reveal **sharply angular exostoses** originating from the caudal cortex of the distal radius at the level of the closed physis. The lateromedial and flexed lateromedial projections are most revealing, but high quality images are required as these exostoses are more difficult to identify than osteochondromas. In addition, endoscopic evaluation of the canal may be necessary to verify that there is a bony spike intruding into the canal because of the undulating nature of the caudal distal radial physis. These exostoses can usually be differentiated from osteochondromas (*q.v.*) radiographically

based on location, and they are also histologically different, lacking a cartilage cap.

Treatment

Tenoscopic removal is recommended, and damaged fibers of the DDFT should be debrided. Simultaneous endoscopic release of the carpal retinaculum may improve recovery rates. The prognosis is good for return to athletic performance.

Enostosis-like lesions (bone islands)

Enostosis-like lesions are focal or multifocal intramedullary radiopacities that have been identified and reported in many long bones, including the radius.

Etiology

The etiology of these **bony densities** remains largely unknown. There has been speculation that they may result from disruption of the medullary vasculature, or infarction ischemia and subsequent bone sclerosis. They can occur in horses of all ages, breeds and performance categories.

Clinical signs

The lesions have been associated with mild to severe lameness in some cases, but other horses are sound and the lesions are an incidental finding. There may be multiple lesions and different long and flat bones can be involved simultaneously.

Diagnosis

These lesions are often first identified on scintigraphy performed when lameness is not abolished with regional anesthetic techniques. On scintigraphic evaluation the lesions are associated with mild to intense uptake. Radiographically the radiopacities range from subtle to very distinct areas of medullary sclerosis, usually on the endosteal surface.

Treatment

Treatment involves stall rest for 2–3 mo, followed by additional paddock rest. Systemic NSAID treatment may be indicated initially depending on the degree of lameness. Repeat lameness evaluation, radiographs and/or scintigraphy should be recommended before returning the horse to work. The prognosis appears to be excellent, although few reports of long-term follow-up are available.

Traumatic periosteitis of the craniodistal surface

Etiology

Periosteitis can be provoked at any site by **impact trauma**. The craniodistal radius is a common site because it is exposed with carpal flexion during the

ascent phase of a jump. Periosteitis at this site also occurs as a result of adjacent **sepsis** in the **extensor tendon sheaths** (*q.v.*). These synovial structures are prone to penetrating injuries, particularly in jumping horses.

Clinical signs

Regardless of the etiology, periosteitis is often accompanied by a local **tenosynovitis** (*q.v.*). This tends to be significantly more severe if sepsis is involved. Reduced and painful carpal flexion may be evident. Periosteal new bone may be palpable and painful to pressure.

Diagnosis

Establishing the inciting process in cases of periosteitis is important in selecting the appropriate treatment. **Synovial fluid analysis** should allow acute sepsis to be differentiated but the distinction between chronic septic and traumatic synovitis is less dramatic. Generally, periosteal reactions following trauma occur more locally, more quickly and are more painful to pressure. Radiographically, lateromedial and craniocaudal oblique projections of the distal radius and carpus are needed for thorough evaluation of the new bone formation and can yield clues regarding etiology. Traumatic reactions tend to be more focal and layered whereas septic reactions tend to be more widespread and palisading. An ultrasound evaluation of the flexor tendons and associated synovial sheaths is also critical.

Treatment

Periosteitis secondary to direct trauma generally responds well to confined rest for a period of 6 wk. Supplemental topical cold therapy and systemic NSAIDs are also indicated. The exostoses persist but are inactive. In the case of sepsis, primary treatment should address the infection (*q.v.*).

Fractures

Etiology

External trauma is responsible for fractures involving the **shaft** of the radius, and these fractures are among the most common **catastrophic fractures** seen in horses. The fracture can be complete or incomplete, transverse or oblique, articular or non-articular, simple or comminuted and open or closed. Most are **oblique, complete and comminuted**. They are often open because of the nature of the impact, e.g. kick, or because fragments penetrate the skin medially where there is no muscular protection.

Foals can develop **physeal fractures** involving the proximal or distal extremity. Although stress fractures of the radius are uncommon, racehorses do occasionally develop fatigue fractures of the radius, and these can occur bilaterally.

Clinical signs

Generally, radial fractures are easily identified on physical examination because of their severity. There is often an associated wound from the initial

injury or due to penetration of sharp fracture fragments. Incomplete non-displaced fractures involving the proximal articular surface may be less apparent but will still usually present with an acute lameness that can be localized to the elbow by careful observation of gait, palpation and manipulation. Rarely, fissure fractures occur causing more subtle lameness. In these cases, pain and swelling can sometimes be detected by palpation.

It is particularly important to carefully evaluate and confine horses that have a history of **acute lameness following a kick**. These horses may have a **non-displaced radial fracture**, and their lameness often improves quickly. However, if they are turned out in pasture the fracture can displace with **minimal exertion**. Stress fractures are difficult to identify on physical signs alone.

Diagnosis

Clinical signs are frequently diagnostic. In the less obvious cases distal fractures may respond to a median nerve block and proximal articular fractures to IA elbow analgesia. Scintigraphic scans may reveal sites of increased bone turnover and are particularly useful for identifying stress fractures. Radiography is essential to accurately map out severe fractures, but may be better left until the horse has been transported to a hospital capable of advanced internal fixation techniques. Incomplete fractures or fissure lines may require several angles of obliquity before the fracture line is crossed and can be recognized. Chronic fissures may be visible because of bone resorption or an adjacent endosteal/periosteal reaction.

If an **incomplete fracture** is suspected but is not visible initially, radiographs taken several days later may reveal the fracture line and/or an endosteal/periosteal response. The horse should be **restrained** in cross-ties, a tie-stall or a sling pending the results of these recheck radiographs. Alternatively nuclear scintigraphy can be used to confirm the diagnosis.

Treatment

Complete, displaced fractures require internal fixation. The limb should be immobilized immediately with appropriately sized caudal and lateral splints to avoid the fracture becoming open (see Table 15.2). Appropriate external coaptation is essential if fracture repair is being considered. Specialist facilities and expertise are required for repair but even then the prognosis for adult horses is guarded and worsens the greater the comminution, contamination and size of patient. There are very few reports of successful repair of complete radial fractures in adult horses, but radius fractures in foals carry a much better prognosis.

Both physeal and midshaft diaphyseal fractures have a good prognosis in foals, and single or double plate fixation is generally required. Incomplete non-displaced fractures can respond to conservative management but this generally necessitates 12–16 wk of strict confinement. In patients with a suitable temperament cross-tying or maintaining the horse in a sling to prevent recumbency is feasible and useful for the first 8 wk. Stress fractures have a good prognosis, and should be managed with stall followed by paddock rest for a total of 3–4 mo.

THE ULNA

Fractures (olecranon fractures)

Etiology

Olecranon fractures are very common long bone fractures, and in adults most frequently result from kicks by other horses. Avulsions of the proximal apophysis can occur in foals from excessive tension on the triceps.

Clinical signs

Sudden onset lameness, often mimicking a radial nerve paralysis (*q.v.*), is characteristic of ulnar fractures. With **displaced fractures** the elbow is typically dropped in position and the horse is unable to fix the carpus (unable to bear weight). With incomplete and non-displaced fractures the horse may stand normally, but will usually show lameness. There is usually swelling over the injury. Fractures can be simple or comminuted and may or may not involve the articular surfaces. The degree of lameness varies between cases. Often there is an associated wound on the lateral surface of the limb and probing this may reveal bone fragments. Crepitus may also be detected.

Diagnosis

Clinical signs are often highly suggestive of fracture. Where the possibility of fracture exists it is advisable to obtain radiographs without delay. Mediolateral projections with the limb held protracted provide the most information, but a craniocaudal projection should also be obtained. It is important to include the whole olecranon on the films. In a young foal, it can be difficult to verify whether the apophysis is normal, but images of the opposite leg can be helpful for making this determination.

Treatment

The horse should be **splinted** prior to transport for further diagnostic evaluation or for surgery, otherwise it will struggle during transport being unable to weight bear on the limb. Effective splinting requires only a caudal splint to fix the carpus (see Table 15.2), and it is not necessary or advantageous to attempt to stabilize the elbow itself.

Although certain non-displaced, non-articular fractures will heal with conservative treatment, **internal fixation** is preferred for the majority of olecranon fractures. The site lends itself excellently to the tension band principle of repair, and a narrow dynamic compression plate applied to the caudal surface is usually the treatment of choice. Some proximal avulsions in juveniles are amenable to pin and wire fixation, and some non-displaced, nonarticular fractures in foals can be managed conservatively with confinement and splinting. Although proximal fragments can be difficult to stabilize and severe comminution occasionally complicates implant application, generally these fractures carry a good prognosis, especially if treated early. If fracture fragments are missing, a locking plate may improve stability of the repair.

The potential of **contaminated wounds** of the lateral radius to lead to elbow joint sepsis (because of the relationship of the ulnaris lateralis tendon to

the joint capsule) should always be considered. Assisted recovery from anesthesia (pool or sling) can prevent early catastrophic implant failures.

THE HUMERUS

Fractures

Fractures of the humerus are relatively uncommon, but occur most frequently in foals and weanlings and racing Thoroughbreds. Fractures can be incomplete/complete, open/closed, simple/comminuted and displaced/nondisplaced, but most are **complete**, **closed and displaced**.

Etiology

External trauma is the usual cause of complete fractures although stress-related fractures are also seen regularly in the racing Thoroughbred. In the case of **tubercle fractures** trauma may be from a kick. Foals sometimes sustain trampling injuries from their dam, and many weanlings present with a history of flipping over backwards during halter breaking. Diaphyseal fractures in adults are the least common and tend to result from propagation of a stress fracture or the forceful impact of a heavy fall at speed. Fractures of the **deltoid tuberosity** usually occur as a result of a kick.

Clinical signs

These are dependent on the site and nature of the fracture. **Tubercle fractures** are typically lateral and sometimes associated with a wound. Patients are weight bearing but very lame and display the guarded, slow limb protraction characteristic of shoulder lameness. Cranial extension of the shoulder joint is resented. **Deltoid tuberosity fractures** are also often open, but tend to be associated with less lameness. **Diaphyseal fractures** are of variable configuration but tend to be oblique and/or spiral. Cases are usually non-weight-bearing with massive soft tissue swelling and a dropped elbow stance. Crepitus may be palpable or audible with the assistance of a stethoscope. Disability is sometimes compounded by a radial nerve paralysis (*q.v.*). Distal fractures may involve the condylar surface and have associated joint effusion.

Stress fractures in racehorses are usually associated with a history of lameness, but the lameness may be transient or intermittent, and nuclear scintigraphy should be pursued in horses with that history.

Diagnosis

Clinical signs are diagnostic in the worst cases. Radiography provides the definitive diagnosis. Mediolateral and craniomedial–caudolateral oblique projections with the limb extended are required. Ultrasound can also be valuable in evaluating humeral fractures, especially those involving the tubercles or the deltoid tuberosity. It is very difficult to assess the status of the **radial nerve** prior to surgery because there is no autonomous sensory zone for the radial nerve in horses.

Stress fractures or an associated endosteal response may be visible on radiography, but these fractures are more commonly diagnosed with nuclear scintigraphy.

Treatment

Prognoses for humeral fractures range from good to hopeless. **Deltoid tuberosity fractures** and **tubercle separations** are amenable to fragment removal when small or to lag screw repair when large. Non-displaced deltoid tuberosity fractures can be managed conservatively with a good prognosis.

Occasionally the muscle mass surrounding the humerus and the hemorrhage and swelling that occur in these tissues offer enough support for healing of diaphyseal fractures to take place by **second intention** even in adult horses, but the end stage can involve considerable deformity. Conservative management involves confining the horse to a small stall, and horses that are putting weight on the injured limb have a better chance of a successful outcome. Internal fixation has been successful in foals and yearlings, either by plating, intramedullary stack pinning, or intramedullary interlocking nail fixation. As with many fractures, the chances of success are inversely related to the size of the patient.

Stress fractures have a good prognosis with prolonged stall and paddock rest (3–4 mo). These horses should not be returned to training until the fracture is healed since they are at high risk for developing a complete catastrophic humeral fracture.

Enostosis-like lesions (bone islands)

Enostosis-like lesions identical to those described in the radius (*q.v.*) can also be detected in the humerus. These should be differentiated from endosteal callus formed in response to a stress fracture (stress fractures are typically proximocaudal or distocranial in location).

THE SCAPULA

Fractures

Etiology

Fractures of the scapula are uncommon and usually occur due to external trauma from a fall or a kick. Stress fractures and resulting complete fractures of the scapula are also seen in racehorses. **Supraglenoid tubercle fractures** can occur with avulsions of the origin of biceps brachii and coracobrachialis muscles or due to direct trauma (*q.v.*). Comminuted fractures of the glenoid can arise when the humerus is driven proximally.

Clinical signs

These vary according to the severity of the injury. Lameness ranges from mild in the case of small tubercle fragments to non-weight-bearing in the case of glenoid and scapular neck fractures. Manipulation and deep palpation will usually locate the area of discomfort, and crepitus is sometimes detectable. Fractures of the spine can lead to sequestration of fragments with chronic sinus formation. Neck fractures may cause damage to the suprascapular nerve.

Diagnosis

Mediolateral radiographic projections with the limb extended provide the best images of distal fractures. Scapular spine fragments may be highlighted

by tangential craniocaudal projections. Fractures through the body require high exposures to penetrate the depth of both forelimbs and should be interpreted cautiously because of the superimposition of thoracic structures and the contralateral scapula. Ultrasound can provide better image detail of many fractures in adults. Stress fractures are usually diagnosed on the basis of nuclear scintigraphy.

Treatment

Many fractures of the spine and body respond to conservative management with the exception that **sequestra** typically **require removal**. Plate fixation of unstable fractures of the body has been reported, utilizing the scapular spine to provide sufficient length for screw insertion.

Many **supraglenoid fractures** are amenable to internal fixation using tension band techniques with screws and wires and/or plates. Transection of the biceps brachii tendon has been reported to prevent postoperative implant failure. Early removal of small supraglenoid tubercle fragments can be successful, but in long-standing cases and in other types of fractures, degenerative scapulohumeral joint disease usually limits success to salvage for non-athletic purposes. Internal fixation of neck fractures is technically feasible in foals. Stress fractures should be managed with prolonged rest.

Enostosis-like lesions (bone islands)

While less commonly reported than those of the radius and humerus (*q.v.*), enostosis-like lesions can be detected in the scapula, and have been associated with similar lesions occurring in the ribs and other flat bones.

THE CALCANEUS (FIBULAR TARSAL BONE)

Osteomyelitis—calcaneal tuber

The prominent calcaneal tuber is prone to traumatic injury and subsequent infection.

Etiology

Calcaneal tuber lesions are often caused when the horse kicks a solid object or is kicked by another horse. Foals can also develop infections of the apophyseal growth plate secondary to hematogenous bacterial spread.

Clinical signs

There are often draining wounds present over the point of the hock, and osteitis generally causes moderate to severe lameness and swelling. Tarsal tenosynovitis may also be noted.

Diagnosis

Both radiography and ultrasound should be considered to confirm the diagnosis and determine the extent of involvement. Lateromedial, flexed

lateromedial and plantaroproximal–plantarodistal (skyline) radiographic views should be obtained.

Treatment

Effective treatment requires **prolonged antibiotic therapy** both systemically and regionally (antibiotic perfusions, *q.v.*). Surgical debridement of infected soft tissues and bone is also frequently necessary. These cases can be very difficult to resolve and generally require prolonged treatment, but they can be managed successfully.

Osteitis—sustentaculum tali

Distension of the tarsal sheath (**thoroughpin**) (*q.v.*) is sometimes associated with new bone formation on the sustentaculum tali.

Etiology

Inflammation of the sustentaculum surface is the trigger factor and can result from direct trauma, e.g. fractures, or tenosynovitis of the adjacent tarsal sheath. Septic tenosynovitis is particularly liable to provoke a proliferative reaction. It is also possible for a systemic bacteremia to seed the sustentaculum causing an osteomyelitis.

Clinical signs

The predominant sign is of **massive tarsal sheath distension** accompanying lameness. Hock flexion is likely to exacerbate the lameness.

Diagnosis

Lameness should improve with intrasynovial analgesia of the sheath (*q.v.*). Bone proliferation is often visible on lateromedial and dorsomedial–plantarolateral oblique radiographic projections but the optimal image is obtained with the flexed plantaroproximal–plantarodistal (skyline) view. Ultrasound should be performed to evaluate the DDFT and the tarsal synovial sheath.

Treatment

Initial treatment should be directed toward the inciting cause, but surgery is often indicated. Early aggressive therapy is required to manage **septic tenosynovitis** (*q.v.*) of the tarsal sheath. Systemic and regional antibiotic therapy is required if infection is present, and sheath lavage with tenoscopic exploration is usually performed in conjunction with surgical debridement of osteomyelitis lesions or traumatic fractures. However, once new bone formation has occurred, the prognosis for athletic performance is poor since surgical removal of the proliferations is often followed by regrowth. Surgical release of the tarsal retinaculum can minimize pain associated with compression of the DDFT in the tarsal groove. Deep digital flexor tenotomy has been described to salvage severe cases, but more recent work suggests that this aggressive technique may be unnecessary for successful management of these difficult cases.

Fractures

Fractures are not common, but a variety of **calcaneal fractures** can occur, including **Salter–Harris type 1 separation** of the tuberal growth plate, chip fractures from the plantar surface and fractures through the body of the bone. The latter are often open and may involve the talocalcaneal or proximal intertarsal articulations.

Etiology

External trauma is the usual cause.

Clinical signs

Fractures are accompanied by local swelling and pain consistent with their severity. **Chip fractures** are frequently associated with open wounds and soft tissue inflammation localized around the plantar border. They may sequester and become a source of chronic purulent discharge. Lameness is typically apparent in the acute phase but often subsides with the resolution of soft tissue swelling. Therefore, at the time of presentation there may be little or no pain. **Physeal fractures** in foals result in a loss of hock extension (dropped hock) due to interruption of the insertion of the gastrocnemius muscle. **Body fractures** may cause similar loss of function if the fragments are significantly displaced. **Open, articular fractures** are likely to develop tarsocrural joint sepsis.

Diagnosis

Standard radiographic projections are required to delineate the fracture, with lateromedial and oblique views being the most informative. Special projections may also be indicated.

Treatment

Chip fractures can be left if they retain a blood supply and are not associated with infection. Otherwise they should be removed surgically via an approach either side of the superficial digital flexor tendon (SDFT). Generally the prognosis is good but some are difficult to locate dorsal to the tendon, and osteomyelitis of the tuber calcaneus has been encountered.

Fractures involving **small fragments** can be repaired by lag screw fixation if accessible, whereas fractures of the body or epiphysis must be stabilized using the tension band principle. Generally, the more complicated the repair needed, the worse the prognosis. An associated septic tarsocrural joint requires appropriate therapy, perhaps more urgently than the fracture itself.

THE TIBIA (CRUS)

Physeal fractures

Etiology

Physeal fractures can be caused by external impact or by intrinsic compressive/tensile forces during exercise. Injuries can involve the proximal or distal

physes, or the tibial crest. Fractures of the proximal tibial physis are particularly common.

Clinical signs

Fractures are usually obvious because of the degree of swelling, pain and loss of function. In the case of proximal and distal separations the limb will deviate markedly distal to the line of separation. Horses with tibial crest avulsions are often non-weight-bearing because of the inability of the quadriceps muscle to fix the patella.

Diagnosis

Craniocaudal and lateromedial radiographic projections are necessary to determine the configuration of the fracture.

Treatment

Except in the minimally displaced distal fractures (in which full limb casting might be considered) internal fixation to stabilize the fragments is generally indicated. The technique is variable according to the biomechanical needs of individual cases. **Salter Harris type 2 fractures** with a lateral metaphyseal component frequently occur in the proximal epiphysis of foals up to the age of 18 mo. These lend themselves to repair by internal fixation (plating, cross pinning, screws and wires) via a medial approach and generally carry a good prognosis. Conservative management can be considered for some non-displaced fractures of the proximal tibia. Fractures of the distal tibial physis that require internal fixation can be repaired with cross pins.

Tibial crest avulsions require tension band fixation to oppose the pull of the quadriceps. This is often best accomplished with a plate applied to the cranial aspect of the tibia. Tibial stress fractures should be managed with strict rest to avoid catastrophic bone failure.

Diaphyseal fractures

Etiology

Extrinsic and intrinsic forces are implicated in the development of tibial diaphyseal fractures, but external trauma from a kick is a common cause. They can be complete or incomplete and may involve either or both articular surfaces. Medial overriding of fragments can create an open fracture because of the limited soft tissue protection on that side. The proximal caudolateral cortex is a predilection site for **stress fracture** in the immature athlete.

Clinical signs

Complete fractures present with sudden onset, severe lameness, crepitus and swelling. Incomplete fractures can be more difficult to detect. There is frequently a history of acute onset lameness with little to find clinically. Some cases will display a localized pain reaction to pressure applied over the bone surface medially. Swellings associated with callus formation may become apparent later.

Diagnosis

Complete fractures are readily diagnosed on the basis of clinical signs. Incomplete fractures may be evident radiographically, but this is not invariable. Nuclear scintigraphy offers a good method of detecting these. At a minimum, craniocaudal and lateromedial radiographic projections are a prerequisite to surgery for complete fractures. For the detection of **incomplete fractures** high definition, multiple, oblique films should be examined.

Treatment

Severely comminuted diaphyseal fractures are a **devastating injury** and euthanasia is indicated. Other fractures may lend themselves to internal fixation, particularly in foals, usually with plates applied craniolaterally and craniomedially.

As with all proximal limb fractures, success is more likely the smaller the patient. The prognosis for complete tibial fractures in adults remains guarded to poor despite studies designed to improve plating and interlocking nail techniques. Incomplete fractures that can be seen on radiographs are frequently spiraling and these are best treated by interfragmentary compression in foals, but conservatively in adults. For less extensive fissures conservative treatment is generally indicated although the potential for incomplete fractures to become complete should always be considered, and tie-stall or sling restraint may be indicated.

Enostosis-like lesions (bone islands)

Enostosis-like lesions identical to those described in the radius (*q.v.*) can also be detected in the tibia. These should be differentiated from endosteal callus formed in response to a stress fracture.

THE FIBULA

The fibula is normally vestigial in the horse. Complete fibulas have been reported as a congenital finding in Shetland ponies and miniature horses, and have also been associated with development of **angular limb deformities**. In those cases, an osteotomy should be performed in conjunction with periosteal elevation and/or transphyseal bridging (*q.v.*).

Fractures

Fractures of the fibula are not common. The bone forms from a variable number of ossification centers, and persistence of these, in some individuals, can lead to a mistaken diagnosis of fracture. Usually, multipartite bones will be bilaterally symmetrical. Even in cases of genuine fracture the clinical consequences are few and they are usually managed conservatively. Mild and transient lameness may be seen.

THE PATELLA

The patella is a **critical component** of the quadriceps apparatus, acting as a lever arm for extension of the stifle.

Fractures

Etiology

Direct trauma to the cranial stifle with the limb in flexion is the most commonly recognized etiology. **Avulsion fractures** are also seen, particularly at the apex, and presumably result from contraction of the quadriceps muscles. Other configurations include sagittal (usually medial to the ridge), transverse and comminuted fractures.

Clinical signs

Depending on the fracture configuration, lameness varies from moderate to non-weight-bearing. Local soft tissue inflammation will usually be present together with femoropatellar joint effusion in articular fractures. Pain and possibly crepitus will be elicited by palpation or manipulation. Horses with small avulsion fractures can present with minimal lameness, but may have marked joint effusion. Flexion usually exacerbates the lameness.

Diagnosis

Intra-articular analgesia of the femoropatellar joint (*q.v.*) will typically improve lameness caused by articular fractures. Lateromedial, caudocranial and flexed cranioproximal–craniodistal (skyline) radiographic views are essential to accurately define the fracture. The latter view can be obtained in the standing horse by flexing the limb and holding the cassette against the horizontal tibia while directing the beam proximodistally. Ultrasound can also be valuable in defining fracture configuration, as well as in determining soft tissue involvement.

Treatment

The least complicated cases, i.e. small non-articular and non-displaced fractures, will heal with a fibrous union given sufficient stall confinement. Sagittal fragments up to one-third the surface area of the patella are small enough such that their removal will not interfere with quadriceps action or femoropatellar mechanics and this is a reasonable option with a good prognosis if performed early.

Fragments off the base of the patella should be removed. Most fracture fragment removals can be performed arthroscopically. In other cases, including complete displaced transverse fractures and large sagittal fragments, internal fixation, usually by lag screw technique, is necessary to restore congruity of the articular surface. These repairs have a relatively high failure rate due to the large distracting forces experienced by this bone. Minimally displaced sagittal, transverse and comminuted fractures should be managed conservatively with prolonged stall rest.

Apical fragmentation

Fragmentation, roughened contour or subchondral lucency at the apex (distal end) of the patella, is occasionally identified on lateromedial radiographs. Many of these lesions develop following **medial patellar ligament desmotomy**

for upward fixation of the patella (*q.v.*). Clinically, the lesions may be associated with lameness, responsive to IA femoropatellar analgesia (*q.v.*), and fibrous thickening of the joint capsule may be palpable. A high success rate has been reported with arthroscopic removal of fragments and debridement of the affected area. Medial patellar ligament desmotomy should be avoided when possible as it apparently creates joint instability or patellar malalignment. Most horses with upward fixation of the patella can be managed more conservatively.

THE FEMUR

Physeal fractures

Etiology

Fractures of the femur are quite common in **foals.** Unbroken, fractious youngsters are prone to epiphyseal fractures when restrained and panicking. Trampling by the dam has also been incriminated in the etiology. Proximal physeal fractures are more common than coxofemoral luxations due to the unique anatomy of the equine hip, including a strong accessory ligament of the head of the femur.

Clinical signs

Animals are usually non-weight-bearing unless there is only minimal displacement. There is typically local pain and swelling at the site of fracture, including a marked **gonitis** (*q.v.*) in the case of distal physeal fractures. Crepitus can often be detected on limb manipulation.

Diagnosis

Distal fractures can be imaged radiographically using flexed lateromedial and craniocaudal projections. **Proximal fractures** require powerful radiographic units and a recumbent patient for adequate penetration and diagnostic images. With capital femoral physeal fractures, the radiographs should be closely evaluated to ensure that the femoral head is secure in the acetabulum (round and accessory ligaments are intact) before recommending surgical repair.

Treatment

Non- or minimally displaced fractures can heal with conservative management given sufficient stall confinement. Otherwise treatment requires internal stabilization and an amenable fracture configuration. Lag screw techniques, buttress plating and Rush pinning of distal epiphyseal fractures have been successful. Proximal physeal fractures have been successfully repaired using pins, cannulated screws, the dynamic hip screw plating system, and other techniques. The prognosis is always guarded for athletic potential but is best in small patients.

Diaphyseal fractures

Etiology

External trauma is the usual cause. In adults the energy dissipation associated with the massive trauma frequently causes severe comminution.

Clinical signs

Non-weight-bearing lameness associated with massive soft tissue swelling of the thigh is characteristic. There is usually excessive mobility of the limb on manipulation and crepitus may be felt or heard. The limb may appear shortened due to overriding of fragments. If the femoral vessels are damaged **massive hematomas** can form, and horses will occasionally exsanguinate.

Diagnosis

Clinical signs are often diagnostic and they may be all that is available since radiography of the adult femoral shaft is largely restricted to referral hospitals.

Treatment

In foals, ponies or very small adults intramedullary pinning and double plating have been successful. In larger animals there is usually no realistic prospect of successful repair, and euthanasia is indicated if the fracture cannot be managed conservatively.

THE PELVIS

Fractures

While the incidence of pelvic fractures has been reported to be low, recent improvements in diagnostic imaging techniques have revealed that there is a **relatively high incidence** of pelvic fractures in all types of horses.

Etiology

Fractures through the **iliac shaft or wing** are the most commonly diagnosed pelvic fracture and are usually associated with the trauma of a fall. **Tuber coxae** fractures can occur with direct impact against a solid object, and these commonly occur when horses charge through **narrow doorways**. Pubic, acetabular and ischial fractures tend to occur in younger horses and may occur during forced abduction of the hindlimbs. Spontaneous stress and complete fractures are also well documented in racehorses and can result in catastrophic injury on the track.

Clinical signs

Tuber coxae fractures ("knocked-down hip") present with local soreness but low-grade lameness, which is usually short-lived. The fragment may be detected by palpation and there is usually a visible asymmetry of the tuber coxae. Sometimes these fractures are open and associated with sequestration and chronic drainage. The signs of other fractures are dependent on the configuration. The worst cases with bilateral comminution will be recumbent. Horses with unilateral fractures have moderate to severe lameness and quickly develop muscle atrophy of the ipsilateral proximal muscle masses.

Asymmetry of the bony landmarks may also be obvious. Rocking the horse from side to side or manipulation of the ipsilateral limb may allow crepitus to be felt or heard. If the fracture splits the pubic symphysis, bilaterally shortened

strides will be evident. **Damage to adjacent vessels** can cause severe or fatal blood loss. Perineal edema in females suggests damage to obturator vessels.

Diagnosis

Definitive diagnosis of a pelvic fracture can be challenging. Clinical signs provide the most important diagnostic features. A **rectal examination** is useful and can reveal otherwise undetectable fragment instability, hematoma formation or, in the chronic case, callus formation. Although a technique for standing ventrodorsal radiographic projections exists, it requires powerful machines and purpose-designed cassette holders to perform without undue radiation hazard. Nonetheless, it can be useful in removing the uncertainty of tentative diagnoses.

Full radiographic evaluation requires ventrodorsal projections obtained under general anesthesia. For this reason it is generally recommended that acute cases are given time to stabilize before the procedure is undertaken. Ultrasound has proven to be invaluable in the diagnosis of pelvic fractures and also facilitates monitoring healing following diagnosis. Both transcutaneous and transrectal exams should be performed. Scintigraphy can also be useful for diagnosis of pelvic fractures, particularly for stress fractures when hindlimb lameness is detected without localizing signs. Unfortunately scintigraphy can be inconclusive and a negative scintigraphic examination cannot rule out even serious pelvic fractures in the acute stage of these injuries.

Treatment

There are currently **no surgical techniques** available to repair pelvic fractures in horses. Fracture fragments sequestered from the tuber coxae may require surgical excision.

For most pelvic fractures, conservative treatment involving **prolonged stall confinement** is the only option available. When unstable pelvic fractures are suspected the risk of **vessel laceration** should be considered, and tying an amenable horse for the first month of confinement can reduce the risk of fatal hemorrhage.

Simple tuberal or iliac fractures have a good prognosis. As a general rule, comminution, fragment overriding and involvement of the acetabulum are poor prognostic signs, but exceptions are frequent. Most horses can at least be salvaged for breeding although it is wise to check that the **pelvic dimensions** have not been compromised when determining suitability of a mare for breeding. The duration of stall confinement is usually at least 2–3 mo, but should ultimately be determined based on ultrasound monitoring, as well as clinical and/or radiographic evidence of fracture healing.

ARTHROLOGY (DISEASES OF JOINTS)

INTRODUCTION

Joint disease is one of the most common problems encountered in equine practice and can be broadly divided into five groups:

1. Developmental
2. Degenerative

3. Traumatic
4. Septic
5. Miscellaneous.

There is considerable overlap between each of these groups.

Diagnosis of joint disease may involve a variety of **diagnostic aids** including (most commonly) local analgesia, radiography and synovial fluid analysis. Nuclear scintigraphy and other computer-assisted imaging techniques are becoming more widespread in availability, but are still primarily confined to referral centers.

ANATOMY

Joints are composed of supporting soft tissues, an articular cartilage surface and a subchondral bone foundation. The soft tissues surrounding a joint include ligaments and tendons. However, of most importance to the understanding of joint disease is the role of the **joint capsule**, which consists of an outer fibrous layer and an inner synovial membrane. These closely linked structures contribute much of the nutrition and sensation to the joint. The fibrous portion of the joint capsule is rich in nerve terminals, through which most **joint pain** is detected. The synovial membrane is the source of many of the components of joint fluid, including **hyaluronan** (*q.v.*), and acts as a permeability barrier that controls synovial fluid composition. Many of the destructive enzymes responsible for articular cartilage damage arise from the synovial membrane, and the structure also plays an important role in phagocytosis.

The articular surface is generally composed of hyaline cartilage, which is divided into four layers. The arrangement of these layers, which are constructed mainly of chondrocytes, collagen fibrils and proteoglycans, imparts much of the characteristic strength, elasticity and resistance to compression of articular cartilage. The **superficial layers** of articular cartilage receive nutrition from the synovial fluid, while the deeper layers of immature cartilage receive nutrition via the vascular supply of the subchondral bone. Articular cartilage has no nerve supply and provides little shock absorption. Most shock absorption occurs in the bone and periarticular soft tissues.

The **subchondral bone** provides support for the articular cartilage. This bone has a rich blood supply and is capable of providing limited repair of articular cartilage when exposed to the joint surface.

Several forms of **lubrication** operate within joints. Synovial membrane lubrication occurs by a process known as **boundary lubrication**, and hyaluronan is primarily responsible for this. Cartilage on cartilage lubrication uses both boundary and hydrostatic lubrication. A glycoprotein aids in cartilage boundary lubrication. At higher loads, however, boundary lubrication is inadequate and **hydrostatic lubrication** takes over, operating by formation of a fluid film composed of joint fluid and interstitial fluid from the articular cartilage that keeps the articular surfaces apart.

DEVELOPMENTAL JOINT DISEASES

The broad category of developmental disorders includes osteochondrosis (including osteochondritis dissecans [OCD]), subchondral bone cysts,

cuboidal bone malformations, cervical vertebral malformation, juvenile arthritis and some angular and flexural limb deformities. Osteochondrosis and angular limb deformities are discussed in more detail in the section on developmental orthopedic disease (*q.v.*).

Osteochondrosis

The most commonly recognized developmental joint disease is **osteochondrosis** (*q.v.*) which is a developmental orthopedic condition characterized and defined by a disturbance in **endochondral ossification**. **Osteochondritis dissecans (OCD)** refers to those cases of osteochondrosis in which a **cartilage flap** is formed.

The appearance of clinical signs associated with osteochondrosis can sometimes be delayed many years, particularly if only mild lesions have occurred and the horse has been allowed to mature before vigorous exercise has commenced. Cases appearing in older animals often present with osteoarthritis (*q.v.*); however, the location and appearance of lesions indicate a long-standing osteochondrosis lesion.

All breeds of horses are affected, and it is important to remember that **any articular surface** can be affected, including vertebral articulations, frequently with more than one joint affected. For these reasons, any evaluation of lameness in young horses, particularly if bilateral, should include osteochondrosis as a differential diagnosis.

Clinical findings

The most prominent clinical sign in cases of osteochondrosis is **effusion** of at least one affected joint. Effusion may not always be evident in the contralateral joint, even when radiographic evidence of disease exists. Lameness is variable, but is usually only mild to moderate. The lameness may be difficult to completely abolish with IA local anesthesia. **Muscle wasting** is often evident in long-standing cases of shoulder and stifle osteochondrosis.

Diagnosis

The age and breed of the horse, its size and sex, and the presence of joint effusion can suggest a diagnosis of osteochondrosis. Intra-articular blocks (*q.v.*) may be necessary to localize the lameness. Confirmation of a diagnosis of osteochondrosis is usually made by radiography. If clinical signs are only apparent in one limb, the **contralateral joint** should always be radiographed. The horse should also be closely examined for abnormalities in other joints. A **neurologic examination** (*q.v.*) may be indicated to determine whether cervical vertebrae have been affected in severe cases.

Treatment

Conservative and **surgical** management have been investigated. Conservative therapy consists of restricting the horse's exercise, slowing the growth rate, and ensuring there are no dietary vitamin or mineral deficiencies or excesses. Excessive feeding of grain should be avoided. Conservative therapy can be successful in carefully selected cases, but is dependent upon the site and

severity of the lesion, how early in the course of the disease the lesion is detected and whether any osteochondral fragmentation or elevation of cartilage has occurred. Up to 12 mo convalescence may be required, and joint effusion and lameness may be present for a considerable period of this time.

The role of **drainage** of the joint and **IA corticosteroid injections** is controversial. In cases of osteochondrosis in which osteochondral fragmentation or loose cartilage flaps have not developed, corticosteroids may provide short-term relief from clinical signs of lameness and joint effusion. However, it is unclear if corticosteroids aid the recovery process and they may hasten the development of cartilage detachment. **Intra-articular hyaluronan** (*q.v.*) or long-term **IM polysulfated glycosaminoglycan (PSGAG)** (*q.v.*) therapy may improve the prognosis in selected cases. However, if severe effusion is present and there is radiographic evidence of fragmentation or undermining of cartilage then surgery is the preferred option if an athletic career is anticipated.

Arthroscopic surgery is the technique of choice. There are estimates that up to 70–80% of appropriately selected cases respond to arthroscopic debridement of osteochondrosis lesions. Of course, prognosis depends on the extent of the lesion, the joint involved and the degree of associated osteoarthritis. Improvement in clinical signs is often evident within weeks of surgery. **Postoperative care** depends on the surgical findings, but generally consists of 4 wk of stall confinement, then 4 wk of hand walking, followed by paddock rest for another 8–16 wk. This can be modified to suit the individual lesions and programs of the affected horse. If required, some horses, primarily those with small intermediate ridge OCD or plantar fetlock lesions, can resume exercise within a week of surgery.

New techniques that may replace simple surgical debridement are being developed. These include stabilizing the OCD flap lesion with absorbable pins to facilitate healing, tissue engineered cartilage constructs to repair the articular surface, and osteochondral autograft transplantation using Mosaic-Plasty or OATS™ (osteochondral autograft transfer system) technologies.

Osseous cyst-like lesions

Osseous cyst-like lesions or **subchondral bone cysts** are most frequently identified in the **medial femoral condyle** of the femur; however, they also occur regularly in many other sites, including the fetlock, pastern, elbow and carpal joints, and cysts can develop in any joint. The etiology of bone cysts is uncertain, but they may be related to dietary abnormalities and may have a similar pathogenesis to OCD (*q.v.*). Trauma to the articular surface can also result in cyst formation.

Conservative therapy can be successful in some cases, but many of these horses will develop **osteoarthritis** (*q.v.*). Surgical evacuation of the cyst contents is the most common surgical technique used when access to the cyst is feasible. **Intralesional corticosteroid** injection without surgical enucleation has recently gained popularity for treatment of medial femoral condyle cysts. Intralesional corticosteroids may slow the progression of cysts if detected at an early stage of development. Improved treatment options are being investigated in an attempt to improve prognosis in these cases. These include cylindrical press-fit osteochondral allografts/autografts, tissue engineered cartilage

constructs, mesenchymal stem cell transplantation and growth factor enhanced repair techniques.

There are several conditions in young horses that can mimic cysts, including lytic areas in the ulnar carpal bone or incomplete development of the distal first phalanx seen in yearling Thoroughbreds. It is important to differentiate conditions that may be "normal", or at least clinically insignificant, from those that can result in lameness.

Incomplete or defective ossification of the carpal and tarsal bones

This condition arises as a result of **delayed ossification** of the carpal and tarsal bones and has been suggested to be a result of prematurity, hypothyroidism (*q.v.*) or a variation of normal ossification rates. Lack of ossification of the cuboidal bones in these joints and uneven pressure distribution result in collapse and deformation of the cartilage; with subsequent ossification, the bones are permanently deformed. In the carpus, an angular limb deformity often develops, while a flexural deformity occurs with tarsal collapse (**curby**, **sickle-hock**) (*q.v.*). In severe cases clinical signs are usually present at, or soon after, birth. In less severe cases, particularly with tarsal bone collapse, a diagnosis may not be made until much later when mild osteoarthritis is detected.

Radiographic examination will confirm either delayed ossification or subsequent deformation and wedging of the cuboidal bones. If a diagnosis is made early, before permanent deformation of the bones has occurred, treatment should be instituted. This consists of straightening the leg and applying well-padded splints or a fiberglass tube cast. Splints should be lightweight to allow the foal to ambulate well, and can be made out of PVC pipe or formed using cast material. In young foals, splints should be reset daily, and casts should be changed every 3–7 days to accommodate the rapid growth occurring at this time and to prevent flexor tendon laxity that can be a major complication of cast application in very young foals. When splints are applied bilaterally, the foal may initially require assistance to stand and nurse at regular intervals.

The prognosis is guarded once bone deformity is identified radiographically. Some horses become sound, but others are left with a chronic osteoarthritis and permanent limb deviation. In mild cases of tarsal bone collapse affecting only the distal intertarsal and tarsometatarsal joints **arthrodesis** can eliminate the associated lameness, particularly if there is no or minimal deviation of the limb.

Young horses can also develop osteoarthritis of the distal tarsal joints, presumably as a result of defective development of the articular cartilage in these joints. This may be a manifestation of OCD. These horses present at a young age with clinical and radiographic evidence of **juvenile bone spavin**.

OSTEOARTHRITIS/DEGENERATIVE JOINT DISEASE

Etiology

Osteoarthritis (OA) or **degenerative joint disease** (DJD) is actually a group of disorders that are defined and characterized by **progressive deterioration** of the **articular cartilage**. Cartilage degeneration is usually associated with

changes in the adjacent soft tissues and subchondral bone, but the term implies progressive and permanent deterioration of the articular cartilage. A wide variety of etiologic factors have been shown to cause osteoarthritis, including trauma, osteochondrosis, IA fractures, chronic low-grade trauma and septic arthritis (*q.v.*), although in many cases no predisposing factors can be identified. In many patients osteoarthritis probably develops due to chronic low-grade articular trauma occurring as a result of joint instability, ligamentous or capsular damage, poor conformation or action, or wear and tear over many years of strenuous athletic activity. In some cases no obvious predisposing factors can be found.

Despite the wide variety of initiating causes, there is considerable commonality in the reactions of the articular tissues. Once the normal architecture of the cartilage is altered, a **vicious cycle** of events begins. The changes that occur include a loss of cartilage elasticity, a decrease in aggrecan or proteoglycan content, and liberation of degradative enzymes. The end result is damage to the articular surface and remodeling of the subchondral bone. In many cases, osteoarthritis can progress to the extent that subchondral bone will fragment from articular surfaces.

Pathophysiology

The articular changes at the cellular level have been well described in a number of review articles. Osteoarthritis can involve changes in the soft tissues surrounding the joint, the articular cartilage and the subchondral bone, but many of the pathologic changes identified also involve the synovial membrane. The initial response is inflammatory, with production of increased amounts of relatively normal synovial fluid. As the inflammatory changes progress there is an increase in the protein levels, as well as an increase in leukocyte numbers and a decrease in viscosity of the joint fluid due to reduced hyaluronan concentrations.

Inflamed synovium is capable of releasing degradative enzymes such as collagenases, proteases and glycosidases, as well as prostaglandins and superoxide radicals. Much of the **pain** associated with joint disease apparently occurs as a result of stimulation of nerve fibers within the synovium.

Grossly, the articular cartilage becomes softened and fibrillated. There may be **cartilage splitting** and fragmentation extending to complete erosion and loss of articular cartilage in the most severe cases. Structural changes include loss of proteoglycan and glycosaminoglycan content, as well as collagen degradation.

Subchondral bone damage results when full thickness articular cartilage damage has occurred. Grossly there is softening of the bone and fragmentation. Subchondral bone damage has been suggested as a cause, rather than a result, of articular cartilage degeneration in young horses whose joints are subject to inappropriate loading during training. However, this is presumably a less frequent cause of osteoarthritis than are primary changes in the synovium and articular cartilage.

There are three basic theories about how cartilage degeneration is initiated in osteoarthritis. First, it has been suggested that trauma stimulates a **biochemical degradative response** in the joint and resident chondrocytes either contribute to this process or are unable to respond adequately to protect the

cartilage from the insult. Second, **excessive mechanical forces** may play a determining role with resulting failure of the articular cartilage. Third, **repetitive concussion** produces changes in the subchondral bone, and cartilage changes develop secondarily. It should be noted that these so-called "biomechanical and biochemical theories" of joint destruction are not mutually exclusive: each of these processes is likely to occur in most cases of osteoarthritis depending on the primary initiating factor. There is a growing trend to suggest that osteoarthritis arises exclusively as a result of changes in the subchondral bone, but the etiology of osteoarthritis is so complex that a single pathologic mechanism is unlikely.

Diagnosis

Initial diagnosis of osteoarthritis is often based on clinical signs (Box 15.1). Horses usually present with a low-grade, chronic lameness. If a fracture has been superimposed on the osteoarthritis, lameness may be more severe. Many horses have reasonably **advanced degenerative changes** before the owner or trainer detects clinical signs. Effusion in the affected joint is variable, with no, or only minimal, distension detected in many cases. For example, due to anatomic constraints, effusion is rarely detected in the distal intertarsal or tarsometatarsal joints.

Response to **flexion tests** (*q.v.*) can often be informative, but a negative response does not rule out the possibility of osteoarthritis. For example, the "**spavin test**" (*q.v.*) for osteoarthritis of the hock can be a useful ancillary diagnostic procedure and is relatively easily standardized between operators. In contrast, many horses with mild carpal osteoarthritis will not respond positively to a carpal flexion test.

Flexion tests of the fetlock must be interpreted carefully, as many horses, particularly older animals, will show some degree of lameness after fetlock flexion, and flexion of the fetlock also affects the proximal and distal interphalangeal joints. Furthermore, variability in pressure applied and duration of flexion makes comparison between operators very difficult. Individual veterinarians should be **consistent** in performing the fetlock flexion test and correlate the response observed with the pathology subsequently detected. Mild pressure for 30–60 s is generally recommended.

Box 15.1 Osteoarthritis—diagnosis

Clinical signs
- Lameness
- Look for joint swelling, pain
- Assess flexion tests

Anesthesia, regional and IA

Radiography
- New bone formation, enthesophytes, lysis, sclerosis

Arthroscopy
- Response to treatment

Diagnostic regional and/or IA local analgesia (*q.v.*) are typically required to localize lameness to a particular area. Scintigraphy may be required to identify some subtle osteoarthritis responsible for a decline in performance without lameness. Radiography is indicated to evaluate the extent of bone involvement, but arthroscopy and MRI can provide information about the articular cartilage.

Synovial fluid analysis is of limited assistance in making a diagnosis of osteoarthritis, however the potential exists for great advances in this area as research continues for a simple, reliable, and accurately interpretable test. Both **serum and synovial fluid biomarkers** are being investigated. Some of the numerous serum and synovial biomarkers being evaluated in horses include: collagenase-1 activity, glycosaminoglycan, aggrecan metabolites, cartilage oligomeric matrix protein, carboxy-terminal propeptides of type II collagen, cross-linked telopeptide fragments of degraded type I collagen, and neutrophil elastase 2A. Work to date suggests that marked fluctuations can be detected with physiologic processes and sampling interventions and careful interpretation of data will be essential.

At present, color and viscosity of the synovial fluid remain as useful indicators of joint pathology. Normal joint fluid is clear to very light yellow in color. The darker yellow (xanthochromic) the fluid appears, the more likely it is that articular pathology is present. In severe cases of osteoarthritis the fluid can appear reddish in color.

Treatment

Treatment should be designed to eliminate the cause of the osteoarthritis whenever possible, for example OCD lesions or joint sepsis (Box 15.2). Articular cartilage has a limited ability to repair, and response to treatment is usually dependent on the severity of the cartilage injury. Partial thickness articular cartilage damage does not repair but full thickness damage can heal as a result of metaplasia of the granulation tissue that forms in the defect. However, the replacement cartilage is fibrocartilage not hyaline cartilage, with lower aggrecan content and little or no type II collagen.

It is important to recognize and to inform clients that **osteoarthritis cannot be cured**. However, a number of management practices can be utilized effectively to keep horses in athletic performance. **Long periods of rest** may also be indicated in conjunction with other treatments, and utilized when the horse's training program allows.

Box 15.2 Osteoarthritis—treatment summary

Arthroscopy and joint lavage
Rest
Medical therapy
- NSAIDs
- Corticosteroids
- Hyaluronan (IA, IV)
- Polysulfated glycosaminoglycan (IM, IA)
- Atropine (IA)

Arthroscopy and joint lavage

In severe cases, or where IA fractures are present, **arthroscopic surgery** should be considered. This allows for removal of loose fragments of bone and cartilage, debridement of degenerative cartilage down to healthy subchondral bone, and a thorough flushing of the joint to remove degradative enzymes and cartilage particles. **Diagnostic arthroscopy** should be considered even if a radiographically identifiable lesion is not present. Experimental evidence suggests that creating full thickness cartilaginous lesions and/or penetrating the subchondral bone plate (i.e. microfracture techniques allow access to cancellous bone without compromising the subchondral bone plate) can enhance cartilage repair. Newer resurfacing techniques including autologous grafting (*q.v.*) are likely to come into clinical use in the near future.

Medical therapy

Medical therapy can be utilized alone or in conjunction with surgery, and includes the use of NSAIDs, corticosteroids, PSGAGs and hyaluronan (*q.v.*). The appropriate use and action of these drugs is similar for all forms of joint disease.

Prior to injection of any substance into a joint (*q.v.*), **meticulous aseptic surgical preparation of the skin surface** must be performed. Evidence suggests that adequate disinfection can be achieved without clipping or shaving the hair provided adequate scrubbing time is allowed, but clipping may still be necessary with a long haircoat and/or excessive contamination. Sterile surgical gloves are recommended for all IA injections.

The most potent anti-inflammatory medications used to treat osteoarthritis are **corticosteroids** (Table 15.3). Their actions are complex and include

Table 15.3 Corticosteroids used in treatment of osteoarthritis

Corticosteroid	Standard concentrations	Typical IA dose per joint[1]	Duration of response[2]
Betamethasone acetate/ sodium phosphate[3]	6 mg/mL	3–18 mg	3 mo
Triamcinolone acetonide	6, 10 and 40 mg/mL	3–18 mg up to 40 mg[4]	Up to 3 mo or more
Methylprednisolone acetate[5]	20 and 40 mg/mL	80–120 mg	Up to 6 mo
Dexamethasone sodium phosphate	5 mg/mL	15–25 mg	1 wk–2 mo
Dexamethasone isonicotinate	1 and 3 mg/mL	9–15 mg	Up to 3 mo
Isoflupredone acetate	2 mg/mL	5–20 mg	3 mo
Triamcinolone and dexamethasone combined		10–40 mg triamcinolone and 15 mg dexamethasone	More potent initial response, 3 mo or more

[1] The dose ranges vary widely and are somewhat arbitrary.
[2] The duration of response can be very variable, depending on the severity of the condition, the nature of the horse and the joint being medicated. The approximate times given above relate to a best-case scenario.
[3] Not currently available on the market.
[4] Reduce if multiple joints are injected. It is advisable not to administer more than a total of 18–80 mg per horse because of a possible risk of inducing laminitis. No research is available to accurately set this limit.
[5] Methylprednisolone acetate may have prolonged detection times in some horses; it also has the most detrimental effects on articular cartilage, and should probably be avoided in high-motion joints.

stabilization of lysosomal membranes (decreasing the release of degradative enzymes), inhibiting prostaglandin, free radical, interleukin-1 and collagenase release, and decreasing vasodilation, edema formation and fibrin deposition. They also suppress leukocyte function, as well as inhibiting other inflammatory pathways. The deleterious effects of corticosteroids are considered to be a result of decreases in proteoglycan content and cartilage elasticity, which can result in cartilage degeneration. However, recent studies have shown that **triamcinolone** (*q.v.*) has very few adverse effects when administered IA and the potent anti-inflammatory effects of this medication are well documented.

Provided corticosteroids are not used in large doses, frequently over long periods, or in an attempt to treat severe IA fractures, the beneficial effects of their use generally outweigh the deleterious consequences. Corticosteroids are often used in combination with hyaluronan. Long-acting agents, such as **methylprednisolone acetate**, can result in improvement for up to 6 mo. Recommended doses of methylprednisolone acetate are 60–80 mg in smaller joints such as the fetlock and carpus, and 120 mg in larger joints. Short- to medium-acting corticosteroids, primarily betamethasone acetate (3–18 mg per joint), dexamethasone isonicotinate (10–15 mg per joint) and dexamethasone (20 mg per joint), can give relief for several weeks up to approximately 3 mo.

Triamcinolone acetonide is one of the most commonly used corticosteroids for IA use in competition horses. The amount of triamcinolone recommended varies from 6 to 40 mg per joint, but many practitioners limit the total quantity of triamcinolone to 18 mg per horse in an effort to avoid the development of laminitis (*q.v.*).

All corticosteroids are readily detected during routine drug testing procedures for racing and competition (*q.v.*). Sufficient time must be allowed following injection to ensure the drug has been excreted prior to competition. Veterinarians must stay current with information regarding detection times of these medications.

Hyaluronan, also referred to as **sodium hyaluronate** or **hyaluronic acid** (HA), is a component of articular cartilage and synovial fluid, and is produced by both synoviocytes and chondrocytes. Hyaluronan is a polyanionic non-sulfated glycosaminoglycan. Under physiologic conditions hyaluronic acid is anionic and can be appropriately referred to as hyaluronate or hyaluronan. Articular surfaces are covered with a fine layer of hyaluronan, which exerts resistance to cartilage compression while still retaining its elasticity. Hyaluronan also confers viscoelastic as well as lubricating properties to normal synovial fluid, and is responsible for the boundary lubrication of synovial membranes. It creates a steric barrier at the synovial membrane, and inhibits release of prostaglandins and free radicals.

Exogenously administered HA is thought to stimulate production of endogenous HA by resident synoviocytes, provide anti-inflammatory benefits, and supplement the action of depleted or depolymerized endogenous HA, but additional documentation of these claims is warranted. Intravenous HA appears to decrease lameness and synovial effusion in horses with synovitis. A number of different hyaluronan products are commercially available for administration to horses (Table 15.4). The properties of HA are listed in Box 15.3.

Table 15.4 Hyaluronan products commercially available for administration to horses

Product	HA conc.[1] (mg/mL)	Supplied	Molecular weight[1] (Daltons)
MAP-5, Enhance[2,3]	10 (9.5) 5	2 mL vial 10 mL vial	750 000 (757 200)
Legend or Hyonate IV[2,4]	10 (10.9)	2 mL vials	300 000 (321 600)
Legend or Hyonate IA[2,4]	10 (10.3)	2 mL vials	300 000 (361 900)
Synacid[2,5]	10 (9.2)	2 mL vial 5 mL vial	150 000–200 000 (82 240)
HY-50[2,6]	17	3 mL syringe	Approximately 750 000
Hylartin V (Hylartil Vet)[7]	10	2 mL syringe	3 500 000 (2 652 703)
Hyalovet, Hyalovet-20[8]	10 (9.8)	2 mL syringe	500 000–750 000 (605 500)
Hyvisc[9]	11 (9.2)	2 mL syringe	2 100 000 (2 449 000)
Hycoat[10]	5	6 mL vial 10 mL vial	 >1 000 000
Equron[11]	5 (5.2)	2 mL syringe	1 500 000–2 000 000 (766 500)
Synvisc[12]	16	2 mL syringe	6 000 000

Product	Protein conc.[1] (ppm)	Intrinsic viscosity[1]	Kinematic viscosity (cps)[1]
MAP-5, Enhance[2,3]	4.03	1387	267.9
Legend or Hyonate IV[2,4]	9.38	711	61.4
Legend or Hyonate IA[2,4]	6.64	780	77.7
Synacid[2,5]	333	246	10.3
HY-50[2,6]	9.76	3978	29 490
Hylartin V (Hylartil Vet)[7]			
Hyalovet, Hyalovet-20[8]	13.83	11.65	158.8
Hyvisc[9]	4.47	3466	30 375
Hycoat[10]			
Equron[11]	4.09	1400	50.6
Synvisc[12]			

[1] *From P. C. Uden and L. M. Lavoie (1997) Laboratory evaluation of commercial hyaluronate sodium products.* Journal of Equine Veterinary Science *17: 123–125.*
[2] *Available in Australia.*
[3] *Bioniche, marketed for embryo cryopreservation.*
[4] *Bayer Corporation.*
[5] *Schering-Plough, Virbac.*
[6] *Delvet, and Bexco Pharma Inc.*
[7] *Pfizer.*
[8] *Fort Dodge and Bioniche.*
[9] *Boehringer Ingelheim (distributor) Anika Therapeutics (manufacturer).*
[10] *Neogen, marketed for wound care.*
[11] *Solvay.*
[12] *Wyeth (distributor) Genzyme (manufacturer).*

Hyaluronan can be given IA or IV. The IA route may be preferred if the lameness has been localized to a specific joint. The IA dose is 20 mg per injection site, and the injection can be repeated in 2–3 wk if clinically indicated. This medication is commonly used **in combination with an appropriate corticosteroid**. The combination can be mixed and injected in the same syringe. Intravenous injections of 40 mg are given once weekly for 3–4 wk often

Box 15.3 Properties of hyaluronan

Molecular weight
The molecular weight (MW) of synovial fluid hyaluronan has been estimated at approximately 2–6 million Daltons. The MW of hyaluronan has been used to compare the relative merits of different hyaluronan products. However, the measurement of MW of hyaluronan products can be difficult and produce misleading results. Contamination of the hyaluronan with proteins and nucleic acid can result in artificially high MW readings. The advantage of higher MW products is not well documented, but higher MW may result in longer duration of effect.

Protein
The measurement of protein concentration in hyaluronan is an indication of purity of the substance. Pure hyaluronan is free of protein. It is acknowledged that it is virtually impossible to totally eliminate all extraneous protein; however, it is suggested that the lower the level present, the less synovial reactions are likely to occur.

Viscosity
It has been suggested that the higher the viscosity of the hyaluronan product used, the more beneficial it will be in terms of assisting in lubrication and shock absorption within the joint.

followed by a maintenance program of decreasing frequency, or given 1–2 days prior to an event. By **combining corticosteroids with the IA administration of hyaluronan** many practitioners have observed a better and longer lasting improvement when compared with corticosteroids alone. Hyaluronan alone is only effective against mild to moderate synovitis.

Two forms of polysulfated polysaccharide medications for intramuscular administration are currently registered for equine use: **polysulfated glycosaminoglycan** (PSGAG) and **pentosan polysulfate**. These agents are reported to have anti-inflammatory properties and anabolic effects on cartilage, to prevent catabolism, to promote hyaluronan synthesis and to have beneficial vascular effects on the joint.

The PSGAG, Adequan (Boehringer Ingelheim), is supplied in an IA or IM ampule. It has chondroprotective and anti-inflammatory effects in osteoarthritic joints, and it is commonly used postoperatively when there is significant cartilage loss. Adequan is reported to inhibit degradation and stimulate synthesis of cartilage matrix, thereby meeting the requirement of cartilage matrix synthesis stabilization, which is deemed most important in the treatment of osteoarthritis. However, the nature and magnitude of its anabolic effects are controversial, while the anti-catabolic effects are more generally accepted. Adequan is a semi-synthetic heparinoid. It is a mixture of highly sulfated glycosaminoglycans, the major component of which is chondroitin sulfate. The product is made from an extract of bovine lung and trachea modified by sulfate esterification. Intramuscular Adequan is recommended at

500 mg (1 mg/kg) every 4–7 days for a total of 4–7 injections. While there are few objective data to support the effectiveness of IM PSGAG, there is a great deal of anecdotal backing. Intra-articular administration has been associated with inflammation and a reduced resistance to infection, and 250 mg of Adequan should be co-administered with 125–250 mg of amikacin sulfate if the IA route is used. Many practitioners have discontinued use of IA Adequan to avoid complications.

Pentosan polysulfate (Pentosan Equine; Nature Vet; 250 mg/mL; 6 mL), is supplied in an IM formulation, but is not licensed for use in the US. Pentosan polysulfate has been used in human medicine as an anti-thrombotic and anti-lipidemic agent for the last three decades and recently its potential as a disease-modifying anti-arthritic agent has been explored. It appears to have chondroprotective but no analgesic properties. Pentosan polysulfate is a linear polysulfated polysaccharide derived from plant extracts. It is prepared from the plant product xylan and contains linked beta-D-xylopyranoses attached to glycoside chains. Pentosan polysulfate has also been used in canine patients with osteoarthritis. In dogs the optimal dosage regimen is 3 mg/kg q 5–7 days by SC injection. In horses, it has primarily been used in Australia, and the dose has been extrapolated from this canine data to 2–3 mg/kg once weekly for 4 wk, repeated after 3 mo as required. Occasional local reactions to IM injection of this product have been observed.

A number of **oral medications** are currently available that are claimed to be of benefit in the management of osteoarthritis. These primarily consist of **chondroitin sulfate** and/or **glucosamine sulfate/hydrochloride**. The efficacy of these products is not well established although there is increasing evidence of their effectiveness. Glucosamine may increase proteoglycan synthesis by chondrocytes as well as having anti-inflammatory properties. Chondroitin sulfate is also reported to have anti-inflammatory and chondroprotective benefits. There is currently debate regarding the efficacy of the two different glucosamine salts on the market (glucosamine sulfate versus glucosamine hydrochloride) but the salt form simply provides the delivery vehicle and the real issue of importance is that of product purity.

Both glucosamine and low molecular weight chondroitin sulfate are absorbed after oral administration to horses, but the levels achieved in the target joint remain unclear. There also appears to be considerable individual variation in clinical results observed following this form of supplementation. When supplementation is used, a reputable product should be selected since many of the glucosamine and chondroitin sulfate products currently on the market do not contain the products listed on the label.

NSAIDs act by inhibiting prostaglandin-mediated activity in the joint, thereby decreasing the pain and inflammation associated with joint disease. Certain NSAIDs **inhibit anabolic activity** in chondrocytes and have deleterious effects, while others **stimulate matrix synthesis**. Clinically, there is little evidence of detrimental effects in the joint even following chronic administration, and these medications are very useful in management of equine joint disease. Nevertheless, there is recent evidence that chronic phenylbutazone administration does suppress proteoglycan synthesis and may potentiate cartilage damage. **NSAIDs should be used judiciously in athletic horses with osteoarthritis**.

The least expensive and most commonly used NSAID is **phenylbutazone** (*q.v.*), which can be given PO or IV. One recommended dosing interval consists of 4.4 mg/kg twice daily for 1 or 2 days, then 2.2 mg/kg twice daily for 3–5 days, then 2.2 mg/kg once daily as required. Toxicity, including gastrointestinal ulceration and renal papillary necrosis, can occur rapidly if the higher dose rate is used for long periods, particularly if the horse is suffering from dehydration or has pre-existing renal or gastrointestinal disease. Toxicity may manifest as protein loss, colic and diarrhea (*q.v.*). A good response is obtained with phenylbutazone when treating **low-grade lameness**. It can assist in resolving clinical signs of lameness when acute inflammation is present, but in chronic lameness clinical signs usually return when medication is withdrawn. As a result **long-term administration** is sometimes indicated to maintain a horse in athletic work. Long-term administration does not usually have adverse effects providing the drug is given at the correct dose and the horse remains well hydrated, but owners should be instructed to monitor the horse for evidence of toxicity. Phenylbutazone can have a prolonged detection time following even short-term use or administration of a single dose, and breed/performance regulations should be observed.

Other drugs in the NSAID group that are used in horses include flunixin meglumine, ketoprofen, carprofen, acetylsalicylic acid, naproxen, meclofenamic acid, vedaprofen, eltenac, etodolac and indometacin. **Meclofenamic acid** (Arquel) is considered to have a wide margin of safety. It has been shown to have similar analgesic properties to phenylbutazone, but may take several days administration to reach peak therapeutic levels. Newer agents such as **meloxicam** are very useful, particularly in foals. They have potent anti-inflammatory and analgesic properties. They are reported to be much less ulcerogenic than traditional NSAIDs. Meloxicam can be given at a rate of 1 mL/75 kg IV or 1 mL/50 kg PO once daily in horses.

Other medications

Dimethyl sulfoxide (DMSO) has anti-inflammatory and antibacterial properties. It can be used as an IA medication, and has significant anti-inflammatory benefits when applied topically. There is some in vitro evidence of detrimental effects on matrix metabolism, but no cartilage pathology was detected following administration in vivo.

Diclofenac is a phenylacetic acid NSAID that has been approved for **topical use**. **Surpass** (IDEXX Laboratories) is a 1% diclofenac sodium cream in a liposomal formulation for locally enhanced targeted delivery. Clinical field trials performed to obtain FDA approval in the US suggest that this medication, applied twice daily, improved lameness and joint mobility of horses with osteoarthritis, and the product has been released for veterinary use.

Atropine sulfate is used regularly in equine practice to **reduce synovial effusion** at a dose of approximately 4–15 mg per joint. A potent anticholinergic, atropine may work by reducing blood supply to the synovium, but there is little objective evidence of its effectiveness. If blood supply is restricted a poor healing response could result. Atropine therefore may be more suitable for use in managing chronic tendon sheath effusions. Doses should be limited to no more than 15 mg total body dose to avoid **gastrointestinal side effects**, and horses should be monitored closely for colic following treatment with IA atropine.

Prognosis

The prognosis for horses with osteoarthritis is dependent on the severity of the disease process, as well as a horse's individual tolerance to pain. No long-term cure can be expected in any case of osteoarthritis since hyaline cartilage does not heal effectively, and many cases require long-term medication to remain in work. Many horses can function adequately as performance horses, despite the presence of osteoarthritis. In more severe cases the best outcome that can be hoped for is for the horse to remain useful as a breeding horse, or be "pasture sound".

TRAUMATIC ARTHRITIS

Traumatic arthritis and degenerative arthritis (*q.v.*) are usually closely linked. There are some occasions when a single traumatic incident, such as a displaced IA fracture, will initiate development of arthritis. More commonly, low-grade repetitive trauma initiates a destructive cycle that results in osteoarthritis. This process is commonly observed in the carpus and fetlock of racehorses, but may be seen at any site. Traumatic arthritis also involves synovitis, capsulitis and articular cartilage damage and it is therefore very difficult to differentiate chronic traumatic arthritis from other causes of osteoarthritis.

SEPTIC (INFECTIOUS) ARTHRITIS

Etiology

Entry of bacteria into a joint can occur as a result of hematogenous spread, penetrating injuries, extension from adjacent soft tissue or osseous lesions, as a consequence of IA injection or as a complication of surgery.

Septic arthritis in foals is often referred to as **joint ill** (*q.v.*). In such cases, a focus of infection can usually be found elsewhere in the foal, such as an infected umbilicus (**navel ill**) (*q.v.*). Foals with bacterial arthritis (*q.v.*) are frequently immunocompromised and multiple joints can be affected simultaneously. Spread of infection is usually via the hematogenous route.

In adult horses, penetrating injuries and injections are the most common cause of septic arthritis. Drugs such as PSGAG (Adequan) and corticosteroids are most frequently associated with infections (Box 15.4). Septic arthritis can occur in any joint. **Iatrogenic septic arthritis** occurs more often than it should and is typically caused by *Staphylococcus aureus* (*q.v.*), which is one of the most common and most resistant joint infections to manage. It is important not to examine any wound, particularly one near a joint, with ungloved fingers, and all IA injections should be performed using strict aseptic technique. The hands are a common source of *S. aureus*, and this organism can also be present in high levels in the nasal passages of some individuals.

Clinical signs

Appearance of clinical signs can often be delayed for several days after the initial bacterial contamination, and this delay can be prolonged up to 14–21 days after corticosteroid injections. Unfortunately any delay is likely to diminish the response to therapy. Horses with septic arthritis are usually **severely**

Box 15.4 Septic arthritis following intra-articular drug administration

Corticosteroids
- Corticosteroids suppress white cell and other inflammatory responses to infection
- The ability to overcome infection is greatly reduced
- Clinical signs may not be evident until 3–21 days following the injection
- Clinical signs are often mild initially
- If in doubt, suspect sepsis following a corticosteroid injection.

Polysulfated glycosaminoglycan (PSGAG, Adequan)
- Adequan suppresses joint defense mechanisms
- Similar infection risk as observed with corticosteroids
- Less ongoing suppression of inflammation following advent of infection
- Administer with amikacin sulfate.

(grade IV/V) lame, with pain on palpation or flexion of the affected joint. There is usually **marked effusion of the joint** and a thickened joint capsule. However, there may be no obvious signs of swelling early in the course of the infection in upper limb joints, such as the shoulder, or joints with limited ability to distend, such as the pastern or tarsometatarsal joints.

Affected horses are often depressed and have a decreased appetite. They may be pyrexic. There can, however, be **considerable variation** in the severity of clinical signs. If the joint capsule is still open following traumatic injury, and there is continual discharge of synovial joint fluid there will often not be as much lameness or effusion detected, although there may be periarticular swelling.

Sometimes a low-grade chronic septic arthritis and synovitis occurs. Affected horses are moderately lame, but have severe synovitis and effusion, as well as pain on palpation of the joints, which are often very warm to touch. Such horses may respond temporarily to treatment but frequently relapse. They are usually only moderately depressed, and often have only a slight temperature rise, to approximately 38.1–38.6°C (100.6–101.5°F).

The typical **clinical signs** of septic arthritis are:

1. Heat, swelling, pain
2. Usually severe lameness
3. Variable pyrexia
4. Variable depression
5. Variable peripheral white cell changes.

Pathophysiology

Once an infection is initiated the synovial membrane responds by becoming inflamed, resulting in increased accumulation of synovial fluid and liberation of **degradative enzymes**. Inflammatory cells, particularly neutrophils, rapidly infiltrate the joint, releasing free radicals and other destructive enzymes. These enzymes result in depletion of proteoglycans and collagen from the articular cartilage matrix, and subsequently cause erosion of the articular surface. The formation of fibrin clots in the joint further compromises synovial

membrane function, provides a supportive environment for bacterial proliferation, and interferes with appropriate nutrition of the articular cartilage.

If full thickness cartilage loss occurs and bacteria penetrate the subchondral bone, a septic osteomyelitis (*q.v.*) will develop. Conversely, osteomyelitis or septic physitis can extend into a joint and initiate a septic arthritis. In such cases, the radiographic abnormalities in the subchondral bone are much more severe early in the course of the disease than would be expected if septic arthritis had been the initiating factor.

Diagnosis

There are few causes of lameness as severe as that observed with joint sepsis; these include hoof abscesses (*q.v.*) and fractures. Therefore when a patient is reluctant to weight bear, and fracture and digital infection have been excluded, it is quite likely that joint sepsis is present. Diagnosis should be based on clinical signs, joint fluid analysis and radiography.

Infected joint fluid will usually have a turbid serosanguineous or seropurulent appearance and a watery consistency. Chronically infected joints will have flocculent synovial fluid. Strong consideration should be given to a diagnosis of joint sepsis when a **synovial fluid** aspirate has a **protein** of $>3\,g/dL$ (often $>4\,g/dL$) and/or a **white cell count** $>5000/\mu L$ (often $>30\,000/\mu L$), of which 80% are **neutrophils**. Cell counts of $>30\,000/\mu L$ with >90% neutrophils are considered virtually pathognomonic for bacterial infection (although some other severe inflammatory conditions can result in cell counts in this range). However, lower values do not preclude a diagnosis of septic arthritis, especially when there is a history of steroid use. Other analyses that have proven valuable include **glucose concentrations** (expect levels below serum glucose with sepsis), **pH** (expect acidic pH, often <6.9), and **lactate** concentrations (expect elevated levels, typically $>5\,mmol/L$, but levels are also elevated following uncomplicated corticosteroid injections). Other reliable markers of joint infection are likely to be identified in the near future.

Samples should be submitted for bacteriology and cytology. Culture of organisms from infected joints can often be unrewarding; however, inoculation of enhancement broths and submitting both aerobic and anaerobic samples for culture can improve recovery rates. In addition, polymerase chain reaction (PCR) analysis is a very sensitive technique for detecting the presence of bacterial DNA and identifying organisms, but it also has a high false positive rate from contaminates or from non-viable organisms.

Joint fluid analysis reveals:

1. Turbid, watery and color altered (slightly red tinged to dark red or cloudy)
2. In severe cases, purulent fluid
3. Protein $>3.0\,g/dL$
4. WBC $>5000 \times 10^6/\mu L$ (usually $>30\,000 \times 10^6/\mu L$)
5. Neutrophils >90%
6. Culture important but often negative despite active infection.

Radiography may reveal evidence of gas within a joint or fractures associated with the sepsis or its initiating factors. Radiographic imaging is particularly valuable in conjunction with contrast studies to determine whether a wound

has penetrated a synovial structure. In long-standing cases evidence of **severe secondary osteoarthritis** may be apparent radiographically. Radiographs are indicated early in the course of disease. When this step is neglected, subsequent images often reveal findings that would have significantly altered either the treatment or the prognosis or both. Such findings include the presence of foreign bodies, osteomyelitis, sequestration or obvious disruption of the articular surface. In utilizing **radiography**, it is important to note that:

1. Radiographs should always be taken as part of the initial examination.
2. Soft tissue changes may be all that is identified initially.
3. Evidence of IA degenerative damage is a poor prognostic sign.
4. Intra-articular osteomyelitis suggests a poor prognosis.
5. Repeat radiographs are recommended at least every seven days during treatment.

Specialized **scintigraphic examinations**, including radiolabeled WBC scans and ciprofloxacin labeled scans, can provide valuable diagnostic tools in challenging cases of infection, but could delay initiation of therapy.

Treatment

Primary treatment for septic arthritis is summarized in Box 15.5. **Early** and **aggressive** treatment is required in order to eliminate the causative organisms and remove damaging inflammatory products from the joint. Treatment can be either **medical** or **surgical**; however, a combination is usually required. It is important to recognize that septic joints are an emergency and often require prolonged medication, and possibly repeated surgical intervention, if a successful outcome is to be achieved. Owners should be advised of this before treatment is instituted.

Initial **emergency treatment** should usually consist of broad-spectrum systemic antibiotics and NSAIDs, arthroscopic examination of the joint, lavage with large volumes of balanced electrolyte solution, regional limb antibiotic perfusion when feasible, and IA antimicrobials. Initial antibiotic selection should be based on the most likely pathogen (i.e. *Staphylococcus* spp. if the infection is iatrogenic), and on susceptibility patterns in the practice area.

Systemic antimicrobials are always indicated (Box 15.6). Ideally, antibiotics should be selected on the basis of culture and sensitivity patterns. Before this information is available, or when culture is unsuccessful, a broad-spectrum

Box 15.5 Primary treatment for septic arthritis

- Systemic antibiotics and anti-inflammatory drugs including NSAIDs
- Surgical lavage and drainage, followed by ongoing treatment either via indwelling catheter or via arthrotomy incisions
- Regional limb perfusion with antibiotics daily or every 2–3 days
- Intra-articular antibiotics daily or every 2–3 days
- Repeat large-volume (10 L) lavage in 1–5 days if not improved
- **Horses with septic arthritis may require treatment for months**

protocol should be initiated. A combination of penicillin and gentamicin, or potentiated sulfonamides can be used depending on resistance patterns in the particular practice area. Antibiotic therapy should be continued for at least 2 wk after clinical signs have resolved. However, up to 3 wk, additional treatment is recommended in foals, where a focus of infection is often located distant from the site of joint sepsis and also needs to be located and treated appropriately.

If *S. aureus* infection is suspected and there has been no response in 48 h with routine broad-spectrum antibiotics, consideration should be given to

Box 15.6 Commonly used systemic antibiotics for septic arthritis

- Preferably dependent upon sensitivity pattern
- Administer for ⩾2 wk after significant improvement in clinical signs
- Often require 3 wk IV/IM followed by 3 wk orally
- Adverse gastrointestinal reactions not uncommon.

Penicillin
- Procaine benzylpenicillin still very useful, but long-term IM therapy a problem
- Avoid under dosing
- Intravenous crystalline penicillin good for initial high levels.

Gentamicin
- Give 6.6 mg/kg IV once daily for an adult horse
- Concentration-dependent efficacy
- Nephrotoxicity a possible but uncommon complication
- In vivo effectiveness against *Staphylococcus* spp. is very disappointing.

Trimethoprim–sulfonamide
- Can be used orally (paste or powder), IV or IM
- Considerable resistance has been detected in some practice areas
- More useful orally for ongoing long-term treatment, particularly when susceptibility testing supports its use
- Susceptible horses can develop colitis.

Ceftiofur
- Appears to have good penetration into bone
- Can be used IV or IM in conjunction with gentamicin
- No advantage to concurrent use of penicillin
- Susceptible (stressed) horses may develop colitis.

Flucloxacillin
- Use 20 mg/kg IM four times per day
- Expensive, but well tolerated
- Extremely effective in vivo against *S. aureus.*

Enrofloxacin
- Broad-spectrum including *Staphylococcus* spp.
- Concentration-dependent efficacy
- Intraveously once daily 7.5 mg/kg
- Orally.

using **flucloxacillin** either systemically if the expense can be justified, or IA. Alternatively, **enrofloxacin** can be administered, but it should be avoided in neonates due to associated cartilage damage in developing joints.

Non-steroidal anti-inflammatory drugs are also recommended for their anti-inflammatory and analgesic effects; **phenylbutazone** or **flunixin meglumine** is often used. Patients should always be monitored for NSAID toxicity, kept well-hydrated and appropriate **anti-ulcer medications** (e.g. **omeprazole** paste s.i.d.) administered when indicated. Concerns about potential detrimental effects on cartilage matrix metabolism are probably unwarranted considering their well-documented beneficial anti-inflammatory effects.

If possible, **arthroscopic** examination of the joint should be performed. This enables a thorough examination and removal of any fibrin clots and other debris. Most importantly it allows **extensive lavage** of the joint. High-volume (⩾10–20 L) frequent lavage of infected joints is critical for effective treatment. Following arthroscopic examination and lavage, an **arthrotomy** can be performed in many cases to facilitate postoperative drainage. The arthrotomy incisions are typically left to heal by second intention, but delayed closure of the arthrotomy incision may reduce subsequent complications. Open joint wounds should be protected by **sterile bandages**, which may need to be changed twice daily if extensive discharge occurs.

When arthroscopy cannot be performed, lavage via a 10–14 G catheter needle or cannula should be performed. Ingress and egress portals should be placed on either side of the joint (or in multiple locations in large joints) and 5–20 L of **balanced polyionic solution** such as lactated Ringer's solution flushed through the joint. Saline should be avoided when possible, as it not physiologic and has been shown to be more detrimental to chondrocyte and synoviocyte function. DMSO can be added as a 5–10% solution for its anti-inflammatory and analgesic benefits. There is some evidence that DMSO is damaging to articular cartilage matrix metabolism, but no gross pathology was detected following its administration in a clinical study. During flushing, the egress cannula/s should be occluded periodically to allow distension-irrigation of the joint.

In refractory cases **continuous lavage** can also be of benefit. An IV fluid administration set-up can be used, with extendable tubing and the end of the drip set entering the joint. This technique is used when appropriate drainage portals are present or have been created to allow free egress of fluid. Lavage solutions can be flushed through under gravity flow for 24–48 h or longer if required, but dedicated nursing care is required to avoid complications. Similarly, indwelling ingress catheters can be used to administer continuous or periodic IA antibiotics. Closed suction drainage can effectively remove inflamed synovial fluid, but also requires careful monitoring to avoid ascending infections.

The use of **IA medications** is generally well accepted. In the past the main objection to their use was that they would create synovitis (*q.v.*), resulting in more damage to the articular cartilage. However, in view of the severity of the disease process induced by the sepsis, the additional synovitis, when it occurs, is probably minimal. Drugs that are known to be irritating should be avoided. The advantage of IA medication is that higher drug levels are present in the joint than can be achieved via systemic administration. The most frequently used IA drugs are **amikacin** (250 mg–1 g IA) and **gentamicin** (300–500 mg IA).

High levels of IA medication can be maintained with the use of IA **antibiotic-impregnated polymethyl methacrylate (PMMA) bone cement**. This can be formed into beads and left within the joint to elute antibiotic. However, recent studies suggest that PMMA beads can damage articular cartilage. Other antimicrobial-impregnated **biodegradable drug delivery systems**, such as collagen, DL-lactide-glycoside copolymers, and plaster of Paris implants have also been described and tested.

Another practiced method for achieving high levels of antibiotics in the joint and surrounding tissues is **regional limb perfusion**. This can be performed by placing a tourniquet on the leg and injecting antibiotics IV, IA or into a medullary cavity in a location distal to the tourniquet. The tourniquet is maintained in place for 30 min following injection. The intramedullary technique is considered particularly beneficial when there is osteomyelitis at the end of a long bone. The injection portal can be left in place so that regular treatments can be performed, and prolonged treatment is usually essential in such cases.

In refractory cases, consideration should be given to **arthrodesis** when feasible. This has the effect of eliminating the joint space and synovial membrane and is occasionally the only means of resolving the problem.

Supportive care should include providing support to the opposite limb and foot to avoid breakdown and/or development of **laminitis** (*q.v.*). Physical therapy should also be initiated including passive range of motion exercises to avoid restrictive joint capsule fibrosis.

Prognosis

The earlier treatment is initiated, the better the chance of successful resolution (Box 15.7). If **sepsis** has been present for 14 days or more the chances of successful long-term resolution are low. Even if the infection is controlled, **cartilage damage** may be severe enough to render the horse chronically lame. Consideration needs to be given to the long-term usefulness of the horse before continuing aggressive treatment in horses that do not respond well initially.

The long-term prognosis can be very good if the infection is controlled early. Several months rest should be provided after any episode of septic arthritis (*q.v.*) to allow the articular cartilage to regain normal extracellular matrix form and function. This **exercise hiatus** should be implemented even if the condition appears to have resolved rapidly with no obvious, immediately apparent adverse effects. Radiographs prior to resuming exercise are also indicated to assess whether any long-term adverse effects have resulted.

Box 15.7 Septic arthritis—summary

1. Early diagnosis and treatment is the key to success
2. There is a requirement for aggressive, often long-term treatment
3. Clients must be advised of prognosis and potentially escalating costs
4. Immediately advise the livestock insurance company when the condition is detected.

MISCELLANEOUS JOINT DISEASES

Immune-mediated joint disease

Immune-mediated joint disease (*q.v.*) is infrequently encountered in the horse, but should be suspected if synovitis is present in multiple joints and no specific etiology can be determined. Synovial fluid analysis will be consistent with a non-infectious inflammatory arthritis. **Polysynovitis** has been documented with **systemic lupus erythematosus** or an immune reaction to ***Streptococcus*** spp. (*q.v.*) or ***Rhodococcus equi*** (*q.v.*) infection.

Treatment with systemic **prednisolone** can be effective if instituted before secondary cartilage damage occurs. A suitable dose rate for oral prednisolone therapy is 1 mg/kg b.i.d. for 7 days, then 1 mg/kg s.i.d. for 7 days, and reducing to 1 mg/kg every 2–3 days for 2–3 wk. Longer periods of therapy may be required to prevent recurrence.

Calcinosis circumscripta

Calcinosis circumscripta manifests as **abnormal calcification** in or adjacent to the joint capsule, and usually occurs as a result of trauma. It is often found in close association with joints, particularly the stifle joint. The calcification is often oval in shape, and is well circumscribed from surrounding tissue. Clinically these calcifications present as firm, non-painful, subcutaneous swellings. The masses have a characteristic radiographic appearance. Removal is recommended if the lesion is large or interfering with joint function. The prognosis is usually good after surgical removal.

Synovial hernia

Herniation of the synovial membrane through a defect in the fibrous joint capsule usually occurs as a result of trauma, but may not become clinically apparent for some time after the initial traumatic episode. A hernia appears as a soft, subcutaneous swelling that is non-painful. Injection of contrast media into the hernia or the joint will reveal a communication between the two, and the communication can also often be documented with ultrasound. The most successful resolution is obtained with surgical repair.

A **synovial hernia** should be differentiated from a **ganglion** (*q.v.*). The latter is a cystic structure containing mucinous material, with no discrete synovial lining, also found in close association to a joint or tendon sheath but not appearing through a defect in the joint capsule. Histologic evaluation is often required to differentiate accurately between these conditions. Treatment for a ganglion is also surgical removal.

DISEASES OF SPECIFIC JOINTS

Scapulohumeral (shoulder) joint

Diagnostic **IA anesthesia**, ultrasound and radiography are usually required to confirm a diagnosis of shoulder lameness. Scintigraphy may also be required to localize the problem, and contrast arthrograms are occasionally necessary to identify cartilage lesions. Intra-articular anesthesia (*q.v.*) is performed through

a needle placed between the cranial and caudal eminences of the greater tubercle of the humerus. Joint fluid should be aspirated prior to injection. Lameness can improve within 15 min, but up to 1 h should be allowed before deciding on a negative result. In some horses the intertubercular (bicipital) bursa communicates with the shoulder joint.

Lateral radiographs can be obtained in the standing horse. The affected leg is simultaneously extended and pulled downward as far as the horse will allow. The plate is held against the affected joint and the beam directed from the opposite side of the horse, under its neck. In this position the articular surface of the joint should overlie the radiolucent shadow created by the trachea. Many horses with shoulder lameness will resent the limb being pulled forward as far as is necessary to obtain good standing radiographs. Oblique radiographs can also be obtained if fractures of the supraglenoid tubercle or lateral tuberosity are suspected. **General anesthesia** may be required to obtain high quality radiographs, and is essential for craniocaudal views.

Scapulohumeral **osteochondrosis** (*q.v.*) usually manifests as a chronic low-grade lameness that may be greatly exacerbated by exercise. The shoulder tends to be one of the most severely affected joints with OCD. Affected horses are reluctant to allow extension of the limb and muscle atrophy is often evident. Conservative treatment is only successful in approximately 20% of cases. Arthroscopic debridement of the lesions improves the prognosis, but the success of arthroscopic surgery is dependent on the location of the lesion and the severity of associated osteoarthritic changes. Instrument access to some lesions on the medial aspect of the humeral head or deep in the glenoid cavity can be difficult to achieve resulting in limited ability to debride the lesion. Intra-articular medication consisting of 20–40 mg of hyaluronan (*q.v.*) can be of benefit.

Intra-articular fractures of the supraglenoid tubercle are relatively common, and horses typically present with severe lameness of acute onset. There is often a history of the horse having run into an object, taking most of the impact on the shoulder. There is usually pain and swelling evident on palpation. Conservative management will result in a very high incidence of **severe osteoarthritis**. Surgical management, consisting of internal fixation or fragment removal, can result in athletic soundness. Best results are observed following removal of smaller fragments via arthrotomy. Larger fragments create more of a problem, as the joint can become unstable following removal. Reasonable results can be achieved following removal of large fragments, but internal fixation has been used more successfully. Fracture reduction can be difficult and the pull of the biceps brachii can result in fixation failure. Consequently, partial or complete transection of the biceps in conjunction with internal fixation has been advocated.

Luxation of the scapulohumeral joint occurs primarily as a result of trauma, although severe osteoarthritis and remodeling, or muscle atrophy occurring as a result of "sweeny" (*q.v.*), can predispose to this. Ponies and miniature horses appear to be at a higher risk for luxation. Since the shoulder has no collateral ligaments, and joint stability is maintained by the joint capsule and surrounding musculature, luxation occurs without ligamentous disruption. Affected horses have a severe lameness, and palpation usually demonstrates luxation. Radiography may be required to confirm the diagnosis if severe swelling has

occurred, and is also useful in determining whether any associated fractures are present. Reduction can be extremely difficult, almost invariably requiring general anesthesia. Once reduced, the incidence of reluxation is surprisingly low, but owners should be advised of this possibility.

Cubital (elbow) joint

Intra-articular fractures of the olecranon are the most commonly diagnosed problem affecting the elbow joint. Horses often have a "dropped elbow" appearance due to loss of triceps function, but this must be differentiated from other upper forelimb fractures, and from radial nerve paralysis. Surgery consisting of internal fixation with either a bone plate or a tension band technique can result in an excellent outcome (*q.v.*). Radiography is essential and the prognosis is dependent on the configuration of the fracture and the age of the horse.

Osteochondrosis and **subchondral cystic lesions** (*q.v.*) are diagnosed infrequently in the elbow. Osteoarthritis is also encountered less commonly in the elbow but may be under diagnosed. Diagnosis of elbow problems is usually reached following IA anesthesia and radiography. Intra-articular blocks can be performed using several alternative approaches but the joint is often approached immediately caudal to the lateral collateral ligament. Radiographic signs are often minimal in osteoarthritis of the elbow, and any remodeling should be considered significant. **Bone cysts** of the elbow are usually detected on a craniocaudal radiographic view.

Prognosis for athletic soundness in cases of bone cysts is guarded, but may be improved if extra-articular surgical debridement can be achieved. Intra-articular medication is usually required if the animal is to pursue an athletic career following development of osteoarthritis in the elbow joint.

Carpus

The carpus is a complex high-motion joint comprised of the **antebrachiocarpal** (radiocarpal), **middle carpal** (intercarpal) and **carpometacarpal** joints. The most common abnormality occurring in this joint is traumatically induced osteoarthritis, which often occurs in association with chip or slab fractures in racehorses.

Lameness resulting from carpal lesions can vary in severity from barely detectable to non-weight-bearing. **Effusion** in the middle carpal and/or antebrachiocarpal joints is usually evident after joint damage has occurred. This is detected as swelling over the joint space medial to the extensor carpi radialis tendon or between the extensor carpi radialis and the common digital extensor tendon. Effusion can also be detected over the palmar lateral surface. The degree of effusion can be variable, and in some instances, particularly following a lay-up period with an injury involving the antebrachiocarpal joint, effusion may not be evident even when a fracture is present.

Response to **flexion tests** (*q.v.*) can also be unreliable in determining whether a carpal lesion is present. While a positive response to flexion is usually reliable, a negative response does not preclude the presence of a carpal lesion.

Although a tentative diagnosis of a carpal injury can often be based on clinical observations, **IA anesthesia** (*q.v.*) is frequently required to localize the source of pain. The middle carpal and carpometacarpal joints reliably communicate and they are anesthetized simultaneously. This can be done through a dorsal approach 1 cm medial or lateral to the extensor carpi radialis tendon with the leg held in flexion, or the joint can be blocked through the palmarolateral pouch with the limb in a standing position. Response should be evaluated after 5–10 min, although up to 30–40 min may be required before a negative result can be confirmed. The distopalmar outpouchings of the carpometacarpal joint can result in inadvertent anesthesia of the proximal suspensory ligament and proximal metacarpus. Similar techniques are used for the antebrachiocarpal joint, which rarely communicates with the other joints.

A minimum of **eight radiographic views** is recommended for complete evaluation of the carpus. These are a lateromedial, flexed lateromedial, a dorsopalmar view, 45° dorsomedial–palmarolateral and dorsolateral–palmaromedial obliques, and a skyline (dorsoproximal–dorsodistal) view of the proximal and distal row of carpal bones, and of the distal radius. The skyline views are very useful, and will often identify lesions that are not evident on any other projection. The dorsopalmar view can identify stress fractures in the proximal metacarpus, and on rare occasions can reveal unusual fractures in the carpal bones. Accurate interpretation of subtle radiographic lesions in the carpus requires experience.

Osteoarthritis

Osteoarthritis of the carpus can be evident in any age, breed or performance category and is probably the most common carpal problem. In racing Thoroughbreds carpal joint disease is seen frequently in younger horses. Clinical signs of osteoarthritis in the carpus frequently go undetected until an IA chip or slab fracture occurs (*q.v.*) and the degree of lameness increases dramatically. Differentiation of osteoarthritis from fractures is often difficult since the two problems are linked. Response to medical therapy for osteoarthritis (*q.v.*) can be variable, with relief of clinical signs ranging from weeks to 6 mo. Repeated treatments are usually indicated. Once fractures occur, arthroscopy is clearly indicated. However, arthroscopic evaluation can also be recommended for horses with unresponsive inflammation in the absence of radiographic abnormalities. CT and MRI scans can also provide important diagnostic information in those cases.

A debilitating syndrome of carpometacarpal osteoarthritis has been described in older performance horses. Arabian and Quarter Horses seem to be predisposed to this condition and carpal trauma appears to be the initiating factor. Conservative management offers a poor prognosis for return to use, and a method of carpometacarpal arthrodesis, similar to that used in the distal hock joints, has been reported with excellent clinical results.

Chip and slab fractures

Osteochondral fragments (**chip**) and **slab fractures** are almost invariably the end stage of a **chronic** low-grade degenerative process initiated by **repetitive loading trauma**. As the disease progresses, the subchondral bone becomes lytic and weakens, eventually resulting in a fracture. Most fragments develop

dorsally. The characteristic location of these fractures can be explained by a combination of factors, including maturity of the horse, conformation and direction of racing. The role of OCD-like changes as a predisposing factor to carpal fractures should be considered, particularly for bilaterally symmetrical lesions. The most common sites are the **medial aspect of the distal radial carpal bone, the medial aspect of the proximal third carpal bone, the lateral aspect of the distal radius, and the proximal aspect of the intermediate carpal bone**. Frequency of fracture at these locations varies between different racing breeds. Multiple fractures may be present in one joint, or be present in both antebrachiocarpal and middle carpal joints. Lesions are often bilaterally symmetrical. For this reason it is recommended that **both carpi** be radiographed routinely when carpal joint disease is present.

Fractures of the **palmar carpal bones** are much less common, and are frequently associated with significant lameness. Horses resent carpal flexion, which tends to impinge on the fragment. Diagnosis is complicated by multiple overlapping lines of the palmar borders of the carpal bones, and CT may be required to confirm fracture location.

Frontal plane slab fractures, which by definition involve both proximal and distal articular surfaces, occur primarily in the third carpal bone. Again, degenerative changes usually predispose to this type of fracture. **Sagittal plane slab fractures** are also most frequently identified in the third carpal bone, but are much less common than frontal slab fractures.

Arthroscopic surgery is usually recommended as the treatment of choice for management of osteochondral fractures. At the time of surgery, any additional fractures can be identified, fracture fragments and degenerative cartilage removed, and the joint thoroughly flushed. Postoperative complications are minimal, and horses can usually return to work 1–6 mo after surgery, depending on the severity of lesions. Approximately 85–90% of horses undergoing arthroscopic surgery of the carpus will be able to return to athletic competition. The prognosis is considered better for lesions in the antebrachiocarpal joint compared to the middle carpal joint. Postoperative IA medication is occasionally recommended, but is not essential for a successful outcome. Palmar carpal fragment removal can be performed arthroscopically or via a small arthrotomy.

Conservative therapy can also be successful, however the time required out of training, the increased requirement for IA medication and a poorer long-term prognosis should be considered if this form of therapy is selected. Many chip fractures will heal with irregularity of the articular margin, which predisposes to more severe OA and re-fracture.

The prognosis for carpal osteochondral fragments is influenced by the severity and location of lesions. When bilateral lesions are present, the prognosis is determined by the severity of the worst lesion.

Many slab fractures are amenable to internal fixation using a lag screw technique or self-compressing screws, and this can usually be performed using arthroscopic guidance. If the fragment is severely displaced and cannot be reduced by carpal flexion, an arthrotomy may be required. **Displaced slab fractures** require internal fixation if the horse is to remain competitive, and the results after this surgery are generally good. Some non-displaced slab fractures do heal with conservative management, while some slab fractures are too thin to support fixation and necessitate removal.

Other articular fractures

Longitudinal fractures of the proximal third metacarpal bone extending into the carpometacarpal joint are occasionally detected (*q.v.*). A similar condition is seen less frequently in the **proximal metatarsus**. There is frequently pain on palpation of the dorsal aspect of the proximal metacarpus. Lameness will be improved or abolished with a middle carpal block (*q.v.*). Conservative therapy is usually effective but surgical management with internal fixation or osteostixis (*q.v.*) may be indicated depending on the pain associated with the fracture, its severity, and chronicity. Intra-articular fractures of the second and fourth metacarpal (splint) bones require internal fixation for the best long-term prognosis. Untreated IA fractures of the splint bones can result in severe osteoarthritis of the carpometacarpal joint and may necessitate arthrodesis (*q.v.*).

Intercarpal ligament damage

Another carpal injury regularly diagnosed in athletic horses is damage to the **medial palmar intercarpal ligament**. This ligament extends between the second and third carpal bones and the radial carpal bone and resists dorsomedial displacement of the radiocarpal bone. Damage ranges from complete rupture to mild disruption of fiber alignment and fraying of the edges of the ligament. Lameness resulting from this damage is inconsistent, and changes are usually seen in association with carpal chip fractures or other joint pathology. Horses typically present with variable forelimb lameness, which has frequently been present for some time. There is usually minimal swelling in the affected joint, and localization requires IA anesthesia. No consistent radiographic abnormalities are evident; however, longer-term signs of osteoarthritis may become evident due to low-grade instability in the joint. Confirmation of the diagnosis is by arthroscopic evaluation, although MRI should also be capable of detecting ligament damage. The condition is usually treated by resting the horse; however, the rate of recurrence is high. Intrinsic repair of the ligament is facilitated if part of the ligament remains intact, when compared to cases with complete rupture. Intra-articular corticosteroids may be required to maintain the horse free of lameness but should be avoided during initial rehabilitation.

A syndrome of **lateral palmar intercarpal ligament avulsion** has also been reported as a clinically significant source of lameness. Treatment involves arthroscopic debridement and rest, and the prognosis for return to athletic competition is good.

Osseous cyst-like lesions (subchondral bone cysts)

Bone cysts can occur in any of the carpal bones or proximal metacarpus. They range in size and can even completely occupy the space within the cuboidal bones. The prognosis for athletic soundness is poor. These cysts should be differentiated from cystic looking areas that are often apparent within the ulnar carpal bones of young Thoroughbred horses, but which resolve with maturity. Incidental cyst-like lesions can also be observed in the second carpal bone and in the base of the second metacarpal bone that are not associated with lameness.

Incomplete ossification of the carpal bones

Carpal bone collapse can occur in young foals, usually as a result of incomplete ossification of the carpal bones in **immature** or dysmature neonates

(*q.v.*). Left untreated, incomplete ossification often progresses to collapse of the cartilage/bones and resulting **angular limb deformity**. Once collapse occurs, treatment is limited to restriction of exercise and the use of tube casts to support the limb, and the condition carries a somewhat guarded prognosis for future athletic performance.

Accessory carpal bone fractures

Fractures of the **accessory carpal bone** are thought to result from direct trauma, hyperextension injuries, or when the bone is crushed between the radius and metacarpus (*q.v.*). These fractures usually result in marked lameness, swelling and severe pain with carpal flexion. The most common configuration is a frontal plane (vertical) fracture through the proximal and distal borders. These fractures have a surprisingly good prognosis when treated conservatively, despite the obvious non-union that develops. Affected horses can resume a normal athletic career following up to 12 mo rest. Attempts at internal fixation are usually unsuccessful. Complications of these fractures include carpal canal syndrome (*q.v.*) and tenosynovitis.

Metacarpophalangeal/metatarsophalangeal (fetlock) joint

Diagnosis of fetlock lesions is generally based on clinical findings and diagnostic regional nerve blocks or intrasynovial anesthesia. Many horses, particularly older horses and those that have had some degree of training, will have a positive **fetlock flexion test** (*q.v.*). Interpreting the significance of such a reaction can be difficult. Lameness originating in the fetlock can often be abolished with IA anesthesia (*q.v.*). A number of alternative injection techniques have been described including dorsal, proximopalmar and distopalmar approaches as well as an approach through the collateral ligament of the proximal sesamoid.

Radiographic evaluation of the fetlock requires careful attention to positioning and exposure. **Five views** should always be taken. These include dorsopalmar/plantar, lateromedial, flexed lateromedial, dorsolateral–palmaromedial and dorsomedial–palmarolateral oblique views. The dorsopalmar/plantar view should be taken with the beam angled down approximately 30° from the horizontal and centered on the joint space, which has the effect of elevating the sesamoids and thereby providing a clear view of the articular surface of the joint. Additional views of the fetlock include a 125° dorsodistal–palmaroproximal (extended dorsopalmar view), and 45° lateroproximal–mediodistal and 45° medioproximal–laterodistal oblique projections. A partially flexed horizontal beam dorsopalmar view can be substituted for the extended dorsopalmar/plantar view if the horse is not in too much pain for flexion.

Synovitis/capsulitis and supracondylar lysis ("osselets")

A precise definition of **synovitis–capsulitis** as a clinical condition is difficult. These horses generally present with either a slight thickening of the joint capsule and/or an increase in joint fluid pressure. These changes are of uncertain significance in some cases, although distension in the fetlock joint is an indication that some abnormality has occurred. In young athletes, synovitis may be a result of abnormal stresses being placed on the joint, and the joint subsequently adapts without more serious injury. However, the distension will

often remain as a permanent record of previous joint damage. In other cases the joint damage can progress and become clinically significant. Horses usually resent fetlock flexion, and are noticeably lamer for 10 strides or more after fetlock flexion. In the initial stages of this condition, no radiographic abnormalities are detectable. If the problem progresses, radiographic signs of osteoarthritis may be present.

Virtually **every young racehorse** will experience this syndrome. The presumed etiology of synovitis–capsulitis is chronic low-grade trauma to the joint capsule and articular surface. Fibrosis in the joint capsule develops, and restricts the range of motion. Lameness is not always evident with this condition, and when capsulitis–synovitis is the sole abnormality, lameness is usually mild. It is important to realize that **chronic capsulitis–synovitis** with effusion is frequently encountered, particularly in performance animals, and may not be contributing to any lameness present at the time of examination. Therefore IA anesthesia (*q.v.*) is recommended to localize the lameness and provide information about the likelihood of a positive response to IA medications.

Treatment for acute cases consists of systemic anti-inflammatory medication for 2–3 wk and 6–12 wk of rest or modified exercise. In most cases, IA medication consisting of hyaluronan and/or corticosteroids (*q.v.*) is indicated, particularly if an exercise program is to be continued. The prognosis is variable, as ongoing trauma necessitates continuous medication and each horse responds differently to the discomfort associated with this condition.

Chronic synovitis can result in erosion of the palmar articular surface. Presumably this occurs as a result of chronic elevation in joint fluid pressure. The condition is identified on radiographs and is referred to as **supracondylar lysis**. The prognosis for these horses is considered guarded by some, although the radiographic change is occasionally seen in horses not displaying any clinical signs. There is no effective treatment but management with IA corticosteroids and hyaluronan is indicated.

Osteochondrosis

Osteochondrosis (*q.v.*) of the fetlock can manifest in several different forms. Lesions involving the **dorsal aspect of the distal third metacarpal/metatarsal bone** (originally referred to as OCD of the **sagittal ridge** of the third metacarpal and metatarsal bones) are the most commonly recognized form of this disease. **Palmar and plantar osteochondral fragments** of the proximal phalanx, and **dorsal osteochondral fragments from the proximal first phalanx** may also represent forms of osteochondrosis. The condition previously referred to as palmar/plantar OCD or palmar/plantar condylar necrosis is apparently traumatically induced and no longer considered to be a manifestation of osteochondrosis.

Osteochondrosis of the dorsal aspect of the distal third metacarpal/metatarsal bones is seen commonly in pre-sale yearling radiographs and is often of little long-term clinical significance. It is also seen in older horses, sometimes as an incidental finding. While the exact significance can be difficult to determine, it is important to assess the degree of effusion in the joint, evaluate lameness and determine if there is any radiographic evidence of a flap of cartilage or underlying subchondral bone damage. All four fetlocks should be radiographed when lesions are identified in one joint.

If there is flattening of the sagittal ridge with no associated clinical signs then no surgical treatment is required. Horses <18 mo of age should usually be managed conservatively at that time as many lesions show improvement radiographically. However, if there is evidence of a flap, or effusion or lameness then arthroscopic examination is indicated. The prognosis following debridement is usually good, providing the entire lesion is treated. Access can be difficult in some cases.

Osteochondral fragmentation of the proximal phalanx

Proximal phalanx (P1) fractures are frequently observed in horses. The most common type is a small osteochondral fracture from the **medial eminence** on the **dorsal proximal aspect of P1**. Fractures from the lateral eminence also occur, and occasionally fractures are found both medially and laterally. These fractures appear to result from impingement by the distal third metacarpal bone that occurs during hyperextension of the joint during high-intensity exercise.

Fractures are frequently seen in association with **chronic proliferative synovitis**, which can also produce abnormal stresses on proximal P1 with impingement during exercise. It has been suggested that some of these fragments are a manifestation of osteochondrosis, particularly when they are identified in yearlings and non-racing breeds, but most fragments are presumed to be of traumatic origin.

Clinical signs vary from no detectable problems to moderately severe lameness. There can be joint effusion and pain on flexion. Intra-articular anesthesia is sometimes required to identify the fetlock as the source of lameness. Confirmation is by radiography. Some P1 fractures are first identified on pre-sale radiographs, and the interpretation of such a finding can be difficult. While some P1 fractures will cause few problems, in the majority of cases some degree of lameness and/or synovitis will be evident. In most instances a non-union develops, and continual movement of the fragment results in pain and inflammation in the joint. Bilateral fractures are common, and the contralateral fetlock should always be examined. The forelimbs are far more frequently affected than the hindlimbs.

If lameness and/or inflammation are present, arthroscopic removal of the fragments is recommended. The prognosis after removal is good to excellent. Affected horses can resume training from 6 to 16 wk after surgery, depending on the extent of cartilage damage.

Palmar and plantar fragments from proximal P1 are more often identified in the hindlimbs than the forelimbs, and are more commonly seen in Standardbreds and Warmbloods. These lesions often appear to be a manifestation of OCD (*q.v.*), although there is increasing evidence that many are avulsion fractures at the insertion of the distal sesamoidean ligaments. The fragments are usually located in the joint capsule between P1 and the base of the sesamoids. They most often occur medially, but can occur laterally or biaxially.

The degree of lameness and effusion associated with these lesions is often only slight, with a gait abnormality only evident at high speeds. Intra-articular anesthesia is often required to locate the lesion, and examination at high speeds after anesthesia may be required to confirm that the lesion is contributing to lameness. The diagnosis is confirmed radiographically. The fragment of bone may only be clearly evident on a lateromedial projection centered on

the base of the sesamoids, or a dorsoproximolateral–palmarodistomedial or dorsoproximomedial–palmarodistolateral oblique projection. The fragments can be difficult to detect on standard 45° oblique projections.

Prior to treatment, it should be determined whether the fragments are causing a clinical problem. In many cases the lesion is detected on survey radiographs and may not be a cause of lameness. However, if lameness is identified as arising from the affected joint, then treatment is by arthroscopic removal. Not all fragments at this site are IA, as some are buried in the joint capsule, and surgery can be challenging. The use of an electrocautery probe or radio frequency technology can facilitate removal. The prognosis after arthroscopic removal is good.

Larger palmar or plantar eminence fractures can result in more severe lameness in the acute phase. These are often traumatic in origin, although large OCD lesions may occur. In acute fractures heat, swelling and pain are evident at the fracture site. However, after this acute phase the degree of lameness may be minimal, although there is usually some obvious thickening of the area. Intra-articular fragments require surgical treatment if athletic soundness is required. Lag screw fixation can be performed if the fragment is large and acute. In many cases, by the time a diagnosis is made an obvious non-union has developed. In such cases removal using an extra-articular approach is usually indicated. The prognosis is generally good, even for larger fragments.

Chronic proliferative synovitis (villonodular synovitis)

Chronic proliferative synovitis refers to an increase in size of the bilobed synovial pad (plica) in the dorsal aspect of the fetlock joint at the distal aspect of the metacarpus. The proliferation occurs as result of **repetitive trauma** from the proximal aspect of the first phalanx that occurs with hyperextension of the fetlock during strenuous exercise. As the tissue increases in size, damage may also occur on the proximal aspect of P1, including cartilage erosion and chip fractures. The forelimbs are affected far more frequently than the hindlimbs, and chronic progressive synovitis is often an underrated cause of fetlock problems in athletic horses.

Villonodular synovitis may represent a progression of chronic proliferative synovitis, being much larger and more pedunculated. This form of the disease can usually be detected on palpation of the joint.

These horses are usually lame, but often the gait deficit is not readily detectable. Trainers may comment that the horse has been unwilling to "stretch out", or has been reluctant to perform or "faded" during a race. The lameness is usually chronic and is frequently bilateral.

There is usually moderate to severe **pain on flexion**, and a markedly positive response to a fetlock flexion test. Intra-articular anesthesia may be required to localize the lameness to this joint. The diagnosis can usually be confirmed with radiographs and/or ultrasound. Plain radiographs reveal a characteristic dishing of the dorsal distal aspect of MC3 ("cut-out"), just distal to the level of the attachment of the joint capsule. There may also be areas of dystrophic mineralization apparent in this defect. The lesion is typically identified on lateromedial radiographs, but can be obscured if even a small amount of obliquity occurs. The opposing aspect of P1 is often roughened, or a chip fracture may be present. Ultrasonographic evaluation can also be used

to confirm the diagnosis and provide a more accurate assessment of the size of the synovial villi. In some instances contrast radiography with 50 mL air or 10–15 mL of positive contrast agent is used to confirm the diagnosis.

Non-surgical treatment, such as IA corticosteroids and alterations in training, can resolve the problem in its early stages, but is often ineffective for advanced cases. A short-term beneficial response may be observed, but clinical signs frequently recur. Arthroscopic surgery is considered the definitive treatment for this condition. The enlarged synovial membrane is removed and any lesions on P1 can also be treated at this time. The response to surgery is excellent, with some horses returning to athletic activity within 4 wk of surgery. Recurrence appears to be uncommon.

Luxation

Luxation of the fetlock joint usually occurs as a result of direct trauma, especially when a horse gets its foot trapped. Diagnosis is usually not difficult. Radiographs are indicated to determine if the luxation is exclusively the result of soft tissue disruption or if concurrent osseous lesions have occurred. Medial and lateral stressed views will confirm joint instability. Ultrasonography is used to evaluate the extent of the soft tissue injury and is the optimal way to identify less extensive collateral ligament injuries. Closed luxations are best treated by external immobilization with a fiberglass cast for up to 12 wk. The prognosis can be good, and some animals are able to resume athletic careers. Recurrent luxation and osteoarthritis are the most frequent complications. Implantation of synthetic mesh to replace the ruptured collateral ligament has been described, and may be indicated with recurrent luxations, but has also been associated with infection.

With **open luxations**, the wound should be thoroughly debrided and the joint flushed. Primary closure can be attempted, but if severe contamination has occurred then the joint is best left either partially or completely open. Casting is then required (again for up to 12 wk), although frequent changes are required until the soft tissue injuries have resolved. The prognosis for these horses is guarded, but some do become useful athletic animals. Septic arthritis, reluxation and osteoarthritis are the major limiting factors.

If severe injuries such as extensive fractures or rupture of the suspensory apparatus (*q.v.*) have occurred in association with the luxation, then arthrodesis may be indicated, either as the initial management option or later when any soft tissue lesions have resolved.

Palmar/plantar condylar necrosis

Subchondral bone damage in the **distal palmar aspect of MC3** has been identified as an athletic injury. Originally considered to be a manifestation of osteochondritis dissecans (OCD), these lesions appear to develop due to focal impact from the base of the proximal sesamoids during strenuous exercise. Young horses are most often affected, and are presented for severe lameness that has often recurred despite rest or other treatments. A diagnosis is made based on clinical signs, response to intrasynovial anesthesia, and radiography. Scintigraphy is very sensitive at detecting these lesions in the early stages. Linear or crescent-shaped lucencies ("flattening") of the palmar or plantar

aspect of the condyles are usually identified on the flexed lateromedial radiographic projection or can be seen on the 125° dorsodistal–palmaroproximal or flexed dorsopalmar/plantar views. The flattening corresponds to severe cartilage erosion and subchondral bone damage. Treatment is unrewarding in most cases, and a very guarded prognosis should be given.

Proximal interphalangeal (pastern) joint

Osteoarthritis of the pastern joint is also commonly referred to as degenerative joint disease, or **high ringbone**, and can be seen in any age or breed of horse. Lameness is usually chronic and low grade. There is typically a positive response to distal limb flexion. In long-standing cases there is often palpable bony enlargement around the pastern joint. Effective regional anesthesia may be achieved by desensitizing the palmar nerves at the abaxial border of the sesamoids. Intra-articular anesthesia can be used for added specificity. Radiography is required to confirm a diagnosis of osteoarthritis.

Early stages of ringbone can often be effectively managed with a combination of IA medication, low dose NSAID therapy and ensuring that the horse is shod correctly with a **well-balanced foot**. A good response will often be obtained initially with this therapy, particularly with IA corticosteroids and hyaluronan. Repeated medication will be required for long-term management. Surgery, consisting of arthrodesis, can provide permanent relief. Arthrodesis can be performed using a number of different surgical techniques. One technique involves placing three parallel 5.5 mm diameter lag screws across the joint space. The screws enter the distal dorsal aspect of P1 and exit through the caudal proximal aspect of P2. Postoperatively the leg is placed in a cast for several weeks.

Fractures

Chip fractures are diagnosed infrequently in the pastern. Any aspect of the pastern can be affected. Most cases appear to be the result of direct trauma, but OCD may also produce fragmentation. A chronic, low-grade lameness is usually present. If the fracture is dorsal, lateral or medial, some swelling may be evident. Many of these fractures result in non-unions, and if lameness persists after rest, surgical removal is indicated. This can be done via arthroscopy or arthrotomy, depending on location and size. The most common complication is long-term osteoarthritis, even though the joint may appear to be relatively healthy at the time of surgery. In severe cases arthrodesis may be indicated.

Osteochondrosis

OCD (*q.v.*) should be considered in the differential diagnosis in young horses, particularly when more than one joint is affected. OCD of the pastern can be very painful and rapidly progress to severe osteoarthritis. Conservative therapy of pastern OCD is usually unrewarding. Most horses require arthrodesis if lameness is to be resolved. Bone cysts can also be found, and multiple cysts are often associated with severe osteoarthritis. The prognosis for these is also poor without arthrodesis as surgical access is very difficult, if not impossible. An extra-articular approach is often the best means of surgically debriding these cysts.

Luxation

Luxation of the pastern joint usually occurs as a result of acute trauma. These are usually medial or lateral luxations. Acute cases that can be reduced effectively can be treated by cast application. However, the results are disappointing. Most pastern luxations either cannot be reduced by closed manipulation or reluxate readily after reduction. Surgical arthrodesis is therefore considered the treatment of choice. Many cases will spontaneously ankylose over a period of 2–4 yr if surgery is not performed.

Subluxation

Subluxation (dorsal or palmar/plantar) can also occur, and is more common in the hindlegs and in younger horses. The etiology is uncertain, but may be related to flexural deformities or deep digital flexor tendon (DDFT) contracture. Subluxation can also occur as a result of reduced weight bearing due to chronic lower limb pain or as a result of acute trauma.

A surgical technique that involves severing the medial head of the DDFT in the hindleg has been reported for resolving dorsal subluxation associated with excessive tension on the DDFT. Conservative treatment can also be effective and includes ensuring relief from low-grade pain if present and dietary management, ensuring that a well-balanced ration is provided and that rapid growth rates are avoided. Arthrodesis provides definitive management.

Distal interphalangeal (coffin) joint

See Diseases of the foot (*q.v.*).

Sacroiliac joint (sacroiliac subluxation/strain/osteoarthritis)

The sacroiliac joint is a true diarthrodial joint although it has virtually no movement and the joint cavity is only a cleft. It is stabilized by the dorsal interosseous and ventral **sacroiliac ligaments**, the sacrosciatic ligament and the iliolumbar ligament. This joint provides the attachment between the pelvis and the axial skeleton, and as such it has to transfer both weight-bearing and propulsive forces.

Injury to the sacroiliac joint is a common problem and source of lameness, particularly in Standardbred racehorses, but diagnosis is challenging. Stresses that produce joint motion may produce subluxation of the joint. These include falls or repeated trauma from strenuous exercise. Apparent prominence and asymmetry of the tuber sacrale reflects previous injury to the sacroiliac joints (**hunter's bump**) or muscle atrophy.

Definitive diagnosis is very difficult. In the **acute stage** of injury the horse is usually lame. Lameness may be manifest as a bilateral shortness of stride or unilateral lameness. Pain can often be elicited with manual pressure applied over one or both tubera sacrale or the surrounding muscles.

A technique for ultrasound-guided **periarticular** administration of local anesthetic has been described to facilitate confirmation that the sacroiliac joint is the source of lameness. This same approach can be used to inject corticosteroids therapeutically. Nuclear **scintigraphy** can be helpful diagnostically in equivocal cases. Ultrasonography is useful to detect damage to the dorsal

sacroiliac ligament or to rule out pelvic fractures. A rectal examination can be used to detect crepitus associated with the subluxation, and to obtain ultrasound images of the ventral sacroiliac ligaments. Radiographs may be required to evaluate associated pelvic fractures.

Lameness can resolve with prolonged rest although some asymmetry with protrusion of one or both tubera sacrale is likely to persist. Asymmetry of the tubera sacrale should be differentiated from muscle atrophy, and many horses with asymmetry do not have sacroiliac subluxation. The prognosis is poor for full recovery due to risk of repeated injury, and return to work should be regulated to minimize this risk.

Chronic pain associated with the sacroiliac joints can result in poor hindlimb impulsion with a tendency to move closely or to plait behind, reluctance to jump, a history of poor performance or much less commonly overt lameness. Other potential causes of lameness should be eliminated before diagnosing this condition. Scintigraphy is particularly valuable for facilitating diagnosis, but images should be interpreted conservatively. Occasionally, irregular widening of the sacroiliac joints can be appreciated radiographically, with or without new bone formation on the caudal aspect of the joint. This may be associated with enlargement of the articular surfaces. Ultrasonography may also be useful for assessment of the dorsal sacroiliac ligament. Affected horses are usually best kept as fit and well muscled as possible and may respond to long-term NSAID therapy. The presence of radiographic abnormalities warrants a guarded prognosis.

Coxofemoral (hip) joint

Abnormalities of the hip joint are infrequently diagnosed in the horse, but **many may be overlooked** due to difficulties associated with localizing lameness in this area. Diagnosis usually relies on the exclusion of lower limb problems, the presence of muscle wasting around the pelvis, and radiography, ultrasound or nuclear scintigraphy. Intra-articular anesthesia can be used to localize the lesion; however, it is a difficult block to perform and ultrasound guidance is often warranted.

The most frequently reported problem is **fracture of the pelvis** (*q.v.*) extending into the acetabulum. This results in moderate to severe lameness, and profound muscle wasting soon develops. Scintigraphy can be valuable, but can also provide false negative results. Pelvic radiography may be required to confirm the presence of an IA fracture, but the risk of recovery from anesthesia often precludes obtaining radiographs in the acute phase of injury. Ultrasound provides a valuable alternative for evaluating the acetabulum and pelvis. Rest for up to 6 mo may result in improvement in some cases; however, the majority of horses remain lame with severe muscle wasting.

Osteochondrosis (*q.v.*) has been reported in the coxofemoral joint. Conservative treatment is frequently used; however, arthroscopic examination of this joint has been described and may improve the outcome. In general, OCD of this joint appears to carry a poor prognosis.

Other conditions include **luxation** of the coxofemoral joint. Luxation is seen more commonly in **miniature horses**, ponies and younger horses. The condition occurs much less frequently in horses than in other species, presumably due to the unique anatomy of the equine hip including an accessory ligament

of the head of the femur. When luxation does occur, the prognosis for recovery is generally poor. Some luxations can be reduced under general anesthesia, but this is ineffective if the rim of the acetabulum is fractured. In appropriate cases, such as miniature horses, femoral head resection can result in a satisfactory outcome, and several other stabilization techniques have also been described for these patients. Osteoarthritis, hip dysplasia, round ligament rupture and joint infection are infrequently observed and also carry a poor prognosis.

Genual (stifle) joint

The stifle is a complex joint that consists of three compartments: the femoropatellar and the medial and lateral femorotibial joints. Diagnosis of stifle abnormalities currently relies on clinical signs including the presence of joint effusion, response to IA anesthesia, ultrasound, radiography and diagnostic arthroscopy. The femoropatellar and medial femorotibial joints communicate in most animals; however, to ensure that adequate local anesthesia has occurred, they may need to be blocked separately. The femoropatellar joint is routinely blocked by injection either medial or lateral to the middle patellar ligament below the patella, but can also be blocked using a lateral approach. The medial femorotibial joint is approached between the medial patellar and the medial collateral ligaments 1–2 cm proximal to the tibia. The lateral femorotibial joint is injected caudal to the lateral patellar ligament or caudal to the long digital extensor tendon just proximal to the tibial plateau.

Osteochondrosis

Osteochondrosis (*q.v.*) **of the stifle** most frequently affects the lateral trochlear ridge of the distal femur, but other sites can be affected, including the medial trochlear ridge, the intertrochlear groove and the patella. Most horses with OCD present for effusion and/or lameness. Radiography and ultrasound are used to confirm the diagnosis. Radiography can reveal a similar clinically silent lesion in the contralateral limb. **Arthroscopic debridement** has significantly improved the outcome over conservative management techniques. However, success rates are dependent on case selection. When there is no evidence of associated osteoarthritis, the lameness associated with osteochondrosis will often improve dramatically shortly after surgery, with resolution of effusion occurring soon after.

Osseous cyst-like lesions

Subchondral bone cysts are most frequently identified in the medial femoral condyle. The lateral condyle and proximal tibia are infrequently affected. Cysts are commonly detected bilaterally. Conservative therapy may be successful in managing small cysts or those with minimal articular involvement. However, the success rate for animals returning to full athletic function may be as low as 20%. An **arthroscopic approach** is recommended for surgical management. The cyst is opened, evacuated and curetted back to healthy subchondral bone. Cancellous bone grafts used to pack the cyst defect following arthroscopic surgery have not improved the surgical prognosis, and forage has been associated with postoperative enlargement of the cyst. Unfortunately, surgical management has failed to return many horses to athletic performance, and treatment

with intralesional injection of corticosteroids has recently been advocated. While this may limit the growth of cysts in young horses and provide short-term relief from lameness, it is less successful in resolving well-established cysts. Newer resurfacing techniques including a combination of bone and chondrocyte grafting with growth factor administration or autogenous stem cell injections may provide better surgical outcomes.

Upward fixation of the patella

Upward fixation of the patella occurs when the medial patellar ligament hooks over the medial trochlear ridge of the femur. Affected horses are unable to flex the limb. The etiology is obscure but appears to be related to conformation, the age and condition of the horse, and poor muscle tone. Horses in very **poor condition**, as well as young horses and those with a straight hindlimb conformation, are predisposed to upward fixation.

Diagnosis is based on the characteristic appearance of the horse, which **maintains the leg in extension with the fetlock flexed**. The condition can be bilateral. Flexion can occur suddenly as the ligament is dislodged, and the condition should not be confused with stringhalt. Subtle forms of this problem consisting of **delayed patellar release** or **intermittent upward fixation** can be more difficult to diagnose. Horses can be worked on an incline to detect any hesitation or jerky movement of the patella. Radiographs and a complete ultrasound evaluation should be performed to rule out concurrent problems including fractures and patellar ligament desmitis.

Treatment of upward fixation of the patella consists of **improving muscle tone** where possible, either by improving the overall condition of the horse, or by exercise to improve quadriceps femoris muscle tone.

In young horses, aggressive treatment should be delayed to determine if the horse will grow out of the problem. Injection of a **counterirritant**, usually 2% iodine based in almond oil, or a **sclerosing agent** such as 5% ethanolamine oleate, into the middle and medial patellar ligament and quadriceps muscles has been used very effectively to reduce ligamentous laxity. Other clinicians inject the medial patellar ligament and distal area of muscle with dexamethasone. The use of conjugated estrogens, which presumably act to reduce ligament tension, has also been found to be effective. Estradiol benzoate or estradiol cypionate (10 mg/450 kg) is administered IM once a week for 4–5 wk to treat this condition. **Most horses will respond to conservative treatment**.

In severe cases in which the patella remains locked, injection of 20–30 mL of **local anesthetic** into and around the medial patellar ligament will often resolve the immediate problem.

In non-responsive or recurrent cases **surgery** should be considered. This consists of cutting the medial patellar ligament. This is best done in the standing horse under local anesthesia, so that the medial ligament is clearly defined. The response to this surgery is usually very good, but the surgery has been associated with patellar instability and subsequent development of apical patellar fractures. Because of the potential for patellar instability after this surgery, the horse should be rested for 6–8 wk, and gradually reintroduced into training. One of the major complications of this surgery is fragmentation of the articular cartilage and subchondral bone at the apex of the patella, in the region of attachment of the middle patellar ligament (*q.v.*). This occurs as

a result of altered biomechanical forces induced by sectioning of the medial patellar ligament. Affected horses have an effusion and low-grade lameness. Arthroscopic surgery is required to remove the fragments if the clinical signs are to resolve (*q.v.*). For this reason medial patellar desmotomy should only be undertaken when non-invasive treatments have failed or when severe clinical signs are present.

An alternative surgical approach has been described in which the proximal third of the medial patellar ligament is split percutaneously to induce a localized desmitis and thickening. The technique has been shown to be effective and allows rapid return to normal activity following surgery.

Luxation and/or subluxation of the patella

Luxation and/or subluxation of the patella, usually in a lateral direction, is seen most often in ponies and miniature breeds of horses, and it is usually **congenital**. With luxation, the quadriceps femoris is disarmed and the foal is unable to lock the stifle joint, resulting in a very characteristic crouching stance. Palpation and radiography will indicate that a luxation has occurred.

Treatment consists of **surgical imbrication** of the fascia on the side opposite to the luxation, with a release incision on the side of the luxation. Trochleoplasty may also be required with trochlear hypoplasia. The prognosis is guarded. Severe OCD lesions of the trochlear ridges can predispose to this problem, but usually only a subluxation will occur with OCD-induced luxation.

Meniscal and cruciate injuries

Meniscal and cruciate injuries usually result in chronic lameness that can be difficult to diagnose and to manage. A preliminary diagnosis can be made on the basis of IA anesthesia as well as radiographic and ultrasonographic imaging studies. Arthroscopy should be used to confirm the diagnosis, and can often provide a more accurate prognosis for the horse. In selected cases meniscal tears can be effectively managed following arthroscopic trimming providing osteoarthritis has not progressed too far.

Osteoarthritis of the patella

Osteoarthritis is seen predominantly in older horses and is commonly a result of trauma or chronic soft tissue injuries, such as collateral ligament or meniscal damage. Some cases benefit from arthroscopic surgery and follow-up corticosteroid medication.

Tarsus (hock)

The hock is a complex articulation comprising numerous joints including the **tarsocrural**, **talocalcaneal**, **proximal and distal intertarsal** (talocalcaneal-centroquatral, centrodistal) and **tarsometatarsal** joints. The tarsocrural and proximal intertarsal joints reliably communicate. The proximal and distal intertarsal joints also communicate in some horses, but this does not guarantee that medication will flow readily from one joint to another.

Most movement in the hock occurs in the tarsocrural joint, which also has the largest joint space. Very little movement occurs in the lower joints. The different joints will be discussed separately.

The tarsocrural joint

Osteochondrosis

The tarsocrural joint comprises the articulation between the distal tibia and the talus (tibial tarsal bone) and calcaneus (fibular tarsal bone). The most commonly detected abnormality in this joint in young horses is **OCD** (*q.v.*). Sites of occurrence in decreasing order of frequency are the **distal intermediate ridge of the tibia**, the **lateral trochlear ridge** of the talus, the **medial malleolus** of the tibia, and the **medial trochlear ridge** of the talus. Affected horses typically present for joint effusion (**bog spavin**), with varying degrees of lameness. Radiography will usually reveal characteristic OCD lesions. The contralateral leg should routinely be radiographed.

The success rate for treatment using conservative or surgical therapy is similar to that seen with OCD in other joints. Conservative therapy, consisting of confinement and dietary management, can result in resolution of clinical signs in approximately 40% of horses. However, many horses will continue to have joint effusion for long periods of time, and osteoarthritis (*q.v.*) can develop.

Osteochondritis dissecans lesions (*q.v.*) are readily operated on, usually using **arthroscopic** techniques. Surgery will be successful in resolving the effusion and lameness in >80% of joints, depending on the location of the lesion and severity of any associated cartilage damage. The **contralateral limb** should be examined arthroscopically if joint effusion is present without radiographic signs, or if radiographic lesions are present without clinical abnormalities. Following removal, resolution of clinical signs of effusion usually takes 4–6 wk. In some horses effusion persists, and IA hyaluronan and/or a corticosteroid may be required.

When OCD lesions are detected in **young horses** (i.e. yearlings) prior to training, the lesions should be removed, even if no associated clinical signs are evident. Left untreated, these lesions can predispose to the development of wear lines and full thickness cartilage erosion once training commences. The secondary changes are often of more consequence than the original OCD lesion.

Effusion in the tarsocrural joint, commonly referred to as **bog spavin** (*q.v.*), can occur in any age or breed of horse. Osteochondritis dissecans is the most frequent cause of bog spavin in younger horses, but in the absence of OCD, the etiology is frequently obscure. Chronic effusion can also occur subsequent to trauma, or septic arthritis (*q.v.*). Resolution of a chronic bog spavin can be difficult even when no underlying pathology can be identified. Confinement and systemic anti-inflammatory therapy may decrease the effusion, but it will frequently recur once treatment is discontinued. Intra-articular corticosteroid, atropine and hyaluronan therapy (*q.v.*) following drainage of the effusion may be successful in resolving the effusion. In refractory cases arthroscopic examination of the joint is indicated.

Fractures

Other abnormalities in the tarsocrural joint are uncommon. **Intra-articular fractures**, luxations and lacerations are seen as a result of trauma. Osteochondral fractures of the lateral malleolus are usually an indication of joint trauma, not of OCD. Treatment of these fractures may require internal fixation if large fragments have occurred, but removal of smaller fragments is recommended. Often

the position and size of the fragment and extensive soft tissue attachments mean that an arthrotomy directly over the fragment is required for removal. The prognosis can be good, but if there has been significant soft tissue trauma associated with the fracture osteoarthritis can develop. There can also be partial subluxation of the joint at the time of fracture, resulting in collateral ligament damage and secondary new bone formation, and ultrasound evaluation is warranted.

The proximal intertarsal joint

The **proximal intertarsal** joint contributes only a small amount of movement and few isolated abnormalities occur. A small portion of this articulation can be examined arthroscopically from the tarsocrural joint. It is relatively common for osteoarthritis of the distal joints to simultaneously affect the proximal intertarsal joint and this can be difficult to manage. Treatment is aimed at controlling clinical signs through the use of IA medication, but the tarsocrural joint will also be exposed to the medication. Arthrodesis of this joint is usually not recommended.

Fractures of the central tarsal bone

Fractures of the **central tarsal bone** occur infrequently, and detection may require multiple radiographic views or nuclear scintigraphy. Conservative treatment of non-displaced fractures has been reported to produce satisfactory results, but can result in non-union and osteoarthritis. Lag screw fixation or a technique using a cannulated self-compressing screw can be successful, providing displacement is minimal.

The distal intertarsal (centrodistal) and tarsometatarsal joints

The **distal intertarsal (centrodistal) and tarsometatarsal joints** primarily consist of the articulations between the central and third tarsal bones, and the second, third and fourth tarsal bones and metatarsal bones, respectively. They are both "**low motion**" joints.

Osteoarthritis (bone spavin)

The primary problem detected in the distal tarsal joints is **osteoarthritis**, or **bone spavin** (*q.v.*). This condition presumably results from **repetitive trauma** to the articular surfaces, and is seen most commonly in racing and western performance horses, particularly Standardbreds and Quarter Horses. Older horses are most frequently affected, and poor hindlimb conformation appears to be a significant risk factor. However, younger horses that have had only light training are sometimes affected and in these animals it is likely that the changes are a manifestation of developmental orthopedic disease such as incomplete ossification of the tarsal bones (*q.v.*).

Affected horses most often present because of **hindlimb lameness**; however, the presenting complaint may be of **back pain** or **poor performance**. Pacers and trotters may lose their gait ("break") and gallop during races. Some horses have extensive new bone production medially (**Jack spavin**) and may respond to manual pressure over the medial joint surface (a "**Churchill test**").

A "**spavin test**", in which the hock is flexed for 1.5–2 min before the horse is trotted off, is a useful means of precipitating lameness. If osteoarthritis is suspected, diagnostic IA anesthesia (*q.v.*) is indicated. This is achieved by

injection into the tarsometatarsal joint immediately proximal to the head of the fourth metatarsal bone, while the distal intertarsal joint can be anesthetized through the space formed by the fused first and second tarsal bones and the third and central tarsal bones. Local anesthesia is important in confirming the hock as a site of lameness.

If a diagnosis is made early in the course of the disease, radiographic signs may be absent or minimal. This is occasionally referred to as **blind** or **occult spavin**. As the disease progresses, radiographic evidence of osteoarthritis often becomes apparent in these horses. Radiographic evidence of osteoarthritis includes the formation of spurring of the articular margins, subchondral bone lysis and sclerosis and decrease in width of the joint space; osteoarthritis can eventually progress to complete obliteration of the joint spaces.

Treatment is dependent on the severity of abnormalities, and the age and expected use of the horse. Initial treatment is aimed at controlling the clinical signs associated with the disease. This can often be satisfactorily achieved with IA injection of a long-acting corticosteroid. Injection of 120–200 mg of **methylprednisolone acetate** often results in improvement in clinical signs for between 1 and 6 mo. Addition of hyaluronan or PSGAGs to the injection is not routinely recommended, primarily due to space limitations in these joints. Corrective shoeing is occasionally advised. This usually consists of elevating the heels and rolling the toe; however, the contribution of these changes to improvement in clinical signs is uncertain. **Ankylosis** can occur in some joints, but this is difficult to predict and may take many years to occur.

When medical therapy fails to give satisfactory results, **arthrodesis** of the joint may be indicated. Both the distal intertarsal and tarsometatarsal joints are routinely fused, even if radiographic abnormalities are present in only one site at the time of surgery. Surgical arthrodesis is best achieved by drilling three holes across the articular spaces from a single entry point. A medial approach is used for this technique and a cunean tenectomy is usually performed simultaneously. Postoperative analgesics are used for up to 6 wk, and a controlled exercise program instituted to promote arthrodesis. Rapid improvement in clinical signs is seen in some cases. Stabilization usually occurs within 6 mo, but up to 12 mo may be required before complete freedom from lameness is evident. A laser technique has also been described for arthrodesis of the distal tarsal joints.

Chemical ankylosis with injection of sodium monoiodoacetate into the affected joints has been suggested as an alternative technique. The recommended dose rate is 100 mg diluted in 2 mL injected IA. Arthrodesis usually occurs within 6 mo, but again, up to 12 mo may be required. However, this procedure has been associated with several potentially serious complications. Prior to injection, contrast studies must be performed to ensure there is no communication between the distal and proximal hock joints or tarsal sheath and also to confirm that the needle is in the joint. The technique can be very painful, and appropriate analgesia including epidural morphine is necessary. Incorrect preparation or storage of the sodium monoiodoacetate can also create problems, and severe sepsis and degeneration can result. Due to the severity of these complications this procedure is not currently recommended.

Other treatments that are used in managing osteoarthritis of the distal tarsal joints include cunean tenectomy, extracorporeal shock wave therapy, and partial tibial and deep peroneal neurectomy. The prognosis for athletic

performance with spavin is guarded, which may explain the large number of different management techniques that have been advocated.

Osteoarthritis can also affect any of the other articulations of the hock, including the tarsocrural joint and the talocalcaneal joint.

Fractures of the third tarsal bone

Fractures of the **third tarsal bone** occur infrequently. They are usually managed in a similar fashion to central tarsal bone fractures (*q.v.*); however, arthrodesis of the distal intertarsal and tarsometatarsal joint can also provide good results if there is not excessive instability of the fracture fragment.

Tarsal bone collapse

Tarsal bone collapse or incomplete/defective ossification of the carpal and tarsal bones (*q.v.*) is a condition usually diagnosed in young foals, in which the third, central or both tarsal bones are crushed and displaced cranially. There can be considerable variation in the severity of this condition. Less severely affected cases may not be diagnosed until training commences, and in some cases a degree of athletic soundness can be achieved with IA medication. The etiology appears to be related to prematurity/dysmaturity and associated incomplete ossification of the central and third tarsal bones at birth. Affected foals may be reluctant to stand, have angular limb deformities, or run with a bunny-hopping gait. Radiography is necessary for an accurate diagnosis. Treatment is limited to minimizing the severity of the changes by supporting the limb with splints or tube casts. Ankylosis may eventually occur; however, most foals have a poor prognosis for long-term soundness.

Tarsal luxation

Luxation of the hock can occur as a result of traumatic damage to one or more joints. Fractures are frequently present with tarsocrural luxations, while severe soft tissue damage occurs with luxation of the distal joints. Treatment is dependent on the amount of stability present at the time of examination. If obvious instability is present, internal fixation may be indicated. If the joint can be reduced and is reasonably stable, which is often the case with luxation of the lower joints, then application of a full limb fiberglass cast can be effective. Many joints subsequently undergo ankylosis, but some horses can continue to be athletes when only the lower joints are affected.

DISEASES OF THE FOOT

INTRODUCTION

The foot is the **most common site of lameness** in horses of all types and activities. Although the hoof is relatively strong, the ratio of a horse's body weight to the weight-bearing surface of the feet is very high, and as a result each foot is continually subject to concussion, stress and trauma.

To understand, diagnose and treat conditions of the foot it is important to have a sound knowledge of its functional anatomy and physiology. Developing a technique of careful, methodical and thorough examination of the foot is of great value in diagnosis. The foot is not an easy structure to examine because

it is encased in a relatively rigid outer hoof capsule and it is necessary for the clinician to develop skills in the use of hoof testers, hammer and hoof knife. In many cases, alterations in the hoof capsule offer clues to underlying problems and these can be detected with careful observation. A fairly consistent indication that there may be a problem is **increased heat** in the foot or feet and/or **increased digital pulses**. The extent of the increase is often related to the severity of the inflammation produced by the underlying condition.

It is also important to have a good appreciation and understanding of the **art and science of farriery** and the value of corrective and therapeutic shoeing as part of the treatment of all kinds of lameness. A good working relationship and communication between the veterinarian and farrier is essential for prevention and treatment of lameness.

LAMENESS DIRECTLY ASSOCIATED WITH TRIMMING AND SHOEING

Quicking (nail prick, hot nail)

Quicking occurs at shoeing when a nail penetrates the sensitive structures of the foot. It occurs most commonly if the horse is restless or fractious, the hoof wall is particularly thin, broken or flared, the shoe is too small, too large a nail has been selected, and/or the nail is simply misdirected.

Clinical signs

Pain and hemorrhage may occur at the time of penetration or when the nail is clinched. Lameness, if present, usually occurs immediately and may persist for 24–48 h accompanied by pain on percussion over the affected area. If infection occurs, the lameness will increase over a 24–48 h period.

Diagnosis

Diagnosis is based on clinical signs and an associated history of recent shoeing. Hoof tester evaluation can be used to locate the offending nail.

Treatment

Quicking rarely gives rise to serious complications. Once the nail is removed and the nail hole irrigated with an antiseptic such as **povidone-iodine**, additional treatment is usually not necessary and lameness will subside after 2–3 days. Appropriate tetanus vaccination status (*q.v.*) should be confirmed. If the hole is infected it is important to establish adequate **drainage**.

Close nail (nail bind)

A close nail occurs when the nail of the shoe is driven close to, but not into, the sensitive structures of the foot resulting in pressure, inflammation and discomfort. A properly placed nail can also cause the problem if the shoe shifts, causing pressure on adjacent sensitive structures.

Clinical signs

Lameness is rare at the time of shoeing, but becomes apparent within 1–4 days. Pain can often be elicited with percussion or hoof tester pressure over the

clinch of the offending nail, and frequently that nail will emerge through the hoof wall slightly higher than the other nails. A close nail rarely results in infection.

Diagnosis

Diagnosis is based on the history and clinical signs.

Treatment

The offending nail should be removed or, if this is not possible, the shoe should be removed. Lameness will usually subside within a few days. If removal of the nail is accompanied by a discharge, or if lameness persists, the wound should be treated as an abscess (*q.v.*).

Over-lowering of the hoof wall (excessive trimming)

Varying degrees of lameness can result if the hoof wall is **trimmed too short**, i.e. below the level of the sole. In these cases lameness is the result of the sole of the foot becoming excessively weight bearing. In some cases, lameness may result from direct damage to the sensitive structures themselves during the trimming process. Over-lowering of the hoof wall is often accompanied by excessive sole trimming, which can cause damage and remodeling of the third phalanx.

Clinical signs

Lameness will be evident almost immediately, or within 24 h of trimming. The degree will vary depending on the extent of damage or pressure on the sensitive structures, and the conformation of the foot.

Clinical signs in the front feet are usually the most obvious. The horse will usually adopt a **laminitic type gait**. If more than one foot is affected this condition can look like acute laminitis.

The lameness will be increased on hard or stony ground and improved on soft ground. A pain reaction can be elicited by pressure with hoof testers over the sole. In severe cases there may be slight serum discharge at the sole/white line junction.

Diagnosis

Diagnosis is based on the history of **recent trimming**, and clinical signs.

Treatment

The horse should be rested on a soft surface or the feet can be placed in protective bandages/boots. Shoeing with a seated out shoe is advisable to take pressure off the sole. In some cases, a **rim pad** between the shoe and the hoof wall may be necessary. The rim pad, however, should not extend onto the sole. Sole pads should be avoided in these cases as they may result in increased pressure on the sole. Most cases will show a marked improvement within 1 wk; more severe cases may take longer. The prognosis for a complete return to soundness is good providing sensitive structures have not been severely damaged.

Sudden changes in hoof length and/or balance

Lameness can arise if an overgrown, neglected foot or a severely unbalanced foot is trimmed back to a normal length and balance in one trimming. The lameness is probably due to a sudden change in the stresses placed on the structures of the foot and the limb.

Clinical signs

Clinical signs will vary depending on the degree and type of change in length and balance of the foot, and the number of limbs involved. If lameness occurs it will usually be apparent very shortly after trimming and will increase if the animal is exercised.

Diagnosis

Diagnosis is based on the history of trimming of overgrown or unbalanced feet.

Treatment

One to 2 wk of paddock rest to allow the feet and limbs to adapt to the new stresses is usually all that is required. If the lameness is severe, box/stall rest and a course of NSAIDs should be given, followed by a gradually increasing controlled exercise program.

Dumping (dubbing)

Dumping is a term given to **excessive rasping** of the outside of the hoof wall, usually at the toe, but it can extend all the way around the wall. It is most often done to make the foot fit a shoe that is too small, or in an attempt to try and trim back an overlong toe, and is most commonly seen in the front feet. This should be differentiated from under cutting the toe, which is an accepted method of shortening the toe and reducing break over. Dumping has several adverse affects:

1. The cross-sectional area of the bearing surface of the hoof wall is reduced and so the shoe will come to rest on the sole, resulting in sole pressure, and the nail holes will invariably be inside the white line, resulting in a higher risk of quicking the horse.
2. If dumping is excessive at the toe or has been present for a long period of time an apparent "reverse rotation/angulation" or "**negative plane**" of the distal phalanx can occur. On lateromedial radiographs of the foot the distal border of the distal phalanx slopes downward at the heels. This results in stress on the dermal laminae at the heels.

Clinical signs

Feet that have been markedly dumped have a characteristic "bull nose" appearance when viewed from the side. The front feet are more commonly affected. Dumping does not always result in lameness. Where lameness is the result of excessive sole pressure or a hot nail, the clinical signs are as for these conditions (*q.v.*). Where it is due to stress on the dermal laminae at the heels the lameness is usually bilateral, accompanied by shortening of the anterior phase of the

stride, and increased when the animal is turned in the direction of the affected foot or feet. There may be no palpable increase in the digital pulses or heat.

A pain response can often be elicited by pressure with hoof testers on the **posterior third** of the foot. A palmar digital nerve block will reduce or abolish the lameness in most cases.

Diagnosis

Diagnosis is based on the appearance of the feet and the clinical signs. In chronic cases lateromedial radiographs may reveal "**reverse angulation**" of the distal phalanx and this is usually accompanied by a "beak-like" projection of horn at the toe of the foot.

Treatment

The shoe should be removed and the wall at the toe trimmed from the ground surface **with reference to radiographs**. The feet should then be shod with wide webbed shoes fit to prevent excessive wear of the dorsal hoof wall, full at the quarters, and the branches should extend slightly beyond the weight-bearing surface at the heels. The horse should be rested until the lameness subsides and then started on a gradually increasing exercise program.

Prognosis is generally good providing the condition has not been present for a long period of time and permanent changes have not occurred in the dermal laminae or distal phalanx.

CONDITIONS OF THE HOOF CAPSULE

Hoof wall cracks

Cracks in the hoof wall can be divided into two categories based on site of origin:

1. Cracks that originate at the **ground surface**, often referred to as **sand cracks**. These rarely extend to the coronary band, involve the deeper structures of the foot or result in lameness. They are usually due to hoof wall overgrowth, training barefoot on hard surfaces, or excessive drying of the hoof, and they frequently involve more than one foot.
2. Cracks that originate at the **coronary band**. These can extend part way down the wall (**incomplete**) or all the way down to the ground surface (**complete**). They can arise due to injury to the coronary band but more commonly they are the result of abnormal stress on the coronary band from hoof imbalance, an overlong concave dorsal hoof wall, or excessive concussion.

In addition to being classified by their site of origin and length, cracks are also characterized by their location at the **toe, quarter, heel or bar**, by orientation with **vertical** and **horizontal** cracks, and by their depth, being either **superficial or deep**. Unstable cracks can cause hemorrhage and can result in infection.

Clinical signs

A **hoof wall crack** is usually obvious on visual inspection of the hoof, but the hoof often fails internally before the crack is visible on the external surface (**blind crack**). Many hoof cracks do not result in lameness, unless the crack is

deep and extensive enough to allow movement of the edges, which causes pinching of the underlying laminar corium, or if the crack becomes infected.

There is often a painful response to pressure applied along the coronary band above the crack, or when hoof testers are applied in the region of the crack. Hoof testers can also be used to assess the degree of instability of the crack. **Hemorrhage** may be evident from the crack, especially after exercise, and bleeding indicates involvement of the sensitive laminae. Purulent discharge indicates infection of underlying structures.

Diagnosis

Diagnosis is based on the clinical signs including response to diagnostic analgesia. In long-standing hoof cracks, or where there is infection, radiograph the distal phalanx for evidence of bone resorption or osteomyelitis, which would affect prognosis.

Treatment

Treatment varies with the location of the crack, the degree to which the crack has invaded sensitive tissues, and whether or not the crack is infected. Small cracks extending from the ground surface of the foot usually only require trimming, balancing and shoeing of the affected foot or feet.

Treatment of larger, **incomplete cracks** is aimed at preventing the crack from extending any further while it grows out, and involves trimming and balancing the foot, **floating** the hoof wall below the crack and shoeing with a bar shoe. The term "floating" refers to trimming the ground surface of the displaced heel shorter than the rest of the hoof wall so that it will not bear on the shoe. This allows transfer of load away from the crack to the frog and remaining wall. Some individuals recommend grooving a **horizontal line** in the hoof wall across the end of the crack; however, this is often not successful in preventing progression of the crack. The technique may be more successful when the hoof is grooved with a **hot file**.

With **superficial cracks**, if the foot is balanced and the horse restricted from strenuous activity, shoeing with a bar shoe will often resolve the problem. With deeper incomplete cracks one of the stabilization methods described for complete cracks may be required.

Treatment of a **complete crack** is aimed at stabilizing the crack to allow solid wall growth from the coronary band. The foot should be trimmed and balanced and breakover eased. The crack should then be pared out to its full depth and length to expose and remove any necrotic or infected tissue and to prevent overlapping of the edges, which would perpetuate the crack. **Heel cracks** are typically associated with proximal displacement of the heel bulb on the side of the crack and can often be managed by floating (*q.v.*) the heel on that side and shoeing the horse with a complete bar shoe or a heart-bar shoe.

Similarly, with **quarter cracks**, the location of the crack typically corresponds to a raised area in the contour of the hairline at the coronary band. Lowering the wall under the crack allows the heel to relax down into a more normal position, encourages normal hoof growth at the coronary band, and reduces the shearing forces that originally created the crack. Removing the shoe, floating the heel and applying frog pressure with a frog support pad for

24–48 h before reapplying a shoe will often allow the raised area to straighten out (relax). Soaking the feet or applying moist bandages can facilitate this process.

The most common techniques for treating a hoof with a complete crack include a combination of a **bar shoe** and **frog support**. In some cases a method of supplemental wall stabilization is required to immobilize the crack. These should generally be applied/tightened with the foot weight-bearing in the case of a toe crack and non-weight-bearing in the case of a quarter crack.

Stabilizing techniques include:

1. A contoured metal plate technique in which one or two plates or sections of hose-clamp are screwed to the hoof wall and tightened.
2. A drill and wire or lace technique done either in a shoelace pattern through holes drilled in the hoof wall at right angles to the crack, or in a figure of eight pattern through two staggered holes drilled in the hoof wall, starting at the ground surface and running upwards, on either side of and parallel to the crack. This technique is most effective for incomplete cracks that do not extend up to the coronary band.
3. Staples placed through the insensitive hoof wall at right angles to the crack.
4. Acrylic hoof wall repair or patching. This should only be performed **after all infection has been resolved**, and the sensitive structures have begun to cornify. In most cases patching is not necessary and can be avoided to prevent complications. When it is performed, the crack is opened to its full depth and length and filled with hoof repair material such as Equilox. A number of synthetic hoof repair materials that bond to the hoof wall have been developed, and some of these materials mimic the consistency of the hoof wall. A pipe cleaner can be used to create a space under the acrylic to allow for drainage of any residual infection, and antibiotics can also be incorporated in the repair material. Because of the high temperatures created during the hardening process of many hoof repair materials they should not be applied directly to sensitive structures, and care should be taken to cool the foot during the hardening process. Some of the newer products such as Equi-Thane Adhere are not as exothermic. A patch of hoof repair material, or a plate and screws, should be applied across the filled crack to strengthen the repair.

The length of time required for healing of a crack is related to the rate of growth of new hoof wall from the coronary band, which is approximately 0.6 cm/mo. In some cases complete healing may take a year or longer.

The prognosis is good for complete healing of superficial cracks not involving the coronary band and for early, uncomplicated cracks involving the coronary band. For long-standing cracks, infected cracks, or cracks accompanied by deformity of the coronary band, the prognosis for complete healing is not as good, and recurrence is common. Identifying and eliminating the biomechanical cause of the crack will reduce the recurrence rate.

Corns

Corns are **bruises** of the sensitive corium and the sole at the angle between the wall and the bars (the "seat of corn"). They are most common in the medial angle of the front feet.

Etiology

The underlying problem when corns develop is that an isolated section of the sole and not the adjacent hoof wall, bars or other supporting structures is receiving pressure during weight bearing. Common causes are:

1. The shoe is left on for too long and, as the foot grows, the heel branches of the shoe are progressively pulled forward off the wall onto the angle of the sole.
2. Improper shoeing, particularly if the shoe is fit short and tight at the heels to prevent the horse from inadvertently pulling the shoe.
3. Excessive weight bearing at the heels, such as the horse with low heels, or the addition of heel calks or studs to the shoe.
4. The heels have been left long and allowed to run forward in an effort to align the pastern.
5. Crushed heels accompanied by a "negative third phalanx plane" in which the distal border of the third phalanx slopes downward at the heels.

Chronic corns can also develop when the wall at the heels is so low and weak that it collapses inward and puts pressure on the "seat of corn", and chronic corns are also detected during the early stages of ossification of the collateral cartilages (sidebone) (*q.v.*).

Clinical signs

The degree of lameness varies depending on the severity of the bruising. Usually there will be bilateral forelimb lameness, with shortening of the anterior phase of the stride and a toe-first landing. Lameness will typically increase with circling and on a hard or uneven surface, and decrease on a soft surface. After removal of the shoe and light paring of the sole, bruising may be evident at the angle between the wall and the bars. Most horses show a pain reaction to gentle pressure in this area.

Corns can be:

1. **Dry**—the surface of the horn is dry but stained red, brown or yellow
2. **Moist**—with more severe bruising the horn over the corn area is moist due to serum seepage from the damaged corium beneath it
3. **Suppurating**—if the corn becomes infected the horn over the area may be a bluish color or there may be a discharge of pus.

Diagnosis

Diagnosis is based on the shoeing history, clinical signs and the appearance of the corn. Radiographic examination of the distal phalanx can be of value in chronic corns to ascertain whether concurrent ossification of the collateral cartilages or pedal osteitis (*q.v.*) exists.

Treatment

Where shoeing is the cause of the corn, the shoe should be removed to provide relief from pressure and pain. Removing a thin layer of sole horn over the corn relieves pressure, but paring out all of the discolored horn is unnecessary (unless suppurative) and weakens the area further. Reshoeing with a shoe fit full may be all that is required along with adequate rest. Heel calks or studs are contraindicated. Infected corns should be treated as for solar abscesses (*q.v.*).

Chronic corns due to low weak/collapsed heels can be very difficult to resolve. Hoof wall that has collapsed onto the seat of corn should be removed enough to relieve pressure. The foot should be shod with a full fit shoe and breakover facilitated. In addition, materials such as Equi-Pac or commercial dental impression material can be used to create "load sharing" with the intent of using more of the caudal sole, bars and frog for support. However, the material should be trimmed away from the bruised angle of the sole.

The prognosis for simple corns is good, but chronic corns due to collapsed heels have a more guarded prognosis.

Bruised soles

Bruised soles are bruises in the sole other than at the "seat of corn". They are more common in the front feet.

Etiology

Bruising can be the result of direct trauma to the sole from stones or rough ground, or a displaced or small shoe. Horses with a misalignment between the hoof capsule and distal phalanx, including a clubfoot or long toe/low heel conformation, are more prone to sole bruising. In addition, excessive paring of the sole, and dropped soles following laminitis (*q.v.*), predispose the horse to bruising.

Recurrent or **chronic bruised soles** may be associated with bony changes to the distal border of the distal phalanx such as pedal osteitis (*q.v.*) or solar margin fractures. Recurrent or chronic bruising at the toe may be indicative of pain elsewhere causing the horse to overload its toe.

Clinical signs

The degree of lameness with sole bruising is quite variable. There is usually a history of sudden onset of quite severe lameness associated with a stone bruise. In cases of recurrent or chronic bruised soles there is often a history of intermittent forelimb lameness. Heat in the foot and increased digital pulse are not consistent findings. The gait adopted by the horse depends on the area affected. Careful examination of the sole may reveal discoloration/bruising in an unpigmented sole or a softer area of horn in a pigmented sole. This discoloration may take several weeks or longer to reach the solar surface, and if the trauma is very recent these changes may not be apparent. **Pain reaction** can usually be elicited by finger pressure or gentle pressure with hoof testers, in the area of the bruise.

Diagnosis

Diagnosis is based on the history, clinical signs and foot conformation, but differentiating sole bruising from other causes of foot lameness can be very challenging.

Radiographic examination of the distal extremity is advisable in cases of persistent severe lameness to rule out fractures or other pathology. In cases of recurrent or chronic sole bruises **pedal osteitis** (*q.v.*) may be detected.

Treatment

Rest is the best form of treatment if the bruise is the result of a single traumatic incident. In cases of recurrent or chronic bruised soles, any predisposing foot

conformation abnormalities should be corrected when possible. The farrier should trim the hoof and place the shoe to bring breakover back toward the distal phalanx, and the weight-bearing surface of the heels should be "backed up" so that support is moved palmarly. Removal of any "live sole" in an effort to shorten the toe should be avoided.

The foot can be shod with a Natural Balance Shoe or with an egg-bar shoe extending back as far as the bulbs of the heels and giving support to the posterior structures of the foot. If necessary to correct the hoof-pastern axis, a **wedge pad** can be used to raise the heels, but this may further decrease the rate of heel growth and possibly contribute to further collapse of the heels. Not all cases of long toe/low heel conformation respond to corrective shoeing: allowing the horse to go barefoot may result in the fastest improvement in conformation, but a horse with sole bruises may not be able to tolerate this.

For horses that are not sensitive to hoof testers in the caudal portion of the foot, dental impression material can be used to load this part of the foot, effectively unloading the bruised front area of the foot.

The use of **complete sole pads** under the shoe has been recommended in some cases. However, if pads are applied to a flat sole they effectively bring the sole closer to the ground and possibly exacerbate the problem. Protective sole pads can also be applied by riveting them at the toe to create a void that will relieve any pressure between the pad and the sole.

The prognosis in the case of a single traumatic incident is good. With recurrent or chronic bruised soles, particularly if the feet do not respond to corrective shoeing or there is concurrent pedal osteitis, then the prognosis is guarded.

Keratoma

Keratoma (*q.v.*) is an uncommon condition involving development of an aberrant keratin mass that originates from the epidermal horn-producing cells of the hoof and extends between the hoof wall and the distal phalanx. While these masses have some clinical characteristics of a benign tumor, they are primarily composed of keratin and squamous epithelial cells.

Keratomas typically form in the epidermal laminae on the inside of the hoof wall and usually originate at or near the coronary band. As the keratoma grows distally it acts as a space-occupying mass, and the resulting pressure on the distal phalanx can cause marked bone resorption. Keratomas tend to occur in the toe or quarter and any foot can be affected.

Etiology

The majority of cases are caused by injury or chronic irritation to the coronary band. However, some cases appear to develop spontaneously, and often the cause cannot be determined.

Clinical signs

Signs vary depending on the size and position of the keratoma. The hoof wall may develop an abnormal buttress shape and lameness may or may not be present. When present, lameness appears to be due to pressure on the dermal laminae and distal phalanx from the growing mass. On examination of the foot, a deviation of the white line toward the center of the foot will often be identified. Once the keratoma has grown down to the bearing surface of the

hoof it causes a break in the continuity of the sole–wall junction that can allow infection to enter, and recurrent abscesses may develop. Pain will usually be elicited by pressure with hoof testers over the area.

Diagnosis

The initial diagnosis of keratoma is based on the clinical findings and, in particular, the deviation of the white line. Radiographic examination of the distal phalanx often reveals a focal area of osteolysis adjacent to the keratoma and increased soft tissue density of the hoof wall. CT or MRI can be used to determine the extent of the mass, and ultrasound can also be utilized to identify the origin of a keratoma at the coronary band. Differential diagnoses include true neoplastic conditions as well as septic osteitis (*q.v.*) of the distal phalanx, and the radiographic changes that occur with keratomas should also be differentiated from the normal crena found at the toe of the distal phalanx.

Treatment

Complete surgical removal of the abnormal growth is necessary and this often requires removing the entire overlying hoof wall. This can be done by making parallel cuts through the full thickness of the hoof wall on either side of the mass and reflecting the horn upward toward the coronary band. Alternatively the keratoma can be resected through a hole made in the hoof wall using a large **Galt trephine**. With either technique it is important to identify the origin of the growth and to make sure all of the aberrant tissue is removed.

Following surgery the foot should be wrapped in sterile bandages until a dry horn cuticle has formed, and then shod appropriately to address any instability created by the hoof wall resection. In some cases this will necessitate a bar shoe, in others a metal band similar to that used to treat complete hoof cracks may be required to adequately stabilize the hoof wall postoperatively.

The prognosis depends on the size of the keratoma and the extent of the damage to the surrounding structures, but is generally good. However, recurrence is expected following incomplete surgical removal.

INFECTIONS OF THE FOOT

Abscesses

Abscesses are the result of **infection** gaining entry to the soft tissues of the foot. This is commonly the result of a penetrating wound through the sole, frog or white line. Infection can also gain entry to the foot through hoof capsule defects such as sand cracks and white line separations, or pressure/traumatic injuries such as corns, sole bruises and lacerations.

The sequelae vary depending on the depth of penetration of the infection and the structures of the foot involved.

Abscesses can be divided into two general groups. **Group 1 abscesses** (subsolar abscesses) are the result of shallow penetration of infection through the hoof capsule. Infection is trapped between the horn (epidermis) and the corium (dermis). The build-up of purulent exudate between the corium and the relatively rigid horn results in an increase in pressure in the foot, pain, and the spread of infection along the line of least resistance. Infection **under the sole** tends to spread backward toward the "seat of corn"; infection under the

wall will usually spread upward to the coronary band (**gravel**), and infection under the frog tends to spread to the heel bulb—skin junction.

Group 2 abscesses are the result of infection penetrating into the deeper structures of the foot and are potentially far more serious. Penetration of the solar surface in the anterior third can result in infection of the corium and/or distal phalanx. Infection penetrating to the middle third leads to the most serious abscesses and can result in infection of the DDFT, digital sheath, navicular bursa, navicular bone and possibly the distal interphalangeal joint. Penetration to the posterior third can result in chronic abscesses forming in the digital cushion, or infection of the collateral cartilages ("**quittor**" [*q.v.*]), while penetration to the white line can result in infection spreading up to and involving the coronary band ("**gravel**"), or to the collateral cartilages. Pain associated with group 2 abscesses is usually the result of infection and destruction of the deeper structures of the foot. These two groups are not mutually exclusive, and untreated group 1 abscesses can progress to group 2 status.

The clinical signs, diagnosis and treatment of septic navicular bursitis, septic arthritis of the distal interphalangeal joint, and quittor (*q.v.*) are covered under the appropriate headings.

Clinical signs

There will often be a history of an **acute onset of lameness**, which may or may not be associated with a known history of foreign body penetration of the foot. The severity and the type of lameness will vary depending on the area of the foot affected and the length of time from onset. At rest, the horse will often point or rest the affected foot. In the early stages, when moving, it will tend to place the foot in a manner designed to keep weight bearing off the affected area. There will be a **marked pain reaction** to light percussion with a hammer or gentle pressure with hoof testers in the region of the abscess.

As the abscess develops, the horse will usually become lamer, the uneven loading of the foot will tend to disappear, and the horse will weight bear only on the toe. Percussion or pressure with hoof testers anywhere on the foot will produce a pain reaction.

Black spots, cracks, soft areas of horn or horn bruising may be found when the shoe is removed and the foot searched. Pus may be found discharging from old nail holes, the edges of the sole or frog or from the coronary band. In group 2 abscesses there will often be a rapid development of severe lameness within 2–3 days of onset.

Diagnosis

Abscesses are **one of the most common causes of severe lameness** in general equine practice. Diagnosis is based on the history and clinical signs. These horses are typically severely lame, with **palpable heat** and **bounding digital pulses**. The site will usually be very sensitive to hoof testers, and often a small black track can be found with careful evaluation of the solar surface. Black, gray or brown colored pus discharging from the foot usually indicates a group 1 abscess and creamy white or yellow colored pus, sometimes blood-stained, is more characteristic of a group 2 abscess.

Radiographs are used to assess the involvement and degree of damage to the deeper structures. Inserting a blunt-ended, malleable probe in the wound tract or injecting a positive contrast agent through a flexible catheter into the

tract can be used to define radiographically the extent and depth of the penetration. If a foreign body such as a nail is found in situ it should ideally not be removed until the foot has been radiographed so that the structures involved can be assessed. However, it is also important to prevent damage from progressive penetration of a nail or other foreign body, so decisions regarding when to pull the nail should be made according to the situation.

Treatment

Group 1 abscesses (subsolar abscesses and gravel)

The first step is the **rapid establishment and maintenance of drainage** by careful paring away of the horn around the abscess tract. Where no abscess tract is evident, but an abscess is still suspected, the use of a **poultice** is advocated. Poultices that encourage the hoof horn to absorb water and become softer should be used. Several different poultices can be used effectively including commercial products such as **Animalintex** that are soaked in hot water and applied to the bottom of the foot under a bandage. Another useful poultice consists of a combination of 2 parts wheat bran and 1 part Epsom salts. Alternatively the foot can be packed with **ichthammol** (sulfonated bitumen). In addition, **foot soaks** containing warm water with dilute povidone-iodine solution and saturated with Epsom salts can encourage drainage and help to eliminate infection, but chronic foot soaking should be avoided.

Once the tract is identified at the sole surface, it should only be enlarged enough to establish adequate **drainage** and allow for **effective irrigation**, and once drainage has been established there is often a rapid improvement in lameness. The debrided surface of the foot should be lavaged with a mild antiseptic solution such as **4% povidone-iodine**, and the foot covered with a **dry impervious dressing** that should be changed daily. This can usually be done with the animal standing, but an abaxial sesamoid nerve block may be necessary to allow adequate debridement.

Submural abscesses that have tracked up and are discharging at the coronary band (gravel) usually respond to removal of the lower portion of underrun wall with frequent through and through flushing of the tract with dilute povidone-iodine. Significant debridement at the coronary band should be avoided as this could result in damage to germinal tissues. Persistent cases may require hoof wall resection under general anesthesia.

Systemic antibiotics are of little value in the treatment of most group 1 abscesses, since in most cases a protective layer of horn covers the corium in the infected area, and antibiotics are unlikely to reach the site of infection at any therapeutic level. However, if there is evidence of cellulitis or swelling around the coronet or pastern region, antibiotic therapy is indicated. **Tetanus prophylaxis** is critical (*q.v.*).

Group 2 abscesses (deep penetrating injuries)

With group 2 abscesses, areas of infected and necrotic corium and/or bone should be removed by **debridement and curettage**, and all underrun areas of cornified tissue should be resected. This is often most easily achieved under general anesthesia, and hemorrhage can be minimized with the use of a tourniquet. A sterile, dry, impervious dressing should then be applied to the foot and changed regularly.

In severe cases that will require long-term treatment, a shoe with a **removable treatment plate** can be applied to the foot to protect the sole while allowing ready access for treatment and reducing the length of time for which the horse requires expensive sterile dressings. In addition, a "**sugardine**" **dressing**, consisting of white granular table sugar mixed with povidone-iodine solution to make a paste, can be applied to the draining area to absorb suppuration and keep the adjacent sensitive tissue dry and healthy.

Systemic antibiotic therapy is indicated in the treatment of many group 2 abscesses in addition to removal of infected tissue. Broad-spectrum antimicrobial coverage such as trimethoprim–sulfamethoxazole 30 mg/kg PO b.i.d. is often appropriate, but bacterial culture and sensitivity results should be used to modify antibiotic selection with more serious and deeper infections. In all cases of abscesses, tetanus vaccination status should be determined and **tetanus prophylaxis** administered if necessary (*q.v.*).

Prognosis

If all the underrun, infected and necrotic material has been removed, the wound will be dry and start to heal within 2–4 days (group 1 abscesses) or 2–3 wk (group 2 abscesses). Once the wound has healed and a firm, dry layer of horn has formed over the corium, the foot can be shod with a flat, broad webbed shoe and a sole pad to protect the sole if required.

The prognosis for group 1 abscesses is good providing treatment is instigated early and all infected tissue is removed. In group 2 abscesses, the prognosis is guarded to poor depending on the extent of the deeper structures involved and the duration of infection.

Septic navicular bursitis

The most common cause of infection of the navicular bursa is **foreign body penetration** through the middle or palmar third of the frog or solar surface of the foot. The shape of the collateral sulci of the frog almost seems to direct nails and other sharp objects toward the bursa, and **all puncture wounds** of the foot should be considered to be potentially serious. Infection can also be introduced iatrogenically with bursal injection or aspiration.

This is a **very serious problem**, and should be dealt with on an **emergency** basis. Infection rapidly spreads to involve the navicular bone and DDFT, frequently resulting in severe irreversible damage. Spread of infection to involve the distal interphalangeal joint can also occur.

Clinical signs

There is usually a **sudden onset of marked lameness** that gets progressively worse within 24–48 h. Foreign body penetration of the foot may or may not have been recognized, and occasionally the foreign body will still be present when the horse presents for evaluation. Often the horse will only weight bear on the toe of the foot and will point the foot at rest. There will usually be a painful reaction to pressure on the DDFT over the middle phalanx, and in more advanced cases a sinus tract may be evident. These horses will also usually respond painfully to flexion of the distal interphalangeal joint, and a palmar digital nerve block (*q.v.*) will improve but not eliminate the lameness.

Diagnosis

Diagnosis is suggested by a history of foreign body penetration and the associated clinical signs.

Radiographic examination can be very useful for determining which synovial structures are involved. A single **nail puncture** can contaminate the navicular bursa, distal interphalangeal joint and digital tendon sheath at the same time. Plain radiographs are taken first; if a puncture tract is found, radiographs should be taken with a blunt-ended malleable probe gently inserted in the tract or with a contrast agent injected along the tract to identify the structures involved. Several radiographic projections (a minimum of two orthogonal views) should be taken to determine accurately the position of the probe or contrast agent.

Plain radiographs may not show much in the early stages although a loss of definition of the navicular bone on a dorsoproximal–palmarodistal oblique projection and possible damage to the flexor surface on a palmaroproximal–palmarodistal oblique projection may be noted. In more advanced cases, osteomyelitis of the navicular bone and secondary osteoarthritis (*q.v.*) may be evident. Normal radiographic findings do not rule out a diagnosis of septic navicular bursitis, and synoviocentesis may be required to confirm involvement. Synovial contrast studies can also be used to confirm a penetrating injury.

Treatment

Rapid treatment is essential. Local debridement and systemic antibiotics are usually unsuccessful if the bursa has been punctured. Traditional surgical treatment involves the establishment of **drainage** and removal of all necrotic and infected material using the "street nail operation".

Under general anesthesia with the affected limb uppermost, and a tourniquet applied, a **sterile probe** is inserted along the puncture tract, and the entire tract is dissected out. A portion of the central part of the frog and digital cushion is removed to reveal the DDFT. A window is made in the tendon over the navicular bone to expose the navicular bursa. All the infected and necrotic tissue is removed and the bursa thoroughly flushed. A cancellous **bone graft** (*q.v.*) can be placed in the defect to encourage granulation. The wound is packed with sterile gauze and the foot bandaged. **Tetanus prophylaxis** (*q.v.*) and broad-spectrum **systemic antibiotics** should be given. The packing and bandage should be changed daily and any further necrotic tissue debrided. Using this surgical approach, the healing period may be prolonged to 6 mo or longer, and the prognosis for a complete return to soundness is poor. The longer the condition has been present before instigation of treatment, the poorer the prognosis becomes.

Endoscopic examination of the navicular bursa has essentially replaced the street nail procedure as the technique of choice for treating acute infectious navicular bursitis. For this surgery, the horse is placed under general anesthesia, and the arthroscope is introduced into the bursa from the medial or lateral side. A cannula or instruments can be introduced through the wound on the bottom of the foot. The bursa is extensively lavaged and any lesions are debrided. Once examination is complete, the puncture tract on the bottom of the foot should be enlarged and debrided to prevent abscess formation. Postoperative management is similar to that with the more invasive

street nail procedure (*q.v.*), but healing is more rapid and prognosis appears to be significantly improved with the endoscopic lavage technique.

Septic arthritis of the distal interphalangeal joint

Infection of the distal interphalangeal joint can occur as a result of **foreign body penetration** of the foot, as an extension of infection from the navicular bursa, or by iatrogenic introduction associated with aspiration from or injection into the joint.

Clinical signs

The condition is characterized by severe, often non-weight-bearing lameness. There may be swelling over the dorsal coronary band from periarticular soft tissues and joint effusion. There will be marked pain on flexion of the joint or pressure over the joint.

Diagnosis

Diagnosis is based on the history and clinical signs. It can be confirmed by arthrocentesis (*q.v.*). Typically the synovial fluid will be cloudy and turbid with low viscosity. With an established infection, the white blood cell count will be $\geq 20\,000/mm^3$ (often $>40\,000/mm^3$) with neutrophils the predominant cell type (characteristically these are degenerate neutrophils). The synovial protein levels will be $\geq 2\,g/dL$ (usually $>4\,g/dL$), and the pH and glucose levels will be decreased (pH often <6.9 and glucose levels significantly below those detected in serum).

A positive **bacterial culture** from the synovial fluid confirms the diagnosis, but it is often difficult to obtain a positive culture with synovial infections and a negative culture certainly does not rule out a diagnosis of septic arthritis (*q.v.*). Sample collection in a nutrient broth or use of antimicrobial removal devices can improve culture success rates. Both aerobic and anaerobic culture should be requested. PCR techniques for identifying bacteria are also gaining in popularity.

Radiographic examination can be helpful to assess the degree of damage to the joint structures. In the early stages, joint effusion may cause a widening in the joint space, and in the later stages areas of bone lysis and periarticular and periosteal proliferation may be seen. Other imaging techniques including CT, MRI or radionuclide imaging using labeled white blood cells can also be of value in cases where diagnosis is difficult.

Treatment

The treatment is as for other forms of **septic arthritis** (*q.v.*). It is generally considered that treatment of this joint is particularly difficult, but the use of arthroscopic evaluation and lavage certainly facilitates effective treatment. The prognosis is generally guarded.

Quittor

Quittor is the term used to describe infection and necrosis of the **collateral (ungual) cartilages of the distal phalanx**. The condition is seen most often,

but not exclusively, in the front feet of the **heavier breeds** of horses. Infection usually gains access to the cartilage via extension from the sole, wall or frog, or from a wound at the coronary band in the region of the collateral cartilage. Since the cartilage is **poorly vascularized**, the body is not able to mount an adequate defense against infection and the condition becomes chronic.

Clinical signs

Lameness may not be present at the time of examination but there will almost always be a history of **intermittent lameness** occurring in the same limb and accompanied by swelling and purulent discharge from the region of the cartilage above the coronary band. Lameness will usually subside following discharge. In many cases, the initial injury or infection that caused the condition may have occurred several months before the first bout of lameness. On examination of the foot, evidence of previous/healed sinus tracts may be found. In long-standing cases there may be permanent damage and deformity of the foot and persistent lameness.

Diagnosis

Diagnosis is based on the history and clinical signs. The number and position of the **sinus tracts** can help to differentiate quittor from submural or subcoronary abscesses (*q.v.*), in which there will usually only be one, if any, sinus tract at the level of the coronary band. Radiographic examination may show areas of ossification of the cartilage. Contrast injections or placement of a sterile flexible metal probe in the fistulous tract can be performed to identify the course of draining sinus tracts, and to rule out foreign body involvement.

Treatment

Systemic or local antibiotics used alone may cause a remission of clinical signs, but unless all of the infected cartilage is removed it will act as a focus for reinfection.

The recommended treatment is to establish **drainage** and to remove **all infected material**. This is best performed under general anesthesia with a tourniquet applied to the limb, but can be done standing. Two surgical approaches are described and are frequently used in combination. An elliptical incision is made through the skin above the coronary band over the cartilage and the infected material is removed through the skin flap. This approach tends to heal quickly, but it does not allow good access to deep-seated infection extending below the coronary band. In the second approach, a hole is drilled through the hoof wall over the affected cartilage giving better access and visualization. The hoof wall can be opened using a large **Galt trephine**. Usually a combination of both approaches is required to effectively debride all of the affected tissue, and the coronary band should be preserved in all cases. **Necrotic cartilage** can be recognized easily by its purple-bluish color. New methylthioninium chloride can also be used to define the tracts and identify necrotic tissue. In addition, great care must be taken to avoid penetration of the distal interphalangeal joint capsule during surgery.

Following surgery, the wound is packed with sterile gauze and the foot bandaged. **Tetanus prophylaxis** (*q.v.*) is required. The bandage should be

changed daily until there is no more discharge and the exposed corium has formed a dry protective cuticle. Healing is slow and reinfection can occur.

Prognosis for a complete return to performance is good for acute cases following complete excision of the necrotic cartilage. However, in long-standing cases and in cases where the foot has become deformed, prognosis for complete soundness is guarded.

Thrush

Thrush is an infection of the **frog and its sulci** that results in degeneration of the horn and the production of **foul smelling gray/black discharge**. In severe or neglected cases the infection can spread to involve the underlying corium. Most commonly it is found in the hind feet.

The degeneration of the horn is due to infection with keratolytic bacteria and fungi; multiple organism infections are most common. *Fusobacterium necrophorum*, one of the organisms responsible for foot rot in cattle, is often isolated when cultures are performed.

Predisposing causes of thrush include wet unhygienic stable conditions, lack of routine foot care, prolonged confinement/lack of regular exercise, overgrown, ragged frogs, and long contracted heels that produce deep sulci.

Clinical signs

Thrush does not typically cause lameness unless the infection spreads to involve the sensitive structures of the foot. In those cases, lameness may be accompanied by swelling of the lower limb. There will be a moist, dark, offensive smelling discharge in the central and collateral sulci and the frog may be **ragged and undermined**. There may be pain on pressure over the frog, and the surface may bleed when being cleaned.

Cases of "**deep thrush**" involving the central sulcus occur even in arid climates can, and often be overlooked. The central sulci will appear closed like a thin slit in the frog, and when probed the depth of the sulcus will extend all the way to the hairline. When opened, the sulcus is usually quite undermined with tracks running over most of the caudal third or more of the frog. These cases resemble early canker (*q.v.*).

Diagnosis

Diagnosis is based on clinical signs and the **distinctive characteristics** of the discharge. Culture is usually not necessary as multiple bacteria are involved, and systemic antibiotics are not generally administered. Thrush must be differentiated from canker (*q.v.*).

Treatment

Debridement of all the infected tissue is important and cases involving the sensitive tissues may require regional anesthesia. Following this, **aeration** of the affected tissues is important and an antiseptic or astringent agent, e.g. povidone-iodine, tincture of iodine, 10% formalin, dilute bleach or oxytetracycline spray, can be applied. Prolonged application of astringents should be avoided as they can damage sensitive structures.

Predisposing factors should be eliminated. The horse should be moved to a clean, dry environment and regular foot care adopted including daily cleaning. In many cases, improved foot balance incorporating more natural frog pressure and regular exercise will eliminate the problem. In severe cases involving the sensitive tissues systemic antibiotics may be indicated, and should provide coverage for anaerobic bacteria, i.e. **IM procaine benzylpenicillin** 25 000 IU/kg IM b.i.d.

The prognosis is good providing there is not extensive involvement of sensitive structures. Of course, prevention should be encouraged for performance horses that are stall confined since proper foot hygiene, regular exercise and **clean stabling** will usually eliminate the problem.

Canker (necrotic pododermatitis)

Canker is a chronic hypertrophic **moist pododermatitis** resulting from infection of the epidermal tissues of the foot. The nature of the infection is not fully understood, and although a number of bacteria have been identified in clinical cases, none has been confirmed as the causal agent. Nevertheless, Gram-negative anaerobic bacteria are consistently identified in the epidermal tissues, and both *Fusobacterium necrophorum* and *Bacteroides* spp. (*q.v.*) are thought to be involved.

The infection causes the production of rapidly growing, friable, filamentous fronds of horn. Canker usually starts in the **frog region** but, if it is not recognized or is left untreated, it can spread to involve the sole and wall. It occurs most commonly in the hind feet, and traditionally draft breeds have been over-represented. However, front feet and non-draft breeds are also regularly affected.

This condition is reported as being rare, however isolated cases do occur and the incidence appears to be increasing. The condition is predisposed to by **unhygienic stable conditions and poor foot care**, but it can occur in clean well-managed stables. The most common risk factor is prolonged exposure to **moisture**, and the condition is seen much more regularly in humid climates or swampy environments.

Clinical signs

Lameness may not be present in the early stages of the disease but develops once neglected infection involves the corium. Lameness can become quite severe and is often accompanied by swelling of the lower limb. Initially, the frog may appear normal but on closer examination there is a **crust** over its surface that is loose and friable and easily splits with slight pressure. Beneath the crust the swollen corium is covered in soft, moist, creamy white, filamentous fronds of horn with a **cottage cheese like, foul smelling exudate**. The proliferative appearance of the frog helps to differentiate canker from thrush.

Diagnosis

Diagnosis is based on the typical clinical signs and can be confirmed histologically with evidence of epidermal hyperplasia, inflammation, intracellular edema, dyskeratosis and necrosis.

Treatment

Once established, canker can be a very difficult condition to treat successfully, and early recognition of the condition dramatically improves success rates.

Horses should be moved immediately to a **clean, dry environment**. Treatment involves removal of the infected horn tissue to allow application of topical antimicrobial medications. This can be done standing under local anesthesia and sedation or under general anesthesia. A tourniquet applied to the limb improves visualization. Superficial and wide debridement of grossly infected horn tissue should be followed with persistent **topical antimicrobial therapy** with metronidazole or antimicrobial mixtures as described (*q.v.*).

Care should be taken not to remove or damage too much of the underlying normal corium as this can result in **permanent hoof deformities**. Surgical debridement and hemostasis can be facilitated with the use of a surgical laser. Some individuals have also reported success with the use of cryotherapy with liquid nitrogen to manage these cases. **Tetanus vaccination** status should be confirmed.

Meticulous postoperative care with topical antimicrobial therapy is essential for successful treatment of these cases. Using **dry, sterile, waterproof dressings**, the foot should be bandaged so that pressure is applied to the wound. Alternatively, a shoe with a **treatment plate** can be applied to reduce the cost of daily bandaging, but pressure should still be applied to the frog and sole under the plate. The dressing should be changed daily, and the area treated with topical **metronidazole, chloramphenicol, or a combination of ketoconazole with rifampicin and DMSO**. To treat the foot topically with metronidazole, a 2% ointment can be used or tablets can be crushed and mixed with water to form a paste. The combination of ketoconazole, rifampicin and DMSO, referred to as "**phycofixer**", is made by dissolving 7.5 g of ketoconazole in 100 mL of heated 0.2 normal HCl in a fume hood. This is added to 4.8 g of rifampin in 400 mL of DMSO, and can be sprayed directly on the affected areas.

Systemic antibiotics including effective coverage for anaerobic bacteria should be considered if lameness is severe or if there is evidence of cellulitis or swelling in the pastern area.

Despite great care being taken in the debridement and postoperative care of this condition, recurrence is common and will usually be apparent within 3–7 days. Regular rechecks and repeated debridement may be necessary before canker can be controlled. Healing tends to be prolonged. **NSAIDs** should be administered to try and encourage weight bearing.

The prognosis is good if the condition is not too widespread but it is important to persevere with treatment. Prognosis is guarded if the condition is widespread and long-standing.

HOOF WALL SEPARATION

Seedy toe

The term **seedy toe** describes a hoof wall separation that occurs as a sequel to **laminitis** (*q.v.*). This separation starts between the dermal and epidermal laminae when rotation or sinking of the distal phalanx occurs, creating

a thickened, stretched or separated white line at the toe. The space is filled with poor quality **soft crumbly horn** and enough separation can occur to allow infection to penetrate between the dermal and epidermal laminae, resulting in submural abscesses. Some of the resulting hoof deformity can be addressed by trimming and/or shoeing the foot to move the breakover point into position with the distal phalanx. This will relieve tension on the DDFT and tends to minimize the separation at the toe as the hoof grows down.

The term seedy toe is also occasionally used to describe the condition of **white line disease** (*q.v.*).

White line disease

The definition and etiology of white line disease are not well established. As a general term, white line disease refers to hoof wall separations at or near the white line that are not due to chronic laminitis. More specifically, white line disease has been described as a **keratolytic process** on the solar surface of the hoof, characterized by a progressive separation of the inner zone of the hoof wall.

The **white line** of the hoof is the junction between the horn of the sole and the soft white horn of the epidermal lamellae, but in most cases of white line disease the separation is not truly in the white line but in the non-pigmented deeper layers of the epidermis, or in the non-pigmented horn at the junction between the stratum medium and stratum internum of the epidermis. This junction can be damaged by mechanical trauma, nutritional deficiencies, excessively wet or dirty environments, dry conditions producing exceptionally dry feet, microorganism invasion or a combination of these conditions.

Hoof wall separations begin at the ground surface and **spread upward** underneath the hoof wall. It is thought that this progressive separation occurs as a result of infection with **anaerobic keratolytic bacteria, fungi or yeasts**, which gain access to the area at the ground surface. These organisms slowly digest the horn of the epidermal laminae and, as the epidermal horn is broken down, the distal phalanx loses its attachment to the hoof wall and can rotate. It is possible that the organisms cultured are all secondary invaders once the keratin becomes exposed by other environmental or mechanical factors.

Clinical signs

Lameness is not usually present in the early stages of hoof wall separations, but the separation will be evident on visual examination and probing the crumbly horn typically reveals a **cavity with separation of the outer hoof wall** from the laminae. The lesion can occur anywhere on or superficial to the white line around the diameter of the foot, and one or more feet can be involved. In severe cases the separation can extend from the weight-bearing surface all the way up to the coronary band. Typically a "**cigarette ash**" type discharge will be found around the edges and in the depth of the lesion, as a result of horn destruction.

Lameness will be evident when the separation is extensive enough to cause instability and some degree of rotation of the distal phalanx. Lameness can be quite marked with the horse adopting a laminitic gait. On examination, the sole may be dropped and there may be evidence of sole bruising and a painful response to pressure from hoof testers. Undermined areas of hoof wall will produce a hollow sound when tapped with a hammer.

Diagnosis

Diagnosis is based on the clinical signs and the insidious nature of the lesion. Radiographic examination is important in order to assess the extent of the separation, to determine whether there is rotation of the distal phalanx, and to detect evidence of **pedal osteitis** (*q.v.*), all of which will affect the treatment and prognosis.

Treatment

The condition is usually refractory to conservative methods of treatment, and treatment of hoof wall separations requires **complete removal** of all the undermined wall and infected, necrotic horn. Infectious agents involved in this condition thrive in an **anaerobic environment**; therefore it is essential to **remove** the entire **undermined hoof wall** to expose the infected area. The edges of the normal horn should be tapered so that no lip is left under which infected material could remain.

In some cases quite large areas of hoof wall may need to be removed and the distal phalanx will require support that can be provided using a properly fit heart-bar shoe. The defects should generally not be replaced with hoof repair material in the early stages of treatment, as this will recreate an anaerobic environment. Some **medicated hoof acrylics** containing metronidazole powder may overcome this problem and allow earlier hoof wall repair. However, if the distal phalanx is supported, and the horse is not lame, hoof repairs for cosmetic purposes are discouraged, as they tend to recreate the anaerobic environment that encourages continued infection.

The laminae in the infected area are usually covered in a protective horn cuticle. Old or necrotic horn over this layer should be carefully debrided and the surfaces treated with an antiseptic solution such as povidone-iodine or dilute bleach. If possible, the foot should be shod with a full bar shoe, or a heart-bar shoe to try and support the foot until the hoof wall regrows. Where a large amount of hoof wall has been removed it may not be possible to fit a conventional shoe. A glue-on shoe can be used, or a shoe can be supported by attaching it with clips screwed into sections of normal wall. Alternatively, the foot can be left bare and the horse kept on a soft dry surface until the hoof wall regrows.

The prognosis is good providing that the distal phalanx and the corium have not been severely damaged. Treatment and healing can be prolonged, so the earlier in the course of the disease treatment is instigated, the better the chances of success. Horses should be monitored closely for evidence of recurrence. **Moisture extremes** (too wet or too dry) apparently provide the optimal environment for the horn-digesting microorganisms that contribute to this condition, so horses should be moved to a different environment when possible. Nutritional supplements including biotin and methionine may also be of benefit in horses with poor quality hoof wall.

CONDITIONS OF THE DEEPER STRUCTURES OF THE FOOT

Fractures of the distal phalanx

Fractures of the **distal phalanx** are a relatively common cause of lameness, and they often occur during exercise, particularly with racing, and may be

associated with hoof imbalance, uncoordinated action or direct trauma from a hard or rocky working surface. Many horses will present with a history of kicking an unyielding object, and these fractures can also arise secondary to other conditions such as foreign body penetration, laminitis, osteomyelitis, nutritional deficiencies or pedal osteitis (*q.v.*).

Seven basic types of fractures are recognized:

1. **Type 1:** Non-articular fracture of the palmar or plantar process (wing fracture).
2. **Type 2:** Abaxial articular fracture that extends from the distal interphalangeal joint (DIP joint) to the lateral or medial distal border (articular wing fractures). These are reported to be the most common fracture type.
3. **Type 3:** Sagittal articular fracture that divides the distal phalanx into two approximately equal parts.
4. **Type 4:** Extensor process fracture.
5. **Type 5:** Articular or non-articular comminuted fracture.
6. **Type 6 adult:** Non-articular fracture of the solar margin. These have also been reported to be the most common fracture type.
7. **Type 6 foal:** Non-articular solar margin fracture of the palmar or plantar process. These fractures are thought to be the result of shear forces generated by tension from the DDFT or by compression.

Extensor process and solar margin fractures most often occur in the front feet and these can be bilateral. There is controversy regarding the etiology of fragmentation of the extensor process, particularly in bilateral cases. Some authorities consider these to be separate centers of ossification and manifestations of osteochondrosis (*q.v.*).

Clinical signs

Type 2, 3 and 5 fractures will usually have a history of sudden onset of non-weight-bearing lameness. In some cases the horse may be unwilling to put the foot to the ground for several days following the onset. Lameness with non-articular fracture may not be as severe, and the lameness associated with extensor process and solar margin fractures can be quite subtle.

Articular fractures and fractures of the extensor process produce distension of the DIP joint and pain on flexion of this joint. A painful response will usually be detected with gentle percussion or pressure with hoof testers in the region of the fracture. There may be a painful response to digital pressure over a fractured extensor process, and if a large extensor process fracture has been present for some time the hoof wall at the toe may become more pointed or buttress shaped (**buttress foot, pyramidal disease**).

Diagnosis

The history and clinical signs may be indicative, but diagnosis is confirmed by **radiography**. Many different oblique projections may be required in order to demonstrate a fracture and to accurately determine its configuration. Artifacts can mimic fractures, and the foot should be well prepared and the sulci packed prior to taking radiographs. Initially the fracture line may not be radiographically evident and in these cases the foot should be radiographed again

in 7–14 days. Alternatively, **nuclear scintigraphy** or **CT** can identify these fractures, and CT is also invaluable for differentiating between type 1 and 2 fractures when the fracture line extends close to the articular surface.

Radiographic examination can help differentiate separate centers of ossification at the extensor process from true extensor process fractures. The former are usually small, round, smooth edged, and sit immediately proximal to the extensor process. Radiographic examination is also important to assess the degree of osteoarthritis (*q.v.*) that may have developed as a sequel to articular fractures.

Treatment

The treatment selected will depend on the type of fracture, the age of the animal and the purpose for which it is used.

For fractures that do not extend into the joint a **conservative approach** will often produce good results. Conservative treatment involves rest, trimming and balancing the foot, and shoeing to stabilize the hoof wall so that it can function like a cast. A number of different shoeing options have been effective including application of a bar shoe with stout quarter clips, a continuous rim shoe, or a bar shoe with cast material applied around the hoof wall. Another alternative is a commercially available Equine Digital Support System P3 and Navicular Bone Fracture Plate for treating distal phalanx fractures. This shoe provides excellent stabilization of the foot, and articular fractures have been successfully treated with this shoe and solid plate combination.

These different approaches are all designed to **limit hoof expansion** and decrease distraction during weight bearing. Releasing tension on the DDFT by raising the heels can also improve comfort and healing with distal phalanx fractures. With the commercial fracture plate system the heels can be raised with adjustable wedge rails that are attached to the shoe with screws placed inside of the nail groove to facilitate turning.

Regardless of the style of shoe selected, it should be reset every 4–6 wk; at least until bone union has taken place (6–12 mo). Even after healing has taken place, the foot may need to be permanently shod in this manner to prevent refracture.

Cast material preventing hoof wall expansion will need to be discontinued earlier in the treatment protocol to prevent permanent hoof contracture. If a long enough period of rest is given after the therapeutic shoe is removed and this is followed by a slowly increasing, controlled exercise program to allow for bone remodeling, refracture is less likely to occur and a return to conventional shoeing is possible.

Many **type 2 and 3 fractures** can be managed conservatively as described for non-articular fractures. Complete hoof casts have also been used in the treatment of type 2 and 3 fractures to give better immobilization, but tend to be associated with more complications. Surgical treatment, using lag screw fixation or cannulated self-compressing screws, has been recommended in early type 2 and 3 fractures to ensure more rapid and efficient healing, particularly in horses over 3 yr old and in performance horses. The risk of **sepsis** and other catastrophic complications is high, and the prognosis for return to athletic performance is still somewhat guarded.

Small **extensor process fractures** can be treated conservatively, but larger fractures should be managed surgically. Most fragments can be removed arthroscopically, although very large fragments may require arthrotomy or in some cases immobilization with lag screw fixation.

Solar margin fractures occur with athletic performance on hard ground or often develop secondary to other conditions such as laminitis and foreign body penetrations. Treatment in these cases is aimed at the primary condition. Where solar margin fractures occur without concurrent problems, conservative treatment consisting of rest is usually successful, and strict immobilization with specialized bar shoes is typically not necessary. The fractures may heal, be resorbed or persist without clinical signs. **Type 6 fractures** in foals usually heal with 8 wk stall confinement alone, but adequate healing should be confirmed radiographically prior to turnout.

The prognosis for a complete return to soundness is influenced by fracture type (particularly whether or not it is articular), degree of displacement, the age of the horse and the foot affected. In general, the prognosis is better in young horses (≤3 yr) and in hind feet rather than front feet. The prognosis for non-articular fractures is generally good providing the animal is given an adequate period of rest and slowly reintroduced to exercise. The prognosis for articular fractures is more guarded because of the rapid development of osteoarthritis that can occur. Prognosis for type 2 and 3 fractures may be improved by surgical treatment in the early stages. Fractures that occur as a result of osteomyelitis (*q.v.*) generally carry a poor prognosis.

Fractures of the navicular bone

Complete fractures occur infrequently, but are seen most often in the front feet. They usually result from direct trauma from exercising on hard or stony ground, or from kicking a solid object. Pathologic fractures also occur as a result of bone demineralization associated with navicular syndrome (*q.v.*) or secondary to osteomyelitis (*q.v.*). The most common complete fractures of the navicular bone are simple, vertical or slightly oblique sagittal fractures close to the central ridge of the bone. Comminuted and transverse fractures of the navicular bone occur more rarely.

Small fractures of the distal border occur more regularly and are typically detected in association with navicular degenerative changes. These fragments may be due to avulsion fractures or may actually be the result of new bone formation in adjacent diseased soft tissue structures. Fractures should also be differentiated from congenital non-fusions that are occasionally identified, and may not be associated with lameness.

Clinical signs

With **complete fracture**, there is usually a history of **sudden onset of severe lameness**. In some cases, the horse will only bear weight on the toe of the foot. Usually there will be a marked painful reaction to flexion of the DIP joint. A painful response can also often be elicited by pressure with hoof testers across the posterior third of the hoof wall. After 2–3 wk the degree of lameness usually lessens but can be exacerbated by flexion of the DIP joint or by exercise.

Diagnosis

Diagnosis is based on history and clinical signs. A palmar digital nerve block (*q.v.*) will often improve the lameness, however a negative response to the nerve block does not rule out a fracture of the navicular bone.

Diagnosis can be confirmed with radiography. Great care should be taken in the preparation of the foot before the radiographic examination, and the **sulci of the frog** should be packed so that **radiolucent air artifacts** are not mistaken for fractures. At least two radiographic projections demonstrating the fracture line are necessary before a definitive diagnosis is made. Fracture lines always end at the bone margins, while lines from the sulci of the frog will typically extend above or below the navicular bone.

Although rare, congenital bipartite and tripartite navicular bones can be distinguished from fractures radiographically by their smooth rounded edges and the overall symmetry of the bone. They can occur bilaterally, and the opposite distal extremity should be radiographed simultaneously.

Treatment

Conservative methods for managing complete navicular fractures involve **prolonged rest** (6–8 mo), combined with trimming and balancing of the foot and shoeing with a bar shoe that does not contact the frog but is fit with quarter clips or a complete rim and has a rolled toe. Alternatively, trimming and balancing the foot and shoeing with a graduated raised heel shoe, fit long in the heels and fashioned with quarter clips, can be tried. There is also a commercial and adjustable Equine Digital Support System P3 and Navicular Bone Fracture Plate system that eases breakover, releases tension on the DDFT and eliminates frog contact. Once shod, the horse is given a minimum of 2 mo of stall rest followed by a gradually increasing, controlled exercise program.

The prognosis for return to athletic soundness is **very poor**. Whatever method of conservative treatment is used, healing will be slow and occur by fibrous union because of the difficulty in immobilizing the fracture. The fracture line will always be evident radiographically and complete soundness is uncommon. Some horses have been returned to performance with a palmar digital neurectomy, but many of these horses develop osteoarthritis of the distal interphalangeal joint, and there is an increased risk of catastrophic failure of the DDFT in those patients.

Surgical treatment by lag screw fixation has been successful in the treatment of a few select navicular bone fractures and resulted in a bony union without excessive callus formation. Repair should be performed as soon as possible after the fracture has occurred to reduce secondary changes. The surgical technique is complicated and sophisticated equipment is required, but several successful cases have been reported.

Osteoarthritis of the distal interphalangeal joint (low ringbone, degenerative joint disease)

This condition resembles osteoarthritis (*q.v.*) in other joints, and it can develop as a result of poor forelimb conformation, foot imbalance or excessive concussion. It also develops in association with other primary conditions causing

instability or joint incongruity such as articular fractures of the distal phalanx, fractures of the navicular bone, osseous cyst-like lesions and navicular syndrome (*q.v.*).

Clinical signs

Lameness is very variable and somewhat non-specific. Lameness may be unilateral or bilateral and will often be increased by trotting on a hard surface, or circling in the direction of the affected limb or limbs. The horse may show a painful reaction to flexion of the distal extremity and lameness is subsequently increased. In some cases, distension of the DIP joint may be palpable just proximal to the coronary band on the dorsal aspect of the limb.

Diagnosis

Definitive diagnosis can be difficult. It is based on clinical signs and history, particularly if there is a history of previous fracture of the distal phalanx or navicular bone.

In most cases, palmar digital nerve block (*q.v.*) will result in a partial improvement in lameness, and an abaxial sesamoid block in a marked improvement or abolition of lameness. A dorsal ring block may be required to eliminate the lameness. Intra-articular anesthesia of the DIP will also improve or eliminate the lameness. Of course, these techniques will also block many other causes of foot lameness, and scintigraphy can be useful in localizing the lameness to the coffin joint.

Changes of osteoarthritis may not be evident radiographically unless severe. A lateromedial projection of the foot is the most useful to demonstrate subtle changes: these include **bone remodeling** and **osteophyte formation** on the dorsal and palmar aspects of the articular margins. Care must be taken to distinguish periarticular changes on the extensor process from true articular changes. Increasing availability of MRI for the distal extremity should improve our detection of early lesions that cannot be detected radiographically.

Treatment

Treatment involves **trimming and shoeing** to correct any obvious foot and hoof–pastern axis imbalance if possible, and to ease breakover. A rocker motion shoe made of steel or aluminum or constructed from double-nail pads can be used to minimize the joint movement required with each stride, and consequently reduce the associated pain. This should be combined with rest, or low dose NSAIDs and a gradually increasing, controlled exercise program.

The systemic use of **hyaluronan** and/or **polysulfated glycosaminoglycan** (*q.v.*) may reduce inflammation in the joint and provide some relief. In addition, IA treatment with hyaluronan, with or without corticosteroids, can be of value in returning these horses to athletic performance. While use of IA corticosteroids has to be balanced with knowledge of their potential adverse effects, in chronic cases these medications have been found to be of value in treatment of this otherwise career limiting condition. Arthrodesis of this joint is difficult and is generally not recommended except for salvage.

Prognosis for a complete or sustained return to soundness is guarded, particularly in cases with obvious radiographic changes.

Desmitis of the collateral ligaments of the distal interphalangeal joint

Injury to the **collateral ligaments** has been identified as a source of severe lameness, typically involving a single forelimb. Medial or lateral collateral ligaments can be affected and they can be simultaneously involved, but **medial desmitis** has been reported more frequently. The lameness can be subtle or severe enough to be seen at a walk. These patients typically have a history of an acute onset of lameness that is not improved with an initial period of stall rest. The desmitis may develop due to a single misstep or with repeated unbalanced landings in which the distal phalanx either slips or rotates, straining the collateral support ligament. Poor footing is a risk factor.

Diagnosis

Soft tissue swelling and pain can be detected in patients with injury to the body or origin of the collateral ligaments; however, many injuries occur at the insertion and are confined to the hoof capsule. Most horses will improve with regional palmar digital anesthesia and/or with IA anesthesia of the distal interphalangeal joint (*q.v.*). **Ultrasound** is probably the method of choice for diagnosis and can be used to detect desmitis involving the origin or body of the collateral ligament, while characteristic radiographic findings include subtle osteolysis or bony irregularity around the insertion of the collateral ligament on the third phalanx. Contrast enhanced **CT** and **MRI** are also valuable for confirming these lesions.

Treatment

Treatment consists of **strict stall rest**, followed by a gradual return to controlled walking exercise over 2–6 mo. Well-balanced wide-web shoes should provide improved support for the joint and reduce strain on the ligament. The prognosis for return to athletic performance is considered fair, although evidence of gross joint instability or associated osteoarthritis is a poor predictive indicator.

Pyramidal disease (buttress foot)

The terms pyramidal disease and buttress foot are used somewhat loosely to describe changes in the appearance of the coronary band and subsequent growth deformities of the toe. **Pyramidal disease** is a term used to describe the triangular distortion of the dorsal hoof wall and coronary band that is frequently the result of new bone growth and subsequent soft tissue reaction in the region of the extensor process of the third phalanx.

The term **buttress foot** is used interchangeably, referring to dorsal hoof wall swelling at the coronary band resulting in a conical deformity of the toe from the coronary band to the weight-bearing surface. Horses with upright conformation, or forward broken hoof–pastern axis, are more prone to develop pyramidal disease.

Etiology

One proposed cause of **extensor process periosteitis** and resulting distortion of the dorsal hoof wall is excessive strain on the insertion of the common or long digital extensor tendon or of the extensor branches of the suspensory ligaments. This results in soft tissue inflammation and fibrosis, reactive periosteitis and enthesophyte formation. Large fractures of the extensor process, advanced osteoarthritis of the distal interphalangeal joint with proliferative exostosis (low ringbone), and keratomas (*q.v.*) can also cause pyramidal distortion of the dorsal hoof wall.

Clinical signs

The clinical signs are clearly dependent on the cause of the hoof deformity. When it is associated with excessive soft tissue strain, there is usually a moderate to severe lameness, accompanied by a shortening of the stride and a tendency for the heels to land first. There may be swelling at the dorsal coronary band and a pain reaction to digital pressure in this area and to flexion of the DIP joint.

In the more chronic stages, the degree of lameness is variable; the swelling at the coronary band will be obvious and firm to the touch, and a painful reaction may or may not be elicited by pressure. Due to the enlargement of the coronary band, the hoof wall develops a **bulge** on the dorsal surface, which will eventually extend down to the bearing surface as the hoof wall grows, giving the foot a distinctive V shape.

Diagnosis

Diagnosis is based on the history and the clinical signs, and can be confirmed by local anesthesia and radiography.

Lameness may improve following palmar digital nerve block, but there should be a marked improvement following an abaxial sesamoid block.

With pyramidal disease resulting from extensor process periosteitis, radiographic examination in the early stages may show no changes other than soft tissue swelling in the area of the extensor process, unless the strain has resulted in a fracture. In the later stages **new bone** and **enthesophyte formation** will usually be obvious.

Treatment

If there is an **extensor process fracture** this should be treated appropriately as described in the section on fractures of the distal phalanx (*q.v.*).

In the early stages, if there is no fracture, the horse should be **stall rested** and treated with systemic anti-inflammatory medications such as phenylbutazone 2 mg/kg PO b.i.d. Immobilization has also been recommended. Rest should be followed by a slowly increasing, controlled exercise program, and the foot trimmed, balanced and shod to ease breakover. In the later stages, once new bone growth is established, lameness may be permanent and **long-term** NSAID treatment or IA corticosteroids may be required to return the horse to any level of work.

The prognosis for a complete return to soundness is guarded in the early stages and poor in the advanced stages.

Phalangeal exostosis (low ringbone)

The term **ringbone** (*q.v.*) was coined to describe bony enlargement of the phalanges below the fetlock joint. The terms **high** and **low** ringbone are used to differentiate between bone production around the proximal and distal interphalangeal joints respectively, while the terms **articular** and **periarticular** ringbone distinguish between new bone production involving the joint and that strictly involving the joint perimeter.

Navicular syndrome (navicular disease, caudal heel syndrome, caudal heel pain)

Navicular syndrome is one of the most common causes of chronic forelimb lameness and it is also one of the most controversial.

The syndrome is generally progressive and usually affects both front feet, while the hind feet are rarely involved. Conventionally, lameness in these patients has been attributed to the navicular bone, the navicular bursa and/or the adjacent DDFT; however, current research suggests that other soft tissue structures may also be involved.

The term "**caudal heel pain**" has gained popularity since it tends to draw attention away from the navicular bone itself, and integrates all of the soft tissue structures thought to be involved in this condition. All breeds and all work categories of horse can be affected, but Quarter Horses and Thoroughbreds appear to be predisposed, while Arabians and ponies are rarely affected.

Etiology and pathogenesis

While a number of different theories have been developed, the proposed **causes remain speculative**. Although historically described as a single disease, it is likely that navicular syndrome includes a variety of different clinical entities, and this could explain the difficulty we have encountered in trying to define a precise etiology. Primary **DDFT tendinitis** (*q.v.*) is usually not included under the heading of navicular syndrome, but can be difficult to differentiate without advanced imaging techniques.

The principal theories are as follows:

1. **Vascular**: The suggestion is that as a result of reduced blood flow, from thrombosis or atherosclerosis of the arterioles supplying the navicular bone, there is ischemic necrosis of the bone, and pain. This theory has fallen into disfavor since histopathology has not confirmed the presence of thrombosis or areas of infarcted bone.
2. **Biomechanical**: This theory suggests that navicular syndrome is the result of non-physiologic forces on the navicular bone such as repetitive concussion, vibration, overloading, or pressure from the DDFT, provoking either a navicular bursitis or increased bone turnover and remodeling.
3. **Degenerative**: It is proposed that changes occurring in the fibrocartilage, subchondral bone, flexor cortex and the synovial fluid of the navicular bursa are similar to those occurring in osteoarthritis (degenerative joint disease) of synovial joints.
4. **Developmental**: This concept is based on observations regarding soft tissue structures in the heel region of pathology specimens from horses

with navicular syndrome. Observations have led to speculation that an increased vascular supply associated with thicker collateral cartilages as well as more fully developed digital cushions may allow improved dissipation of concussion in horses with "good feet". In addition, abnormal shearing forces between the impar ligament and the DDFT are thought to lead to painful inflammation in the heels of horses with "bad feet". Recent work suggests that **regular exercise** is essential for development of healthy foot architecture in horses as they mature.

The above theories point to **abnormal conformation** and **foot imbalance** as predisposing factors in the development of the condition. Abnormal foot conformations implicated are:

1. **Broken back hoof–pastern axis**—probably the most common, and almost always the result of long toe/low heel imbalance
2. **Upright pastern**
3. **Feet smaller than normal** in relation to body size
4. **Mediolateral foot imbalances**
5. **Sheared heels**.

Clinical signs

There will often be a history of **intermittent and progressive forelimb lameness** involving one or both forelimbs. On examination, the degree of lameness can be variable and may initially appear to be unilateral, but on further examination, such as circling or flexion tests, is usually found to be **bilateral**. The degree of lameness may be the same in both forelimbs, resulting in a very short "**pottery**" forelimb gait. Lameness is usually accompanied by shortening of the anterior phase of the stride, with the toe of the foot contacting the ground first. Affected animals are inclined to **stumble** and there is often marked **wearing of the toe** of the shoes.

At rest, the horse may "point" the most severely affected foot, or alternately point one foot and then the other. In advanced cases the horse may adopt a "rocking horse" stance with the forelimbs placed in front of and the hindlimbs placed behind their normal position.

If the condition has been present for some time, the affected foot or feet will have **changed in shape**. Because of lack of normal use of the posterior third of the foot, the foot becomes smaller, narrower, and higher in the heels. A marked disparity in shape may be evident between the front feet. A painful response may be elicited with hoof tester pressure applied across the heels, or across the middle third of the frog to the opposite heel. Flexion of the DIP joint often produces a painful reaction and a significant increase in lameness. An increase in lameness may also follow extension of the DIP joint. The palmar hoof or hoof extension **wedge tests**, in which the frog or toe regions are temporarily elevated on a block, also frequently exacerbate the lameness.

Diagnosis

A tentative diagnosis based on the history and clinical signs should be confirmed by local anesthesia and subsequent diagnostic imaging studies.

A **palmar digital nerve block** (*q.v.*) will usually produce a marked improvement, or abolition of the lameness, and lameness will often become more obvious in the **opposite forelimb**.

Intra-articular anesthesia of the DIP joint will also usually significantly improve the lameness, presumably due to diffusion of anesthetic to the area or to the palmar digital nerves that are located subsynovially in the DIP joint. The volume of local anesthetic placed in the DIP joint may influence the time required for the block to improve lameness in horses with caudal heel pain, but research suggests that it is difficult to differentiate between DIP joint and caudal heel pain on the basis of IA anesthesia alone.

Navicular bursal blocks can also be used to confirm a diagnosis of navicular syndrome, but these are more difficult to perform and are usually performed in conjunction with bursography or with medication of the bursa.

Lameness caused by disease of the DDFT within the digit often fails to improve with analgesia of the palmar digital nerves, the DIP joint or the navicular bursa, but does typically improve following an abaxial sesamoid nerve block. Intrathecal analgesia of the digital sheath can also be used to identify horses suspected of having an injury of the digital portion of the DDFT.

For radiographic examination of the navicular bone a minimum of three radiographic views are needed: **dorsoproximal–palmarodistal** oblique view, **lateromedial** view, and a **palmaroproximal–palmarodistal oblique** (flexor) projection. Great care should be taken in the preparation of the foot prior to radiography to avoid imposition of artifacts.

Radiographic findings associated with navicular syndrome include an increase in number and change in shape (from a normal cone shape to rounded or mushroom shapes) of the **synovial fossae** on the distal border of the navicular bone; the presence of synovial fossae (regardless of shape) in the distal border of the wings and proximal border of the navicular bone; areas of radiolucency or **cyst formation** within the navicular bone; thinning or roughening of the flexor cortex (flexor view); loss of normal trabecular pattern in the medullary cavity; remodeling of the proximal and/or distal border; **enthesophyte formation** on the proximal border of the wings of the navicular bone (spurs); and avulsion fractures of the distal border of the navicular bone.

The degree of lameness and radiographic abnormalities are often poorly correlated. In fact, many of the radiographic findings associated with navicular disease are found in sound horses, and no single radiographic feature is diagnostic. Similarly, the absence of radiographic abnormalities does not rule out a diagnosis of navicular syndrome. Radiographic findings should be assessed in conjunction with the clinical findings and the results of local anesthesia.

Alternative diagnostic imaging methods that facilitate evaluation of soft tissue involvement have become increasing popular. Magnetic resonance imaging provides optimal anatomic detail, and its increased use has confirmed the frequent involvement of the DDFT in horses with caudal heel pain. Computed tomography provides excellent three-dimensional detail of the bone and, when used with contrast injections, can provide excellent soft tissue detail. Ultrasound can be used to evaluate a narrow portion of the DDFT, impar ligament and navicular bursa by imaging these structures through the bottom of the foot. Appropriate **preparation of the foot** with thinning of the frog and soaking the foot improve image quality.

Scintigraphy can be used to localize the area of involvement in the foot, but it often does not provide much anatomic detail, and there is a high incidence

of false positives. Bursography is occasionally used to confirm effective injection of the navicular bursa, and it can also give valuable information regarding cartilage pathology and adhesion formation. Thermography can be used to assess relative blood flow to the region, but must be performed under appropriate temperature controlled conditions, and should not be over interpreted. Endoscopic evaluation of the navicular bursa has been described, but is usually reserved for penetrating injuries to the foot.

Treatment

Selection of treatment for navicular syndrome depends on the stage of the disease process and the duration and degree of lameness. **Correction of any foot abnormality or imbalance** should always be the first line of treatment. The trimming and shoeing technique used depends on the individual animal's conformation.

The most common foot imbalance predisposing to navicular disease is the **long toe/low heel** resulting in a backward broken hoof–pastern axis. This configuration places excessive stress on the DDFT and navicular region, and can result in development of **underrun heels**. Some correction can often be achieved with corrective trimming and shoeing. Underrun **heels should be trimmed** to move support for the hoof back under the foot. The hoof–pastern axis can be realigned using wedged heels, wedge pads or rails as necessary. Leaving underrun heels long in an effort to align the hoof–pastern axis naturally only forces the heels to grow farther forward. **Breakover**, or the last part of the hoof to leave the ground, should be moved back using appropriately designed and placed shoes (this will reduce tension on the DDFT). The **toe should be trimmed** as short as is practical, and the horse shod with a commercial Natural Balance shoe or in a wide webbed egg-bar shoe extending back to meet a line dropped vertically from the bulbs of the heels.

Over time the use of bar shoes in low-heeled feet can crush the caudal region of the frog and offer little weight-bearing support to the third phalanx. The use of a **frog insert** can help by redistributing weight over more of the foot, and will also provide better support to the heels on soft ground. The feet should be trimmed and shod every 6 wk until the desired correction is achieved. In some cases, the heels are so low and collapsed that even supporting the heel structures will not encourage development. In those cases, it is recommended that the shoes be removed, the collapsed portion of the heels trimmed, and the horse kept on a very soft surface until enough strong wall has grown at the heels.

When the horse is very lame, or the disease is advanced and the feet have become small and upright, it may be more beneficial to shoe the horse with a wide webbed, graduated raised heel shoe with a rolled toe and fit well beyond the weight-bearing surface at the heels to give some support. This shoe will lift the heels mechanically to take tension off the DDFT and help straighten the hoof–pastern axis. However, because of the increased thickness of the shoe at the heels, there may also be increased pressure and wearing of the wall at the heels.

Wedge pads or wedge rails added to the Equine Digital Support System shoe can also be utilized to elevate the heels. While the chronic use of wedge pads has been associated with further collapsing already weak heels, this

problem can be minimized through the use of sole loading materials such as Equi-Pac or dental impression material. By incorporating the sole in weight bearing, loading of the hoof wall at the heels is reduced, protecting that area.

In some cases of navicular syndrome, particularly in the early stages, correction of the foot imbalance combined with a gradually increasing exercise program is all that is necessary to return the horse to athletic performance. Other cases may also require medical and/or surgical intervention.

Intrasynovial medication of the DIP joint or of the navicular bursa is used regularly to manage these patients. Typically, a combination of corticosteroid and hyaluronan (*q.v.*) is used. Results and duration of effect vary between patients, but can be outstanding with even long-term improvement in lameness recorded in some horses. If necessary the treatment can be repeated, and careful aseptic technique should always be used.

NSAIDs are used routinely, although they are **largely palliative**. In chronic cases with advanced bony remodeling changes, the use of oral NSAIDs can be invaluable for returning horses to work. These patients should be monitored for adverse systemic effects. The anti-inflammatory effects of these drugs can also be beneficial in management of acute cases of caudal heel pain, although the benefits must be weighed against the **adverse effects** of encouraging increased loading on the affected area, particularly when DDFT involvement is suspected.

Vasoactive drugs and hemorheologic agents have been used extensively in an effort to improve circulation to the foot. With increasing evidence that thrombosis and ischemia are not responsible for the development of navicular syndrome, use of these medications has been questioned. Recent data indicate that orally administered isoxsuprine hydrochloride, pentoxifylline and propentofylline are poorly absorbed and do not increase blood flow to the foot. Nevertheless, there is considerable clinical as well as research evidence that these medications can be beneficial, and practitioners continue regularly to recommend their use. Oral warfarin therapy for navicular syndrome has largely gone out of favor.

Other systemic medications that are routinely used include IV **hyaluronan** (Legend), IM polysulfated glycosaminoglycan (Adequan), and oral feed supplements such as glucosamine HCl and chondroitin sulfate. In addition, intravenous tiludronate, a bisphosphonate used to normalize bone metabolism, has been shown to be beneficial in treating some horses. This drug currently requires FDA approval for use in the USA.

Palmar digital neurectomy is the most commonly performed surgical technique used to manage horses with caudal heel pain. It is **purely palliative**, and should probably be considered a last resort when more conservative methods of management are no longer effective. Palmar digital nerve block should always be carried out before a neurectomy is considered in order to assess the likely results of surgery. Owners should be informed of associated risks of injury as well as of the possibility of nerve regrowth or painful neuroma formation.

Desmotomy of the medial and lateral collateral (suspensory) ligaments of the navicular bone is also used as a surgical treatment. Under general anesthesia the ligaments are sectioned on the medial and lateral aspects of the pastern just below the level of the pastern joint. The effects of this treatment are not well documented and clinical improvements may actually be due to

sectioning of sensory nerve fibers. Variable results have been reported, and clinical improvement is usually short term.

Other treatments that have been described include shock wave therapy, desmotomy of the accessory ligament of the DDFT, temporary chemical neurectomy or percutaneous cryoneurectomy, surgical drilling of cysts and acupuncture.

Prognosis for a complete return to soundness is good in the early stages, providing the condition is recognized and treatment is instigated at that stage. The prognosis is guarded once the disease is established, and poor in the advanced stages when the lameness is persistent and there is radiographic evidence of cortical and medullary erosion involving the flexor surface of the bone.

Laminitis

Laminitis (or **founder**) is a complex systemic metabolic disease that results in **acute degeneration of the laminae** that form the supportive bond between the distal phalanx and the hoof wall. Occasionally, simple mechanical overloading of the laminae can cause the same changes.

Because laminitis is a **systemic disease**, all four feet are often involved to some extent, but the condition is usually more severe in the front feet. Ponies are more often affected than horses, but laminitis in the horse tends to be more severe and life threatening.

The disease can be divided into three phases: the **developmental phase** when the trigger factors initiate the complex pathway of events that lead to disintegration of the lamellar attachments and changes in the foot; the **acute phase** from the onset of clinical signs until the **chronic phase** begins; and the chronic phase when there is either 48 h of continual pain or evidence of distal phalanx rotation and/or sinking.

Etiology and pathogenesis

There are many **predisposing factors** that can trigger the development of laminitis. These include alimentary carbohydrate overload with grain starch (grain founder), lush grass overload on fructan rich pasture (grass founder), obesity, endometritis, retained placenta or severe systemic infection, colic, stress and/or exhaustion, ingestion of toxins, hormone imbalances, systemic or IA administration of corticosteroids, and viral respiratory disease. Horses with **equine Cushing's disease** (*q.v.*) caused by a pituitary adenoma and those with peripheral insulin resistance are also predisposed to developing laminitis.

Over-exercise on hard ground (road founder) and excessive weight bearing on one limb due to an injury or a surgical procedure in the opposite limb can cause the same changes to occur in the foot as a result of mechanical overload.

The pathogenic mechanisms involved in development of laminitis are not fully understood, but recent work performed by the Australian Equine Laminitis Research Unit (AELRU) has contributed substantially to our understanding of the pathogenesis of this difficult disease. The primary pathology identified with development of laminitis involves a **failure of attachment** between the dermal and epidermal lamellae, ultimately resulting in a loss of the attachment between the hoof wall and distal phalanx. This failure specifically involves the **lamellar basement membrane**.

AELRU have identified molecular up-regulation of **lamellar matrix metalloproteinase-2 (MMP-2)** as a critical early event in the pathogenesis of laminitis. Structural components of the lamellar basement membrane are targets of the activated MMP-2, and the increased proteolytic activity promotes degradation and structural failure of the hoof lamellae at the dermo-epidermal junction. The basement membrane and anchoring filaments connecting the epidermal cells to the basement membrane may be the primary targets for MMP activity. In fact, enzymatic separation of basement membrane from lamellar epidermal cells is well underway before clinical signs of laminitis are apparent. Targeted inhibition of MMP-2 has the potential to prevent laminitis, but preventive strategies must be in place early to avoid permanent structural damage.

In addition to MMP activation, there is also substantial evidence that **peripheral insulin resistance** during stress, injury or infection could contribute to laminitis through **glucose deprivation**. Adequate glucose levels are required for maintenance of lamellar integrity, and glucose deprivation may contribute to the dermo-epidermal separation that characterizes laminitis. Inadequate glucose levels can result in depletion of the normal hemidesmosomes required to support epidermal cell attachments to the basement membrane, and similar reductions in the number or size of these crucial supporting structures have been observed with naturally occurring laminitis. Medical conditions contributing to the loss and failure of hemidesmosomes through insulin resistance and subsequent glucose deprivation, such as pituitary pars intermedia dysfunction (Cushing's disease, *q.v.*), may contribute to laminitis development.

An alternative hypothesis regarding the pathophysiology of laminitis proposes that digital hypoperfusion during the developmental stage of laminitis leads to ischemia and separation of lamellar tissue. Shunting of blood through arteriovenous anastomoses, vasoconstriction and perivascular edema are thought to contribute to the vascular compromise. Recent reports indicating that digital and laminar blood flow is increased during episodes of acute laminitis, as well as evidence that digital vasoconstriction is protective during the developmental stage of laminitis, do not support this vascular compromise theory of laminitis.

If the developmental phase is severe or prolonged, there will be laminar degeneration and breakdown of the epidermal–dermal **laminar bond** that suspends the distal phalanx within the hoof. Since the dorsal laminae are usually more severely compromised, the distal phalanx loses its dorsal support first. This, combined with the downward force of the body weight and the pull of the DDFT, results in the **distal phalanx rotating** down at the toe. The amount of rotation depends on the extent of the laminar degeneration. In severe cases, rotation can take place within a few hours of the onset of clinical signs.

In extreme cases, where all or virtually all of the laminae are involved, there is total loss of support for the distal phalanx and it "sinks" within the hoof (vertical distal displacement). In many cases, a combination of rotation and **sinking** may be present.

Clinical signs

The clinical signs vary depending on the severity of the attack. Most often both front feet are involved. In the acute phase, there will usually be a **sudden**

onset of signs. In severe cases, the horse may lie down for long periods and be reluctant to rise. There may be increased respiratory rate, muscle tremors and sweating. In milder cases, the gait is short and stilted and it can be difficult to lift a forefoot.

When standing, the front feet are usually held out in front of their normal position to transfer the weight to the heels and the hind feet are tucked under the body to take weight off the front feet. The back is usually arched and the muscles of the back and quarters are tensed, which may give the impression of a back injury. When the horse moves it will place the heels of the affected feet to the ground first in an exaggerated manner (**laminitic gait**), and it may show hyperflexion and short steps with the hindlimbs, which can be mistaken for a hindlimb problem.

On examination, the feet will usually be **hot**, particularly around the coronary band, and there will typically be a marked increase in **digital pulse strength**. A painful response can usually be elicited using light pressure with hoof testers over the sole. In horses with rotation of the distal phalanx the foot is usually most sensitive over the toe, while "sinkers" or horses with vertical displacement of the distal phalanx tend to be sore over the entire sole. Areas of bruising may be evident.

In the **chronic phase**, the degree of rotation and/or sinking of the distal phalanx influences the degree of lameness. With a mild to moderate degree of rotation, initially the sole is pushed down and becomes flat or slightly convex (**dropped sole**) and there will be increased sensitivity to light pressure in this area. There will be a slight depression at the dorsal coronary band. Over time, the foot will develop characteristic changes due to the disparate growth rates between toe and heels, associated with the position of the bone and compromised blood supply. The dorsal hoof wall becomes concave, the heels grow long, and there will be distinct **laminitic rings** around the wall. These are growth rings that are wider apart at the heels than they are at the toe. The white line also becomes wider as the laminae are stretched.

With severe rotation of the distal phalanx, which is often accompanied by some degree of sinking, lameness will be severe and the horse may be recumbent for long periods, often resulting in development of **decubitus** ulcers. There is usually a soft semicircular bulge of the sole just in front of the point of the frog indicating imminent prolapse of the distal phalanx. Serum may be oozing from the surface of the bulge, or the horn may break to reveal the corium covering the bone.

In complete vertical displacement without rotation of the distal phalanx, the degree of lameness may initially subside markedly and the horse may even weight bear evenly. Often, the only external feature will be a distinct depression at the coronary band all the way around the foot. However, the lameness eventually increases accompanied by discharge and separation of the hoof wall at the coronary band.

Diagnosis

Laminitis can often be mistaken for other conditions, such as muscle injuries, colic and back pain. Diagnosis is based on the history and on the characteristic clinical signs.

Serial radiographs should be taken, starting as soon after the onset of the condition as possible. These are very useful in assessing if, and to what extent, rotation has taken place and in subsequently monitoring the progress of the case and selecting treatment. A lateromedial view with one marker placed at the apex of the frog and a second linear marker taped to the front of the hoof wall from the hairline down is the most helpful. A horizontal dorsopalmar view can detect medial to lateral rotation.

Treatment

Each case must be considered individually. The selection of treatment will depend on the predisposing factors and the severity and duration of the disease.

Acute laminitis should always be treated as a **medical emergency** since changes can take place within a matter of hours of the onset of the disease. It is important to instigate intensive therapy as soon as possible to prevent these changes occurring.

Treatment is aimed at removing the initiating cause, preventing or reducing the degree of pedal bone rotation or sinking, as well as minimizing delivery of "trigger factors" to the foot. **Forced exercise is contraindicated** as it places stress on an already weakened lamellar attachment apparatus causing further damage; however, once appropriate treatment has begun the horse should be allowed limited free movement whenever possible. Nerve blocks are not recommended because the degree of pain relief that they produce can result in increased weight bearing and movement, which in turn will cause further damage to the lamellar attachments.

Medical therapy of laminitis should include aggressive treatment of the primary disease process. Unfortunately there is no known treatment protocol that can effectively arrest the development of laminitis, although there is ongoing research investigating methods of inhibiting MMP activation. **Stall or small paddock rest** should be continued to prevent further damage.

Antimicrobial and **antiendotoxin** therapy are indicated when bacterial infection or endotoxemia are suspected. **Non-steroidal anti-inflammatory medications** including phenylbutazone, flunixin meglumine or ketoprofen are usually indicated to reduce inflammation and pain. Horses with acute laminitis will usually require at least 2 wk of NSAID therapy. Chronic administration of large doses of NSAIDs should be avoided due to risk of adverse systemic effects, and also because the analgesic effects of the NSAIDs may encourage the horse to ambulate more, increasing damage to the already compromised lamellar attachments. When NSAIDs are required for long periods, weekly fecal occult blood, PCV and creatinine levels should be performed to monitor for systemic toxicity.

Continuous cryotherapy using a slurry of ice and water for 48 h during the developmental and acute stages of laminitis can be used as a preventative strategy. Up-regulation of MMP enzymes is thought to contribute to the pathogenesis of acute laminitis, and cryotherapy applied during the developmental stage of laminitis can **limit MMP activity**. In addition, cold-induced vasoconstriction may limit delivery of laminitis trigger factors such as

cytokines and bacterial products. Aggressive cryotherapy for 24–48 h using boots containing ice and water or circulating cold water can effectively prevent development of acute laminitis in horses with conditions that put them at risk of developing acute laminitis.

Therapy designed to increase blood flow to the foot, including hot water footbaths and vasodilating drugs such as isoxsuprine hydrochloride, acepromazine and nitroglycerin, is **contraindicated** during the developmental phase of laminitis as it may increase exposure to circulating trigger factors and activate MMPs. Use of these therapies later in the management of laminitis is currently debated. There is little evidence that they do effectively increase blood flow to the foot, and the benefits of increasing laminar blood flow are not well established. However, acepromazine may also encourage a horse in pain to spend more time down, consequently protecting the lamellar attachments.

Hoof care and mechanical support are absolutely critical for effective management of laminitis at all stages. The goal of hoof care is to minimize damage to the lamellae by minimizing the forces that produce rotational or vertical displacement of the distal phalanx. The forces favoring displacement include the weight of the horse, the pull of the DDFT and leverage on the hoof wall, especially at the toe.

In the **developmental and acute phases** of laminitis the goal is to prevent distal displacement of the distal phalanx by providing optimal support for the distal phalanx. In these early stages shoeing is usually not indicated, but if the horse is already shod, removing the shoes may also be **contraindicated** as this often increases discomfort.

Stress on the wall and damaged laminar structures can be minimized by increasing the dimension of the weight-bearing surface by transferring weight from the wall to the **caudal solar surface** of the foot. Specifically, the frog and caudal sole can be recruited for weight bearing through application of dense Styrofoam pads, frog support pads and/or the use of soft supportive bedding materials like sand or peat moss. The toe can be unweighted by beveling or rockering it with a rasp, or by beveling the foam pad. Foam pads cut from sheets of very dense Styrofoam insulation provide an economical and effective method of supporting these patients. The pads can be applied using duct tape and flexible adhesive bandaging material. Alternatively a commercial system using a cuff with wedge pads and rubber impression material is available (Redden Ultimates) and provides excellent support.

Once the disease has become chronic, treatment is aimed at preventing further laminar damage and rotation or sinking of the distal phalanx, minimizing infection and necrosis, and resolving any systemic problems. Eventually an attempt should be made to re-establish normal alignment between the third phalanx and the wall and sole. Therapeutic trimming and shoeing are extremely important in the treatment of **chronic laminitis**.

The methods chosen will depend on the individual animal and the degree of damage in the foot. What will be effective in one animal may not be effective in another. Discussion and collaboration with the farrier and reference to lateromedial radiographs of the feet are essential in the selection of hoof management techniques.

The fundamental principles to follow when designing a treatment plan should include the following:

1. Utilize as much of the palmar aspect of the ground surface as possible for support.
2. Avoid removing sole, particularly under the toe of the distal phalanx.
3. Bring the breakover back toward the toe of the distal phalanx (in this context breakover refers to the last part of the foot or shoe to leave the ground).
4. Raise the heels when necessary to reduce tension from the DDFT, but continue to trim the heels to re-establish the relationship between the distal phalanx and the sole.

In mild cases with only **slight rotation**, removal of the shoe, trimming of the toe to reduce its fulcrum effect, lowering the heels to start realignment of the distal phalanx and maintaining the horse on a soft surface may be all that is required. Realignment of the distal phalanx, hoof wall and sole is brought about gradually by trimming based on serial radiographs. Some animals are more comfortable if frog support is continued or they are shod with a flat wide-webbed shoe with a rolled toe.

Where there is a **moderate degree of rotation**, the hoof wall at the toe should be trimmed back more radically to reduce the fulcrum effect, but use caution to avoid compromising sole thickness under the toe of the distal phalanx. The heels should be trimmed and a variety of shoes can be applied, with or without the addition of early frog support, depending on the response of the horse.

Different types of shoes that have been used effectively include flat wide-webbed shoes, full-bar shoes, egg-bar shoes, reverse shoes (these allow more radical removal of the hoof wall at the toe, but should never be used if the laminae are still friable as they can induce further rotation), glue-on shoes of any configuration, Equine Digital Support System (EDSS) shoes, heart-bar shoes, and steel or plastic adjustable heart-bar shoes. The **heart-bar** and adjustable heart-bar shoe should be used with caution. These are shoes with a built-in frog support bar that puts varying degrees of pressure on the frog depending on how it is made. These shoes require considerable experience to fit correctly, they do not compensate for growth or changes in hoof capsule to bone alignment, and more damage can be done with an incorrectly fitted heart-bar shoe than any other shoe or no shoe at all.

One of the most effective techniques for shoeing horses with **chronic laminitis** and moderate to severe rotation involves application of a shoe that transfers weight bearing to the palmar aspect of the foot and provides optimal support for the third phalanx. Hoof testers should be used first to confirm that the caudal third to half of the sole is relatively pain free, and a commercial shoeing system marketed by Equine Digital Support System Inc. can often be used with excellent results. The **EDSS** system includes a shoe that automatically reduces the length of breakover, a sole pad, wedge rails and frog inserts with various elevations, as well as dental impression material. The system offers a highly adjustable shoeing method that effectively allows the horse to dictate what feels best. The shoe and pad are designed to protect the toe of the distal phalanx and improve circulation by creating a gap between the anterior sole and the foot surface of the pad. The system seems to facilitate **minimizing**

NSAID doses, and free movement can be encouraged at this stage of treatment as the system provides dynamic support to the distal phalanx instead of static pressure. If the wall cannot effectively hold nails, or the horse cannot tolerate the concussion, the shoe can be applied using a cuff and screws placed into the insensitive wall.

A common problem in chronic laminitis is **recurrent abscess formation** and septic pedal osteitis (*q.v.*). Abscesses should be drained, and infected bone debrided as needed. Distal limb perfusion with broad-spectrum antimicrobials may help to resolve distal phalanx infections, and topical application of a mixture of povidone-iodine and sugar ("**sugardine**") (*q.v.*) is also commonly recommended to encourage drainage. If there is radiographic or clinical evidence of **seroma** formation (a sterile accumulation of serum) or infection under the hoof wall, a **dorsal wall resection** may be required. This involves removal of all undermined hoof wall, facilitates drainage, and encourages new hoof growth. Infected and necrotic laminae are removed and the foot bandaged with frog support until the laminae have produced a dry protective cuticle. The hoof wall resection technique was very popular at one time and was probably over utilized. Removal of the dorsal hoof wall is no longer recommended in horses with acute laminitis. However, the principles behind the procedure are still valid for management of chronic laminitis with extensive laminar damage and can benefit some horses.

Transection of the DDFT has also been advocated for treatment of horses with laminitis. The rationale behind performing the tenotomy is that it will reduce the pull of the DDFT and decrease shearing forces on the lamellae. In addition, the surgery facilitates lowering of the heels to realign the distal phalanx. Guidelines for when to perform the surgery are not well defined. In general the surgery is used in management of chronic recurrent laminitis cases, and it is usually considered a salvage procedure. Reported results have varied between practices, and this may reflect the timing of the procedure. The tenotomy can be performed in the mid-metacarpal or mid-pastern region. **Transection of the accessory ligament of the DDFT** (carpal or inferior check ligament desmotomy) has also been advocated to reduce tension on the DDFT in less severely affected horses.

Coronary grooving is a technique in which a groove extending from the medial to the lateral quarter is created through the hoof wall parallel to the coronary band and approximately 1.5 cm below the hairline. The groove extends to the depth at which soft translucent horn is visualized. The theory behind this technique is that it will relieve pressure on the dorsal coronary band and promote new hoof wall growth. In addition, grooving the area of the hoof wall associated with the extensor process in an effort to relieve pressure and suppuration created by rotation of the distal phalanx has provided pain relief in some cases.

The **prognosis** in laminitis should always be considered guarded and depends to a large extent on the degree of internal damage that has taken place and the number of feet involved. Horses that recover from one attack tend to be prone to further attacks. It is always important to find the initiating cause in order to try and eliminate this from the animal's environment or management. In cases of severe rotation or sinking, particularly if more than one foot is involved, or where extensive infection or necrosis of the feet

occurs, prognosis is very poor and destruction on humane grounds may be necessary.

Ossification of the collateral cartilages of the distal phalanx (sidebone)

Ossification of the collateral cartilages is most often found in the front feet in heavier breeds of horses. Ossification usually starts at the cartilage–bone junction or can originate at a separate location in the center of the cartilage, and is thought to be part of the normal aging process.

It is not unusual to find some degree of **sidebone** formation on radiographs of older horses, or young draft horses without associated lameness. Ossification is typically more extensive in the lateral than the medial cartilage. Excessive, abnormal or premature ossification can occasionally cause lameness. Increased loading and/or concussion on the collateral cartilages may predispose to ossification, and these tend to occur as a result of poor foot conformation or improper trimming and/or shoeing. Occasionally direct trauma to the cartilage can result in an area of ossification.

Clinical signs

Lameness associated with sidebone is considered to be rare, and when present it is usually thought to be associated with an inflammatory reaction at the onset of ossification or with excessive ossification. Recent evidence from detailed anatomic studies of healthy and diseased feet suggests that well-developed collateral cartilages and their associated vascular architecture may be critical for dissipation of concussion within the hoof capsule. Future studies may confirm that pliable, non-ossified collateral cartilages are essential for long-term pain-free locomotion.

In the early stages, lameness associated with sidebone development is often slight but will be increased on a hard or rough surface or when the horse is turned in the direction of the affected foot. Pain may be elicited on pressure with hoof testers over the heels. Paring of the foot may reveal hemorrhage at the "seat of corn" on the affected side(s). Lameness usually subsides given rest.

If the cartilage becomes **extensively ossified**, lameness may be more marked, and there is often pain on palpation of the area as well as a loss of pliability of the cartilage. With loss of normal expansion accompanying extensive ossification, the hoof wall from the heels to mid-quarter on the affected side(s) tends to become more upright and the coronary band bulges in this region.

Diagnosis

The diagnosis is based on clinical signs and shape of the foot in advanced cases. It should be confirmed by uniaxial or biaxial palmar digital nerve blocks and with radiographs. Radiographic evidence of ossification of the collateral cartilages does not necessarily mean that this is the cause of lameness and the findings should be correlated with the clinical signs and the results of nerve blocks (*q.v.*).

Occasionally what appear to be "**fractured**" sidebones may be identified radiographically. Usually these are actually separate **centers of ossification**, but traumatic fractures have also been described.

Treatment

Foot imbalance should be corrected and the feet shod with a flat, wide-webbed shoe with a rolled toe, fit wide at the quarters and heels, and extending beyond the weight-bearing surface at the heels to support the posterior foot and encourage expansion. Combined with 6–8 wk rest this may be successful in the early stages.

In more advanced cases, treatment is mainly palliative and includes correction of any foot imbalance and shoeing as above, making sure that there are no nails behind the mid-quarters. **Long-term NSAIDs** may be necessary. Grooving or thinning the hoof wall at the quarters and heels may encourage expansion and reduce pain, but does tend to weaken the foot.

The prognosis for a complete return to soundness is good in the early stages, and guarded to poor if ossification is extensive.

Pedal osteitis

By strict definition, the term **pedal osteitis** refers to inflammation of the distal phalanx, and this diagnosis has commonly been made to explain chronic forelimb lameness. However, pedal osteitis is actually a very poorly defined condition that was traditionally diagnosed on the basis of radiographic evidence of bone demineralization, new bone formation and widening of the vascular channels in the distal phalanx.

These radiographic changes have been attributed to persistent trauma occurring as a result of **abnormal foot conformation**, including long toe/low heel imbalance, flat thin soles and clubfeet or when concavities or flares have developed in the external hoof wall. However, demineralization can also develop secondary to other conditions of the foot, such as abscesses, hoof wall cracks, laminitis and corns. In addition, there is considerable variation in the appearance of the distal phalanx between horses, and demineralization is probably over diagnosed. Furthermore, once radiographic demineralization of the distal phalanx develops, it tends to persist, and it is difficult to document active inflammation or bone resorption without scintigraphy.

Clinical signs

The clinical signs usually attributed to pedal osteitis are varied. The degree and type of lameness will vary depending on the initiating cause, the area of bone affected, and severity of damage. There will often be a marked increase in lameness on a hard or uneven surface and a decrease in lameness on a soft surface. There may be diffuse areas of bruising evident in the sole, and a painful response to pressure with hoof testers in these areas.

Diagnosis

There is increasing evidence that lameness is often incorrectly attributed to "pedal osteitis", and many experts do not think that there is a discrete clinical syndrome associated with inflammation of the distal phalanx.

Radiographic changes in the distal phalanx include areas of demineralization around the solar margin, widening of the nutrient foramina at the solar margin, new bone growth on the solar margin of the wings and occasionally type VI fractures of the solar margin. Since many of these radiographic findings are found in sound horses and will persist indefinitely once they do develop, their significance should be assessed in conjunction with clinical signs and results of local anesthesia.

Treatment

Treatment depends on the cause, and should be aimed at the primary condition when that can be determined. If there is associated severe or chronic bruising, shoeing changes should be implemented and the horse should be rested until lameness subsides.

CONDITIONS OF THE HEELS

Sheared heels

The condition of sheared heels involves a loss of structural integrity of the tissue between the medial and lateral heels, and is probably a more common cause of lameness than is generally recognized.

The structural breakdown between the medial and lateral heels appears to occur as a result of **uneven loading** of the heels and disproportionate use of one heel. When the foot is examined from behind with the foot in a weight-bearing position, the bulb of the heel on the affected side is higher, and wall of that heel is longer. In severe cases the heels can be manipulated to displace them, confirming shearing of the structures between the two heels. This condition can be caused by a single incident of severe uneven loading but is usually the result of persistent slight uneven loading due to mediolateral foot imbalance.

Sheared heels are usually the result of **improper trimming** and/or shoeing, and poor conformation is often a contributing factor. Once the condition is created it tends to be perpetuated, since a disproportionate amount of the weight-bearing load tends to be shifted onto the affected heel when the hoof contacts the ground, displacing it further upward. The use of heel calks ("stickers") or studs will exaggerate this effect.

Horses with long toe/low heel imbalance are more prone to develop sheared heels because of the already weak heel structure. Sheared heels may also follow long-term corrective trimming for a conformational defect in young horses, or occur as a result of a painful lesion elsewhere in the foot or limb that causes an alteration in the way the foot contacts the ground. Front feet are usually more severely affected, and the medial heel is most commonly displaced proximally.

Clinical signs

Lameness is usually insidious in onset, but the degree depends on the duration and severity of the deformity. The anterior phase of the stride will be shortened with the toe of the foot contacting the ground first. The affected heel may be seen to strike the ground first on landing and to move proximally

relative to the other heel. The central sulcus of the frog appears unusually deep, with the heel bulb on the affected side higher than the other. The hoof wall at the heel and quarter on the affected side is steeper, and on the non-affected side it will usually be flared. In severe cases, the hoof wall on the affected side may be rolled under the foot.

On manipulation, the heel bulbs may be able to be displaced in opposite directions proximally and distally and the horse will usually react painfully to this manipulation. However, with chronic upward displacement of one heel, it can be difficult to detect instability with manual manipulation. A painful reaction may also be elicited by pressure with hoof testers across the heels or from mid-frog to the opposite quarter. Radiographs are indicated to rule out other problems.

Diagnosis

Diagnosis is based on the clinical signs and characteristic appearance of the foot. There will usually be a marked improvement in, or abolition of, lameness following palmar digital nerve block (*q.v.*).

Treatment

The aim of the treatment is to restore normal foot balance and shape and relieve pain. Since each animal is an individual and may react in different ways, no set technique for correction can be applied, but guidelines can be considered.

In mild cases, the heels should be trimmed to the same length and a **bar shoe** fit to stabilize the heels. In more severe cases, the affected heel should be trimmed or "floated" so it will not make contact with the shoe, and in time the horse's body weight will push the heel back down into alignment. To encourage more rapid realignment of the heels prior to shoeing the foot can be maintained overnight in a "**foot-soak bandage**" (consisting of water-soaked wrap material or commercial baby diapers applied to the foot with an impervious covering of duct tape) with a frog support insert (i.e. Lily Pad). If there is a flare on the unaffected side, this should be rasped to try and return the wall to a normal angle. This can rarely be achieved in one trimming. The foot is shod with a **full bar shoe**. When the hoof wall on the affected side is rolled under, the shoe should also be fit wide at the heels and quarters on the affected side to give support and encourage the wall to grow down without collapsing. Trimming and shoeing may be required several times in advanced cases before balance is restored.

The prognosis is good in most cases although some horses may require a prolonged period of corrective trimming and shoeing. If there has been severe structural damage, the prognosis is guarded and permanent shoeing with a full-bar shoe may be necessary.

Avulsion of the hoof wall at the heel

This is a separation of a portion of the hoof wall from the underlying structures at the heels. It may involve the corium and coronary band. The most common causes include standing on or kicking a sharp object, trapping the

foot in wire, prolonged foot imbalance or incorrect removal of the shoe. It can also occur secondary to submural infection. Avulsions can be complete or partial.

Clinical signs

The degree of lameness will vary depending on the position and extent of avulsion and the depth of the injury. With an **acute avulsion**, the horse will often be very lame, resenting any examination of the foot. In **chronic cases**, lameness is usually less marked unless there is involvement of deeper structures. Wound healing may be evident but this is often delayed by infection.

Diagnosis

The diagnosis is usually straightforward but careful examination of the foot is needed to determine the full extent of the injury.

Radiographic examination can be of value in assessing involvement of deeper structures. Contrast radiography can be useful.

Treatment

In cases of **acute partial avulsions**, attempts at repair rarely work, and it is best to completely remove the separated portion of hoof wall. This is best done under general anesthesia so that the damaged area can be assessed and thoroughly cleaned. The exposed corium should be lavaged with an antiseptic solution and the area packed with a non-caustic antiseptic astringent agent such as "sugardine" (*q.v.*). The foot should then be dressed and bandaged, and the bandages changed every 2–3 days until protective cuticle has formed over the corium.

In cases of **complete heel avulsions** where there is involvement of the sensitive corium, any remaining separated pieces of hoof wall should be removed, the corium cleaned and debrided and any wounds in the coronary band sutured. The wound should be packed, and dressed as above. The use of a **foot cast** covering the entire hoof and extending up to the level of the pastern is often recommended to reduce the amount of movement, which can delay healing. If secondary infection occurs, the presence of the cast makes it difficult to detect and treat.

Once a **firm dry cuticle** has formed, a full-bar shoe can be applied to the foot with an extension in the area of the avulsion to give added support. Hoof repair materials can be used to fill the defect and protect the area, but should be used with caution since covering the area prevents inspection and cleaning, and can create an ideal **anaerobic environment** for bacterial infection.

Where there is evidence of infection and/or involvement of deeper structures, chronic heel avulsions should be treated as described previously for group 2 hoof abscesses (*q.v.*).

The prognosis depends on the extent of the avulsion and the structures involved. In cases of partial avulsions the prognosis is usually good. Where there is damage to the coronary band and dermal laminae the prognosis is more guarded.

Heel bulb lacerations

Because of their distal location on the limb, the foot and pastern regions are particularly susceptible to trauma. Lacerations are most frequently found over the bulbs of the heels. These heel bulb wounds usually involve one heel and appear as an inverted U, and they often occur when the horse kicks at or steps on a sharp-edged object such as barbed wire or roofing sheet metal. **Overreaching** with a hind foot can also result in serious injuries. Open wounds quickly become contaminated with feces, urine and dirt.

Diagnosis

The diagnosis is straightforward but careful examination of the foot is needed to determine the full extent of the injury. Possible complications include coronary band injury, arterial laceration, nerve damage, collateral cartilage injury (could result in quittor) as well as joint capsule penetration (*q.v.*). The integrity of the DIP joint, navicular bursa and digital sheath should be assessed. Radiographs can be taken to assess involvement of deeper structures.

Treatment

Carefully evaluate wounds and consider potential complications prior to initiating treatment. The branches of the laceration may extend through the coronary band, but there is seldom much loss of tissue—it is usually pulled loose as a flap. As the horse moves, these wounds alternatively gape open and close, and this constant motion will result in delayed healing and excessive granulation tissue (**proud flesh**) (*q.v.*).

Usually a combination of **suturing** and stabilizing the repair in a **foot cast** (*q.v.*) will provide the best cosmetic and functional end result. Fresh clean wounds can be closed primarily, but delayed primary closure generally is recommended for the acute contaminated laceration.

SOFT TISSUE INJURIES AND DISEASES

INTRODUCTION

Soft tissue injuries and diseases, apart from injuries to the flexor tendons and suspensory ligaments, have previously been underestimated as causes of lameness or poor performance. It should always be borne in mind that when there has been trauma to a joint or bone it is likely that there is **concurrent soft tissue pathology**. Advances in diagnostic techniques, notably local analgesic techniques, diagnostic ultrasonography and arthroscopy, have made us more aware of the incidence and importance of these injuries, either alone or in conjunction with bone pathology.

DISEASES OF THE SUSPENSORY APPARATUS

Superficial digital flexor tendinitis in the metacarpal/metatarsal region

Superficial digital flexor tendinitis is predominantly an injury affecting one or both forelimbs of horses that work at speed, especially racehorses and

advanced level event horses. However, any type of performance horse can be affected. It is considered to be an **overstretch injury** and muscular fatigue is probably a predisposing factor. Foot imbalance and conformational abnormalities may be underlying factors, aggravated by sudden alterations in ground conditions or irregular surfaces. It is likely that multiple episodes of submaximal strain induce **microdamage** that accumulates and predisposes to eventual injury. Lesions can range from minor tearing to complete tendon rupture.

Clinical signs

There is usually **localized heat with swelling** from fluid accumulation or palpable thickening of the superficial digital flexor tendon (SDFT). Pain can often be elicited by direct palpation of the margins of the tendon. Lameness may be present but is frequently absent in mild injuries, and this emphasizes the need for diligent observation to pick up subclinical injuries.

The **degree of swelling** is often proportional to the severity of the injury, but core lesions tend to swell less than peripheral injuries. In mild cases, clinical signs often resolve with confinement to box rest and application of a bandage, with or without cold therapy, but the potential significance of the underlying lesion should not be overlooked, and these horses should have an ultrasound evaluation before returning to work.

Diagnosis

Diagnostic ultrasonography is essential to assess the extent, type and severity of injury, and to monitor progress. One important caution is to recognize that examination of a recent SDFT injury may not reveal the full extent of the injury. If the SDFT appears only slightly enlarged or even normal on ultrasound, but clinical signs suggest that there could be an injury, the horse should be managed conservatively and the examination **repeated** in 3–7 days.

In most cases both forelimbs should be assessed since lesions are frequently **bilateral** although overt clinical signs may only be detectable in one limb. High quality images are essential for accurate diagnosis and prognosis. Abnormalities that can be detected include enlargement of the tendon, poor definition of one or more of its margins, and a reduction in echogenicity in a localized or more diffuse area (e.g. a central, anechoic core lesion or a diffuse hypoechoic area involving the entire cross section of the tendon). High-resolution images and experience in evaluating these images are critical for accurate interpretation.

Treatment

The aims of treatment are to reduce inflammation and pain, minimize further damage, restore normal fiber alignment as soon as possible, promote increased speed of healing and enhance the quality of the repair tissue. However, even under optimal conditions the **repair tissue** will not be as strong as an undamaged tendon.

A prolonged period of stall rest with gradually increasing controlled exercise is required for adequate healing to occur. **Scheduled exercise**, which usually involves walking in the early stages, stimulates optimal collagen fiber

alignment. Healing should be monitored with ultrasound on a regular basis (30–60 days) in order to determine when increased exercise is warranted. Uncontrolled turnout should be avoided. Appropriate rehabilitation is probably the most important aspect of treatment, and must be performed regardless of the other treatments that are used.

NSAID medications, cryotherapy with ice and/or cold water, pressure/compression wraps, topical DMSO and therapeutic ultrasound can help to reduce inflammation, swelling and pain. The use of systemic and intralesional corticosteroids should generally be avoided as they appear to retard healing.

Surgical options for managing SDFT injuries include **percutaneous tendon splitting**, in which ultrasound-guided incisions are made into the lesion. By evacuating the area of hemorrhage, reducing lesion size and possibly enhancing resolution of inflammatory edema, this procedure may be helpful in the acute stage of central core lesions. **Transection of the accessory ligament of the SDFT** (superior check ligament desmotomy) has been reported to reduce the incidence of re-injury in some horses, and is considered most valuable for Standardbred racehorses. **Annular ligament desmotomy** can be beneficial in the management of distal SDFT tendinitis in which the tendon is constricted by the palmar annular ligament.

Various drugs including intralesional hyaluronan, PSGAGs (*q.v.*) and most recently ACell Vet Powder (a derivation of extracellular matrix of swine urinary bladder) have been used to improve the quality of the repair tissue. In addition, bone marrow, stem cell and growth factor (i.e. insulin-like growth factor) injections are currently being advocated. Bone marrow injections are likely to provide high concentrations of **growth factors** as well as some **primordial stem cells**. Vet-Stem Inc. offers stem cell therapy technology on a commercial basis. The injured horse's fat is collected and mailed to the company, where stem cells are isolated, concentrated and sent back to be injected into the tendon injury. Treatment within 28 days of injury is recommended to minimize fibrosis. Additional research is needed to document the benefit of these treatment modalities.

Prognosis is dependent on the severity of the initial injury. Severe injuries result in **peritendinous adhesions** (*q.v.*), which predispose to re-injury. Repair tissue is mechanically inferior to normal tendon tissue and the incidence of re-injury is high. Once returned to performance, the horse should always be maintained as fit as possible for the work it is required to do.

Superficial digital flexor tendinitis in the pastern region

In the pastern region the SDFT divides into two branches that encircle the DDFT before inserting on the palmar aspect of the middle phalanx. Injury to the SDFT in this area may be a sequel to a previous injury in the metacarpal region, or occur in isolation. It occurs much more commonly in the forelimb than in the hindlimb.

Clinical signs

There is usually associated lameness, greater in degree than a comparable injury to the SDFT in the metacarpal region, and **localized heat, pain and swelling** on the palmar lateral and/or medial aspects of the pastern. Usually

only one branch is affected. In the acute stage there may be lameness that is improved or alleviated by perineural analgesia of the palmar (abaxial sesamoid) nerves but no detectable swelling.

Diagnosis

The diagnosis is confirmed ultrasonographically: the affected branch is enlarged, its margins may be poorly defined and it is of irregular echogenicity. This should be differentiated from injury to a distal sesamoidean ligament, DDFT tendinitis, or peritendinous trauma (*q.v.*).

Treatment

The same principles of treatment apply as for SDFT tendinitis in the metacarpal region (*q.v.*). The incidence of re-injury is very high, regardless of the method of management.

Deep digital flexor tendinitis

Deep digital flexor tendinitis in the metacarpal or metatarsal region is less common than SDFT tendinitis but is seen alone, or in association with the palmar (plantar) annular ligament syndrome. Subtle lesions of the dorsal margin can also be seen in association with desmitis of the accessory ligament of the DDFT.

Clinical signs include localized heat, swelling and pain and associated lameness; in some cases there is no detectable enlargement of the DDFT and in others the degree of swelling is too extensive to determine definitively, with palpation alone, which structures may be involved. Involvement of the DDFT within the digital sheath can result in **distension of the tendon sheath** and marked lameness.

Diagnosis is generally confirmed using diagnostic ultrasonography, although tenoscopic evaluation of the digital flexor tendon sheath may be required to appreciate some linear tendon defects. The same treatment principles apply as for SDFT tendinitis (*q.v.*); the incidence of re-injury is high.

Deep digital flexor tendinitis in the **pastern region** or in the **foot** occurs more frequently. There is localized swelling on the midline of the pastern region and associated heat and swelling although lesions further distally may have no detectable palpable abnormalities. There may be associated distension of the flexor tendon sheath. There is usually associated lameness.

Pastern lesions are confirmed ultrasonographically. The appearance of the DDFT is dependent on the **angle** of the transducer head, and hypoechoic areas should be interpreted with great care. Injuries within the hoof capsule typically require specialized ultrasound techniques, MRI, or contrast enhanced CT imaging for diagnosis.

Treatment is prolonged rest and rehabilitation. Intralesional therapy with stem cells on ACell have been used to improve the quality of repair tissue. The prognosis for return to sustained full athletic function is guarded.

Deep digital flexor tendinitis progressing to partial or complete rupture can occur following **palmar digital neurectomy**. Pre-existing pathology in the DDFT and/or flexor cortex of the navicular bone may be predisposing factors. Following rupture, there is **marked swelling** in the palmar aspect of the

pastern, severe lameness and often subluxation of the distal interphalangeal joint. The horse appears to walk on its heel. The prognosis is grave.

Accessory ligament of the deep digital flexor tendon (inferior check ligament) desmitis

The accessory ligament of the DDFT or **check ligament** is a substantial supporting structure in the forelimb that is similar in diameter to the DDFT itself. It arises from the palmar carpal fascia and joins the DDFT in the mid-metacarpal region. In the hindlimbs it is generally much smaller and less prone to injury.

Clinical signs

Injury almost invariably results in sudden onset of lameness during work. Localized swelling (medial and lateral), heat and pain develop within the following 24 h. Lameness usually resolves relatively quickly, long before healing is complete.

Diagnosis

Diagnosis can be confirmed ultrasonographically, and healing monitored with serial examinations.

Treatment

Treatment is as for SDFT tendinitis (*q.v.*). Uncontrolled turnout will result in exacerbation of the injury, but **controlled exercise** is important to minimize the risk of adhesion formation. Horses are often able to resume work within 6 mo. The prognosis for future athletic function is fair. Severe injuries may be associated with the development of adhesions and a secondary flexural deformity of the metacarpophalangeal joint, or SDFT tendinitis. These patients, and horses with chronic recurrent desmitis, may benefit from desmotomy of the accessory ligament.

Palmar/plantar annular ligament desmitis

The **palmar annular ligament** traverses the palmar aspect of the digital tendon sheath at the level of the fetlock joint. The annular ligament with the sesamoid bones and intersesamoidean ligament create an inelastic fetlock canal around the SDFT, DDFT and digital sheath. The annular ligament is in part contiguous with, and attaches to, the digital sheath so that they appear as one structure on ultrasound. This ligament maintains the position of the flexor tendons.

The ligament itself can be injured by direct trauma or with hyperextension of the metacarpophalangeal (or metatarsophalangeal) joint. Direct trauma can cause thickening and contraction of the ligament, effectively reducing the diameter of the fetlock canal. Desmitis is often grouped with other conditions including tenosynovitis of the digital sheath (*q.v.*), SDFT or DDFT tendinitis, adhesions between the sheath and tendon and combinations of these problems under the heading of **palmar annular ligament syndrome** (*q.v.*) or constriction of the annular ligament.

Clinical signs

There is localized heat, swelling (resulting in a **bulge** on the palmar aspect of the limb at the level of the ligament, as opposed to the notch observed with primary tenosynovitis) and pain. Lameness is variable in degree and can be due to the desmitis or due to compression of the flexor tendon or restriction of free movement of the tendons.

Diagnosis

Diagnosis is based on clinical signs and ultrasonography. With acute injury there is enlargement of the ligament and focal or diffuse areas of reduced echogenicity. All other structures should be examined carefully to exclude concurrent injury.

Treatment

Treatment involves rest, NSAIDs, bandaging, cryotherapy and topically applied anti-inflammatory agents (e.g. DMSO). The period of rest required is variable. Usually localized swelling persists. Sometimes **local adhesions** develop, resulting in recurrent lameness.

Suspensory ligament desmitis—body and branch lesions

The **suspensory ligament** originates from the proximal palmar aspect of the third metacarpal bone and the palmar carpal ligament in the forelimb, and it originates from the plantar aspect of the third metatarsal bone in the hindlimb. The ligament divides in the mid-metacarpus/tarsus, and the resulting medial and lateral branches insert on the ipsilateral proximal sesamoid bones. Extensor branches are given off and join the extensor tendons. With respect to routine injury the suspensory ligament can conveniently be divided into its proximal third and the remainder of the body and branches. Injuries of the proximal part of the suspensory ligament are considered separately.

Sprain of the body and/or branches of the suspensory ligament is usually seen in horses that work at speed and/or race over fences, although **localized** soreness of the suspensory ligament branches is regularly detected in dressage horses. Straight hindlimb conformation and/or hyperextension of the metacarpophalangeal (metatarsophalangeal) joints and/or foot imbalance may predispose to injury of the suspensory apparatus.

Clinical signs

There is usually **palpable enlargement** of the body and/or one or both branches of the suspensory ligament with associated heat and localized pain. In some cases **swelling is so extensive** initially that identification of individual structures by palpation is difficult, especially if there is a concurrent fracture of the distal second or fourth metacarpal bones. When detected, lameness is often not proportional to the extent of the injury but may be **worse on soft ground**. There is usually pain on passive flexion of the metacarpophalangeal (metatarsophalangeal) joint and accentuation of lameness following flexion. In some horses there is concurrent pain associated with the metacarpophalangeal joint.

Diagnosis

Diagnosis is based on clinical signs and ultrasonography. Unfortunately, there is considerable variation in the normal appearance of the suspensory ligament, including an inconsistent amount of muscular tissue, and images must be interpreted with care. Lesions often persist for a long time ultrasonographically and serial imaging is less useful for predicting when a horse may be returned to work compared with SDFT lesions. Nevertheless, some improvement including a reduction in the cross sectional diameter of the ligament may be observed and **serial ultrasound** examination is strongly recommended even after the horse returns to work.

The second and fourth metacarpal bones should be evaluated radiographically together with the proximal sesamoid bones to eliminate the possibility of concurrent fracture, sesamoiditis or mineralization within the ligament.

Treatment

The same principles of treatment apply as for SDFT tendinitis (*q.v.*). There is a high incidence of recurrent injury.

Suspensory ligament desmitis—proximal

Proximal suspensory desmitis refers to lesions in the suspensory ligament in the proximal third of the metacarpus (or metatarsus). This is a **common injury in athletic horses** from many disciplines, and it is associated with either a sudden or insidious but often transient onset of lameness. With hindlimb involvement the lameness is often more severe and persistent.

Clinical signs

Since the suspensory ligament lies between the bases of the second and fourth metacarpal (metatarsal) bones there is frequently no detectable enlargement of the ligament, although further distally its margins may feel slightly rounded. There can be localized heat with or without distension of the medial palmar vein.

Pain can often be elicited by pressure applied over the origin of the suspensory ligament. Lameness varies from mild to moderate and usually improves considerably with rest. Lameness is typically worse on soft surfaces, especially with the affected limb on the outside of a circle. The condition can be **unilateral or bilateral**, in which case the horse may present for a loss of action.

Diagnosis

Pain should be **localized** to the proximal metacarpal (metatarsal) region using perineural analgesia although interpretation of these blocks can be complicated by diffusion and inadvertent synovial analgesia. In particular, care should be taken to eliminate the middle carpal and tarsometatarsal joints as potential sources of pain.

Diagnosis is confirmed ultrasonographically but requires high quality images for accurate interpretation. There may be enlargement of the suspensory ligament, poor definition of one or more of the margins, ectopic mineralization, loss of fiber pattern, a central hypoechoic lesion and/or a more

diffuse decrease in echogenicity. Comparison with the contralateral limb is often useful.

The proximal metacarpus/metatarsus should be examined radiographically, together with the carpus or tarsus to exclude the possibility of an avulsion fracture at the origin of the suspensory ligament, a palmar cortical fatigue fracture, and/or osteoarthritis of the middle and/or carpometacarpal or tarsometatarsal joints (*q.v.*).

Treatment

Treatment consists of **prolonged stall rest** with gradual introduction of controlled exercise. The speed of recovery is often proportional to the duration of lameness prior to inception of treatment and to the severity of the injury. Recurrent injury in hindlimb proximal suspensory desmitis is common and prognosis is generally poor.

Many of the treatments discussed for SDFT tendinitis (*q.v.*) can be used for proximal suspensory injuries. **Extracorporeal shock wave treatment** has been particularly successful in management of chronic unresponsive injuries (Box 15.8).

Owners should be cautioned to allow the horse **adequate time** to heal before returning it to work since shock wave therapy also provides analgesia. Intralesional bone marrow, stem cell and ACell Vet Powder (a commercially marketed derivation of extracellular matrix of swine urinary bladder) injections have also been advocated, and there is some preliminary evidence that lesions heal more rapidly and effectively. Infiltration of proximal suspensory lesions with 2% iodine in almond oil has been used for many years, but creates considerable scarring.

Surgery may be necessary in unresponsive cases. **Suspensory desmoplasty** (surgical fasciotomy and splitting) can be performed with ultrasound guidance on the front or hind limbs. Alternative surgical interventions including tibial neurectomy, neurectomy of the deep branch of the lateral plantar nerve and fasciotomy of the deep plantar metatarsal fascia have all had some reported success in returning horses with hindlimb proximal suspensory desmitis to athletic function.

Proximal suspensory desmitis often occurs **concurrently** with some other cause of lameness or in association with poor foot balance. Obviously, all problems diagnosed should be addressed.

Complete breakdown of the suspensory apparatus

Traumatic rupture of the suspensory apparatus during racing or training is uncommon in Europe but relatively common in racehorses in the US. It is often **catastrophic** since extreme hyperextension of the metacarpophalangeal joint ensues, with potential disruption of the blood supply to the distal limb.

Loss of the suspensory apparatus can occur with fracture of the proximal sesamoids, disruption of the body or branches of the suspensory ligament, rupture of the distal sesamoidean ligaments, metacarpal fracture, rupture of the intersesamoidean ligament or with a combination of those injuries. Traumatic disruption of the suspensory apparatus is also seen in **young foals**

Box 15.8 Extracorporeal shock wave therapy

- Acoustic pressure waves with peak pressures of 10–100 MPa
- Rapid pressure rise times of 30–120 ns
- Variable pulse frequencies
- Dose-dependent effects on bone and soft tissues
  - Analgesia
  - Hemorrhage and hematoma formation
  - Increased regional blood flow
  - Microfracture of cortical bone
  - Stimulation of osteogenesis
- **Radial** shock waves expose broad areas of tissue
  - Low peak pressures and shallow depth of penetration
- Radial shock waves generated:
  - **Pneumatically**
- **Focused** shock waves converge on a target point guided by ultrasound or radiography
  - High peak pressures and greater depth of penetration
- Focused shock waves generated:
  - **Electrohydraulically**
  - **Piezoelectrically**
  - **Electromagnetically**
- Exact mechanisms of action are unknown
- Various treatment protocols are used ranging from one to three treatments at 3–14 day intervals
- Equine conditions treated with shock wave therapy include:
  - Proximal suspensory desmitis
  - Superficial digital flexor tendinitis
  - Osteoarthritis of distal tarsal joints and interphalangeal joints
  - Stress fractures
  - Bucked shins and dorsal cortical stress fractures of the metacarpus
  - Navicular syndrome.

running out in pasture, and this is usually associated with fracture of both sesamoids.

Immediate emergency treatment is essential to prevent vascular trauma by maintaining the metacarpophalangeal joint in flexion. This may be achieved by application of a specially designed commercially available splint (**Kimzey Leg Saver Splint**) or by attaching a wood splint to the sole of the foot and strapping this to the palmar aspect of the metacarpus.

The prognosis for athletic function is grave. However, if the blood supply and skin are intact, some horses are salvaged for breeding, usually by performing a metacarpophalangeal joint arthrodesis. Conservative management with long-term splinting has also been used successfully.

Degenerative suspensory ligament desmitis or atraumatic degeneration and breakdown of the suspensory ligaments associated with hyperextension of the fetlock joints is a progressive degenerative syndrome recognized in

horses that have intense workloads as well as in older broodmares. This syndrome also occurs spontaneously in certain breeds (**Peruvian Paso**, **Andalusian**). The hindlimbs are most commonly affected, and it is usually bilateral (can be quadrilateral) and unresponsive to treatment, although shoeing the horse with flat shoes with long heel extensions can provide some support for the fetlock. Horses may only appear stiff initially, but lameness can become quite severe.

The etiopathogenesis of this problem is unclear, but there is no sex, age or work-related predisposition in Peruvian Pasos. In that breed, the degenerative changes and progressive enlargement are typically most severe in the branches, and the disorder often involves all four limbs. A genetic component has not been confirmed, but the etiology of this condition may be different in Peruvian Pasos than that in older horses with a history of heavy exertion.

Distal sesamoidean ligament desmitis

There are three distal sesamoidean ligaments, the paired **deep** or **cruciate**, the paired **middle** or **oblique** and the **superficial** or **straight**. With the advent of improved ultrasonographic equipment and expertise, injury to these structures has been recognized as an important source of lameness problems in performance horses. Ultrasonographic evaluation of the soft tissue structures over the palmar/plantar pastern is quite complex, and results should be interpreted with appropriate reference to normal anatomy and common artifacts. MRI can also be valuable in identifying these injuries. These ligament injuries should be differentiated from tendinitis (*q.v.*) of the medial and lateral branches of the SDFT in the pastern region.

There is usually some degree of lameness and associated enlargement of the palmar aspect of the pastern, and some horses will have digital sheath effusion. The lameness should improve following an abaxial sesamoid nerve block. Many horses will also improve with a palmar digital nerve block, presumably due to diffusion. It is usually not possible to determine which structure is involved with palpation alone.

Treatment involves a **prolonged period of rest** and rehabilitation (with corrective trimming and shoeing as appropriate). The incidence of re-injury is relatively high.

Injury to the middle distal sesamoidean ligaments is the most common, and tends to be associated with moderate to severe lameness. Enthesopathy at the site of insertion on the palmar aspect of the proximal phalanx is a common incidental radiographic abnormality. Desmitis of the straight distal sesamoidean ligament is an unusual cause of lameness, and usually involves the forelimbs when it occurs.

MISCELLANEOUS TENDON AND LIGAMENT INJURIES

Gastrocnemius tendinitis

The gastrocnemius tendon lies caudal to the SDFT in the mid-tibial region and then passes laterally and cranially to insert on the calcaneal tuber beneath the SDFT. The **intertendinous calcaneal bursa** is interposed between the tendons

of the SDFT and the gastrocnemius, while the **subtendinous calcaneal bursa** (or gastrocnemius bursa) is located deep to the gastrocnemius tendon near its insertion. The proximal part of the gastrocnemius tendon contains some muscular tissue and has an irregular echogenicity but, when it has assumed a position dorsal to the SDFT, has a more uniform echogenicity. Tendinitis of the gastrocnemius is unusual, but should be included among differentials for upper hindlimb lameness.

Clinical signs

With tendinitis there is usually slight to moderate enlargement in the region of the **Achilles tendon** (which includes the gastrocnemius and soleus tendons), with or without localized heat. It is usually difficult to elicit pain by palpation, and lameness varies from mild to severe. There can be associated distension of the calcaneal bursa/bursae, with or without a capped hock appearance.

Diagnosis

Lameness is usually improved by perineural analgesia of the tibial nerve (although this may reflect local diffusion of local anesthetic). Diagnosis is confirmed ultrasonographically.

Treatment

Mild cases may respond adequately to conservative treatment of box rest and controlled walking exercise for 3–6 mo but moderate to severe lesions carry a guarded prognosis for return to full athletic function. Ultrasonographic abnormalities of the tendon usually persist.

Biceps brachii tendinitis

The proximal tendon of biceps brachii attaches to the supraglenoid tubercle of the scapula and passes over the intertubercular groove of the humerus enclosed within the intertubercular (bicipital) bursa. At the level of the humeral tubercles the tendon has distinct lateral and medial lobes that are connected by an isthmus, and the tendon is partially cartilaginous.

Tendinitis of the biceps brachii from an **athletic injury** occurs most often in racehorses and results in acute onset lameness of variable severity. The tendon can also be injured traumatically. There may be focal pain induced by firm pressure applied over the region of the tendon and intertubercular bursa, or pain induced by manipulation of the upper forelimb, especially retraction. Lameness is **characteristically improved** by analgesia of the intertubercular bursa (*q.v.*).

Diagnosis is confirmed with ultrasound, although radiographs are warranted to rule out an underlying bony injury. Mild injuries may be difficult to identify since the curvature of the normal tendon creates artifacts, and images should be interpreted cautiously. The medial and lateral lobes of the biceps brachii tendon should each be evaluated. Biceps tendinitis should be differentiated from injury to the infraspinatus tendon and/or bursa (*q.v.*).

Treatment consists of box rest and controlled exercise for 3–6 mo. Intrasynovial injection of hyaluronan and/or corticosteroids can reduce the synovitis. Endoscopic as well as open surgical evaluation of the intertubercular bursa and underlying bone has also been described. Serial ultrasonographic examination may be useful to monitor healing. The prognosis for return to athletic function is guarded.

Luxation of the superficial digital flexor tendon

The SDFT of the hindlimb becomes flattened and wider as it passes over the tuber calcaneus, and it is held in position by strong medial and lateral fascial attachments. **Luxation or dislocation** of the SDFT from the point of the hock is an uncommon injury, but it can occur with racing, strenuous exertion (i.e. endurance) or trauma. The luxation is usually lateral.

Clinical signs

Displacement of the SDFT is usually a **sudden onset** injury; the SDFT slips off the tuber calcaneus and lies laterally, or less frequently, medially. It can remain mobile and slip on and off the tuber calcaneus. The unstable position of the SDFT in the acute state often results in lameness and **considerable apprehension**, and the horse may appear very distressed.

Usually considerable swelling develops within the initial 24–48 h, and this makes accurate palpation of the tendon increasingly difficult. However, if NSAIDs are used to control the development of swelling, the tendon may remain **more mobile** and cause more distress. Ultrasound can be used to determine the extent of soft tissue injury, while radiographs are recommended to rule out bone involvement. In some cases the tendon is only subluxated and unstable, and those horses have a better prognosis for future soundness.

Treatment

Although replacement of the SDFT and surgical stabilization has been attempted using various techniques, the results are often disappointing and generally require long-term cast immobilization. With conservative treatment (stall rest) pain-related lameness usually resolves, although the horse may be left with a mechanical gait abnormality. This does not necessarily significantly impair jumping ability.

Plantar ligament desmitis (curb)

The plantar ligament originates at the top of the tuber calcis, runs down the plantar aspect of the calcaneus and inserts on the distal tuber calcis, the plantar aspect of the fourth tarsal bone and fourth metatarsal bone and the plantar fascia. **Curb** is associated with thickening of the plantar distal aspect of the tarsus. However, it is important to confirm what structures are involved in horses that have thickening in this location (or a so-called "**curby**" appearance) as many conditions can mimic curb. In fact, the term **curb** is often used more generally to describe a whole collection of plantar tarsal soft tissue injuries including SDFT tendinitis, injury to the peritendinous/periligamentous tissues, and long plantar ligament desmitis.

Clinical signs

Racing Standardbreds are the most commonly affected, and poor hindlimb conformation, especially a **sickle hock conformation**, may predispose to ligament injury. There is usually localized heat and swelling and pain on palpation. Lameness is often absent, but if present is usually mild.

Diagnosis

Initial diagnosis is based on clinical signs but care should be taken to differentiate the swelling from a prominent base of the **fourth metatarsal bone** or from synovial effusions. Ultrasonography is necessary to differentiate a curb involving the plantar ligament from **subcutaneous edema, peritendinous/periligamentous inflammation** or **SDFT tendinitis**, and radiographs can be used to identify horses with **tarsal collapse**, which can also produce a curby appearance.

Horses with "curb" or swelling over the plantar aspect of the fibular tarsal bone are actually more likely to have swelling and injury of peritendinous and periligamentous tissue and/or SDFT tendinitis than an injury of the plantar ligament.

Treatment

Treatment for plantar ligament desmitis typically involves rest, or moderation of the exercise program, and local application of cold and topical anti-inflammatory agents such as DMSO. Rarely is there recurrent lameness, but some swelling may persist. With peritendinous/periligamentous inflammation, local treatment with corticosteroids and Sarapin (an extract of the pitcher plant) may be effective. Substantial SDFT injuries will require longer rehabilitation and ultrasound monitoring before return to work.

Supraspinous ligament desmopathy

The supraspinous ligament caudal to the withers region consists of a strong cord of white fibrous tissue attached to the summits of the dorsal spinous processes. Sprain of the supraspinous ligament causes **acute onset back pain** often associated with localized thickening and sensitivity to palpation, and results in a restricted gait. Tearing of the attachment can result in linear radiopacities proximal to the summits of one or more dorsal spinous processes. In association the horse may develop some atrophy of the longissimus dorsi muscles. Focal hypoechoic areas may be detected in the ligament using diagnostic ultrasonography.

Treatment is a prolonged period (3–6 mo) of rest; ultrasound therapy may be beneficial in the acute stages. Prognosis is usually fair to good.

DISEASES AND INJURIES OF ARTICULAR SOFT TISSUE STRUCTURES

Intercarpal ligament desmitis

Small ligaments cross the dorsal aspects of both the proximal and distal rows of carpal bones, attaching to each bone. Pulling or tearing of the attachments

results in periosteal new bone formation or **enthesopathy**. This is rarely associated with clinical signs, since the new bone is far removed from the joint margins. However, the development of enthesopathy probably reflects mild instability of the carpus that may predispose to osteoarthritis. Enthesopathy should be differentiated from periarticular osteophyte formation (*q.v.*). If enthesopathy is detected radiographically the radiographs should be examined carefully for modeling of the articular margins.

Several palmar carpal ligaments connect the proximal and distal rows of carpal bones on the palmar aspect of the joint. A large **medial palmar intercarpal ligament** attaches the radial carpal bone to the second and third carpal bones, and a lateral ligament joins the ulnar to the third and fourth carpal bones. **Desmitis** of one (or both) of these ligaments is associated with moderate to severe lameness and/or effusion of the middle carpal joint. Lameness is usually improved following IA analgesia.

Diagnosis is made by arthroscopic evaluation of the joint. The entire joint should be assessed for concurrent damage. The injury occurs most commonly in racehorses but has been seen in other performance categories.

Treatment involves rest and rehabilitation, although the prognosis for return to full athletic function without recurrent injury is guarded.

Collateral ligament injury

Most diarthrodial joints are supported medially and laterally by collateral ligaments. Sprain of a collateral ligament can occur within the body of the ligament and/or at the site(s) of bony attachment. Injuries to the collateral ligaments are most commonly recognized in the femorotibial, tarsocrural, distal interphalangeal and metacarpo/metatarso-phalangeal joints, and include desmitis, insertional desmopathy, avulsion fractures and rupture.

There is usually an **acute onset of lameness**, the degree being proportional to the severity of the injury. **Desmitis** (*q.v.*) may result in localized soft tissue swelling, heat and focal pain, with pain on passive manipulation of the joint (especially rotation).

Lameness is usually not immediately improved following IA analgesia of the joint (unless there are concurrent IA lesions), but is improved by local perineural analgesia or by local infiltration. In a suspected case of collateral ligament desmitis an **ultrasonographic** evaluation should be performed. **Radiography** should be performed to exclude other concurrent damage, and "stressed views", in which medial to lateral force is applied to the joint during image acquisition, can confirm joint instability and ligament damage. Secondary insertional desmopathy may not become radiographically apparent until 2–3 wk after the onset of lameness. If lameness is severe the axial stability of the joint should be assessed carefully, and stressed radiographs obtained, in order to assess better the integrity of the collateral ligament and the possibility of subluxation of the joint.

In some cases no clinical signs referable to the collateral region can be detected clinically but **nuclear scintigraphy** subsequently indicates increased bone activity or blood supply at the site of collateral ligament attachment. Several weeks later, new bone formation may be apparent.

Treatment is prolonged (many months) rest, preferably stall rest combined with controlled exercise. If there is discernible joint instability with

a metacarpophalangeal joint collateral injury, some external support may be required. **Rupture of the collateral ligament** can be treated conservatively by immobilization of the limb in either a Robert-Jones bandage or a cast, or with surgical implantation of an implant.

Avulsion fractures occur most commonly in the metatarsophalangeal and metacarpophalangeal joints with displacement of a fragment from one or more of the plantar (palmar) processes of the proximal phalanx. If the fragment is displaced or a significant proportion of articular surface is involved, it should either be removed (if small) or stabilized by internal fixation (if large). Prognosis depends on the degree of articular damage and of damage to the collateral ligaments. Fracture of the lateral malleolus of the distal tibia can also occur due to an avulsion fracture of the lateral collateral ligament of the tarsocrural joint. Treatment usually involves surgical removal of the fragment or conservative management. The prognosis is good.

Cruciate ligament injury

The cranial cruciate ligament attaches to the lateral wall of the intercondylar fossa of the femur and to the tibia just cranial to the intercondylar eminence. The caudal cruciate ligament lies medially and attaches to the cranial part of the intercondylar fossa of the femur and to the region of the popliteal notch of the caudal tibia. Both structures are extrasynovial, not within the femorotibial joints, but between the synovial sacs of the medial and lateral compartments. Associated pain may not be alleviated with IA analgesia of either compartment but it is often improved.

Cranial cruciate ligament damage is recognized far more frequently than caudal cruciate ligament damage. Other structures, including the menisci, collateral ligaments and articular cartilage, are often damaged in horses with cruciate injuries.

Lameness is usually sudden in onset and relatively severe, although it can be insidious in onset and less severe. There may be palpable distension of the medial femorotibial, lateral femorotibial or femoropatellar joint capsule. Flexion of the stifle is usually resented; the horse may avoid flexion by exaggerated lifting of the limb. Manipulation of the stifle usually accentuates lameness. Lameness may be improved by IA analgesia of the medial and/or lateral compartments of the femorotibial joint. A drawer sign cannot usually be elicited in the conscious horse.

Ultrasonographic evaluation of these ligaments is extremely difficult. Radiographic abnormalities associated with cranial cruciate ligament injury include remodeling of the tibia, avulsion fracture of the intercondylar eminence and cranial displacement of the tibia. However, many horses will have no radiographic abnormalities. In chronic cases, there may be evidence of **secondary osteoarthritis**, as well as remodeling of the intercondylar fossa of the femur. Nuclear scintigraphy can reveal increased bone activity at one of the attachment sites. A definitive diagnosis is made with arthroscopic evaluation. The cranial cruciate ligament is most easily assessed from the lateral femorotibial joint, while the caudal cruciate ligament is best viewed through cranial and caudal approaches to the medial femorotibial joint. The prognosis for athletic function is guarded.

Meniscal injury

The crescent-shaped medial and lateral menisci are composed of fibrocartilage, and are interposed between the femur and tibia. They are stabilized by substantial cranial and caudal meniscal ligaments.

Lameness associated with **meniscal injury** can be sudden or gradual in onset and is usually moderate to severe when recognized. There may be distension of the femorotibial joint capsule and pain on manipulation of the joint. Lameness is usually substantially improved by IA analgesia of either the lateral femorotibial joint (lateral meniscus) or the medial femorotibial joint (medial meniscus).

Care must be taken in interpreting radiographs since apparent narrowing of one side of the femorotibial joint space can be a positional effect. Occasionally there is **sclerosis** of the subchondral bone of the tibial plateau of the affected side and infrequently mineralization of the affected meniscus. In long-standing cases there may be radiographic evidence of secondary osteoarthritis.

Ultrasound is very effective in evaluating the menisci, and should be recommended routinely. Diagnosis can often be confirmed with arthroscopic evaluation of the meniscus and the meniscal ligaments. The cranial meniscal ligaments are visible with cranial approaches to the joints; however, only the cranial and caudal poles of the menisci themselves can be viewed arthroscopically, and some pathology will be missed. Tears should be debrided when indicated. Damage to the meniscus or cranial meniscal ligament appears to warrant a guarded prognosis for return to athletic function.

Patellar ligament injury

The medial, middle and lateral patellar ligaments attach to the patella and the tibial tuberosity/crest and are effectively the tendons of insertion of quadriceps femoris and biceps femoris. Injury to one or more ligaments usually results in acute onset mild to moderate lameness, pain on pressure applied over the affected ligament and pain on manipulation of the stifle. Intra-articular anesthesia may not improve the lameness but local infiltration of anesthetic often will. Diagnosis can be confirmed with ultrasound. Treatment consists of rest with rehabilitation, and the prognosis is usually good.

Impar ligament desmitis

The **distal sesamoidean impar ligament** attaches to the distal border of the navicular bone and to the flexor surface of the distal phalanx. Injury to this ligament can be difficult to differentiate clinically. Associated lameness is likely to be improved by perineural analgesia of the palmar digital nerves or intrasynovial analgesia of the navicular bursa. Ultrasound images obtained through the frog following meticulous flattening of the surface with a hoof knife as well as **soaking** the foot overnight, can detect impar ligament injuries, adhesions and/or bursal distension. However, the optimal imaging technique to detect impar desmitis is probably MRI.

Discrete osseous or mineralized opacities distal to the distal border of the navicular bone are often identified radiographically. These may represent an

avulsion fracture from the distal border of the navicular bone, mineralization of a hematoma in the impar ligament or dystrophic mineralization within the ligament (*q.v.*). The clinical significance of these changes is unclear, however they are seen with higher incidence in horses with navicular syndrome (*q.v.*).

Intersesamoidean ligament injury

The intersesamoidean ligament (also referred to as the **palmar/plantar ligament of the fetlock**) attaches to the palmar and axial surfaces of the medial and lateral proximal sesamoid bones, and the flexor tendons glide across this surface. With fetlock extension the intersesamoidean ligament is under significant tension and compression as the suspensory apparatus restricts dorsiflexion.

Injuries to this ligament, including desmitis and enthesitis, have been recognized and associated with lameness. Horses can develop areas of bone lysis along the axial insertion sites of the intersesamoidean ligament with enthesitis, or avulsion fractures may be detected. Lameness is generally moderate. Severe injuries, including rupture and abaxial displacement of the proximal sesamoids, can also develop and can occur in association with complete breakdown injuries. Infectious desmitis and osteomyelitis can develop with puncture wounds or hematogenous inoculation (*q.v.*).

Lameness should be improved by **perineural analgesia** (*q.v.*) of the palmar (at mid-metacarpal level) and palmar metacarpal nerves. Intra-articular analgesia of the metacarpophalangeal joint and digital sheath will frequently improve but not eliminate the lameness. Diagnosis is usually based on diagnostic ultrasonography and radiography, although lesions have also been diagnosed via tenoscopy of the digital sheath or localized with scintigraphy. With insertional damage there may be radiographic evidence of radiolucency on the axial surface of the proximal sesamoid. The collateral ligaments of the proximal sesamoid bones can also be injured.

TENDON LACERATIONS AND RUPTURES

Suspensory apparatus lacerations

Clinical signs associated with tendon lacerations depend on what tendon is involved and whether the tendon is partially or fully transected. **Transection** of the SDFT typically results in **sinking of the fetlock** while transection of the DDFT allows the **toe to turn up**.

Tendon healing is compromised by a poor blood supply, concurrent contamination, and the biomechanical forces that create a gap between the lacerated tendon ends regardless of the repair technique utilized.

For a successful outcome, **radical aggressive treatment** is required. The wound must be thoroughly cleaned and debrided and the nature of the tendon injury assessed. The site of the lesion (metacarpus/metatarsus or pastern), the condition of the ends of the tendon and the degree of contamination will influence to some extent what method of repair is instituted.

Alternatives include attempts to repair the tendon with **specialized suture patterns** (e.g. locking-loop and 3-loop-pulley) using monofilament nylon,

polypropylene or polydioxanone; gap healing with multifilament scaffolds such as Dacron or carbon fiber; cast immobilization; splint immobilization or fitting raised and elongated heel shoes. Newer techniques, including semicylindrical biodegradable plates sutured to the transected tendon, are being investigated and appear to be significantly stronger than sutured tenorrhaphies. Frequently a combination of these different techniques is employed.

Prognosis depends on the tendon (or tendons) involved (extensor tendons have a much better prognosis than flexor tendons), the site of the injury (injuries entering tendon sheaths have a much more guarded prognosis), the degree of contamination, and whether a forelimb or hindlimb is affected. Prognosis for salvage for breeding is good; prognosis for return to full athletic function is more guarded. Repair of flexor tendon lacerations has a reported success rate of 11–18% for return to athletic function. There are no repair methods that provide adequate tensile strength for primary tendon healing.

Superficial digital flexor tendon rupture

Complete rupture of the SDFT is relatively uncommon. It occurs more often in forelimbs than hindlimbs and results in sinking of the fetlock.

Treatment requires **elevation of the heel** to bring the ends into apposition, application of a splint or cast for up to 3 mo and a prolonged period (often 12 mo) of rest. Implants such as carbon fiber or Dacron to provide a multifilament scaffold have been reported to enhance the speed and quality of repair, but they also dramatically increase the risk of infection. The prognosis for athletic function is poor but the horse may be salvaged for breeding.

Deep digital flexor tendon rupture

Rupture of the DDFT is uncommon and usually occurs as a sequel to previous palmar digital neurectomy (*q.v.*). Rupture is probably predisposed by preexisting tendon damage, adhesions and bone remodeling. Rupture rarely occurs with advanced navicular degenerative changes when a neurectomy has not been performed. Once the tendon ruptures there is swelling on the palmar aspect of the pastern and lameness is generally severe. The foot is placed on the ground heel first, and the toe flips up with weight bearing.

The prognosis is hopeless for return to athletic function. Immobilization of the distal limb for 8–12 wk may allow sufficient healing to take place to salvage the horse for breeding, but most cases will require humane euthanasia.

Common digital extensor tendon rupture

Rupture of the common digital extensor tendon occurs in **young foals** and can be **congenital** or **acquired**. The etiology is poor understood, but there may be a heritable component. It results in a characteristic soft tissue swelling in the associated tendon sheath on the dorsolateral surface of the carpus, often occurs bilaterally, and is frequently seen in foals with **flexural deformities** of the carpus or fetlock. The ends of the tendon can usually be identified on palpation, and can also be seen with ultrasound. Foals are often able to stand normally or may appear bowlegged, but **knuckle forward** at the fetlock as they

walk. The intact lateral digital extensor tendon often allows them to move normally at slow speeds, but the gait deficit becomes more noticeable as they move quickly.

Treatment for this condition is **conservative**, and surgery to repair the tendon is not necessary. The use of bandages to reduce swelling and support the carpus is recommended and **stall confinement** is advised. A well-padded splint can prevent knuckling, but should be changed regularly and removed periodically to prevent tendon laxity. The prognosis is excellent. Associated flexural deformities may require more aggressive management and carry a more guarded prognosis.

Extensor carpi radialis tendon rupture

Rupture of the extensor carpi radialis tendon also usually occurs in **young foals** and can be congenital or traumatic. It results in soft tissue swelling on the dorsal proximal aspect of the carpus. The ends of the tendon can usually be identified on palpation, and can also be seen with ultrasound. Mild lameness may be observed.

Treatment is conservative with stall confinement for 6–8 wk and the prognosis is excellent. Although immobilization of the limb using a **Robert Jones bandage** (*q.v.*) or a cast may facilitate repair, flexor tendon laxity is likely to develop.

Gastrocnemius rupture

Rupture of the gastrocnemius, with or without rupture of the SDFT (the combination is referred to as the **Achilles tendon**), is a rare injury resulting in severe lameness and an inability to extend the hock. This condition also occurs in foals with flexural deformities or following overexertion. With complete rupture the hock is dropped even at rest, and as the horse attempts to weight bear the hock drops further while the stifle extends (loss of reciprocal apparatus).

If the entire Achilles tendon is lost, the horse cannot support weight on the limb. There is localized soft tissue swelling proximal to the hock and/or lateral to the stifle. With **partial rupture** the signs are more subtle with moderate lameness and an exaggerated hock drop. With **complete rupture** the prognosis for athletic function is very poor and the prognosis for survival is guarded.

Most surgical treatments to salvage the horse for breeding have failed, but some horses have been managed successfully with full limb support. Partial rupture should be managed with protracted stall rest.

TENDON SHEATHS

Digital flexor tendon sheath tenosynovitis

The digital flexor tendon sheath extends from the junction of the third and fourth quarters of the metacarpus (or metatarsus) to the distal pastern and encloses the SDFT and DDFT.

Mild distension of the tendon sheath, proximal to the metacarpophalangeal (metatarsophalangeal) joint, and sometimes distally as well, is a

common incidental finding, particularly in the hindlimbs. Such non-articular "**windpuffs**" or "**windgalls**" may fluctuate according to the amount of work the horse is doing, the hardness of the ground and the environmental temperature. Bandaging the horse while it is stabled may control their size.

Enlargement of the tendon sheath may also be due to thickening of the sheath wall which can result in a firm nodular swelling at the proximal reflection of the sheath wall, or in a somewhat loculated appearance to the enlarged sheath, and a slight notch at the level of the palmar (plantar) annular ligament. The latter two features occur more commonly in hindlimbs than in forelimbs.

Sudden onset of distension of a digital flexor tendon sheath associated with heat, pain on flexion of the fetlock and moderate to severe lameness can be due to tenosynovitis. Diagnostic ultrasonography should be performed to exclude the possibility of concurrent tendon pathology. Unfortunately, some longitudinal tendon defects may not be detected with ultrasound.

Most cases respond relatively rapidly to **local application** of cold pressure bandaging and systemic NSAIDs. Topically applied DMSO and IV hyaluronan therapy (*q.v.*) may also be beneficial. If lameness persists, **intrathecal** injection of a corticosteroid and/or sodium hyaluronan should be considered. The prognosis for acute cases is good provided that the injury is solely due to tenosynovitis and does not involve structural damage of the sheath wall or damage to supporting structures. When other structures are involved, healing can result in **intrathecal adhesion formation**, peritendon sheath fibrosis and/or effective constriction by the palmar (plantar) annular ligament (**complex tenosynovitis**). Intrathecal adhesion formation can be diagnosed either by ultrasonography or radiographic contrast studies and may necessitate surgical treatment.

Treatment of chronic cases of tenosynovitis can be challenging. Initial management usually involves drainage of fluid and intrathecal injection of hyaluronan and corticosteroids. Horses that do not respond or that have ultrasonographic evidence of complex tenosynovitis are surgical candidates. A tenoscopic approach is typically recommended as this allows diagnostic evaluation, as well as annular ligament desmotomy when indicated, and resection of granulation tissue masses and adhesions.

Palmar/plantar annular ligament syndrome (annular ligament constriction, stenosing palmar ligament desmitis)

The palmar annular ligament passes around the palmar aspect of the digital flexor tendon sheath. It is contiguous with it on the most palmar aspect of the limb, and attaches to the proximal sesamoid bones.

Overextension of the metacarpophalangeal joint can result in overstretching of the ligament and associated annular ligament **desmitis** (*q.v.*) with thickening.

Similarly, **distension** of the digital flexor tendon sheath and/or tendinitis and **tendon swelling** within the sheath can result in effective constriction by the relatively inelastic palmar annular ligament creating a notch on the palmar aspect of the limb, often best assessed when the limb is clipped. Slight notching can also be an incidental finding of no current clinical significance.

Clinical signs

Lameness associated with constriction by the palmar annular ligament may be insidious or acute in onset and varies from mild to severe. Often these patients have a history of **persistent lameness** that does not respond effectively to rest. Lameness is usually improved, but rarely alleviated, by intrathecal analgesia; perineural analgesia of the palmar and palmar metacarpal nerves is usually required to eliminate the lameness.

Diagnosis

Diagnostic ultrasonography is useful to assess the size of the ligament and its structural integrity, the thickness of the sheath wall and associated fibrosis, the presence of intrathecal adhesions and the presence of associated tendon pathology. The latter warrants a guarded prognosis. Adhesions have also been identified using radiographic contrast, but that technique has largely been replaced by ultrasound.

Treatment

In the absence of adhesions, **closed palmar annular ligament desmotomy** may result in resolution of lameness, but in most cases breakdown of adhesions is required. This can be performed tenoscopically or with an open incision into the sheath.

Prognosis is fair to guarded. Postoperative administration of intrathecal and IV hyaluronan (*q.v.*) may help to reduce reformation of adhesions. Deep digital flexor tendinitis (*q.v.*) occasionally occurs following constriction by the palmar annular ligament and carries with it a guarded prognosis for return to full athletic function.

Tarsal sheath distension (thoroughpin)

The tarsal sheath extends from approximately 7 cm proximal to the medial malleolus of the tibia distally to about the proximal third of the metatarsus, and surrounds the DDFT (or more correctly the lateral digital flexor tendon). It lies in close apposition to the sustentaculum tali of the calcaneus. Enlargement of the tarsal sheath is colloquially referred to as **thoroughpin** (*q.v.*).

Clinical presentation

Distension is visible in the distal caudal crus. The filling extends laterally proximal to the tuber calcaneus between the common calcaneal tendon and the tibia, and tends to be somewhat less prominent medially. Occasionally swelling extends further distally and is detected medial to the DDFT in the proximal metatarsal region. Mild distension may be seen without other associated clinical signs. The swelling must be differentiated from the caudal outpouching of the tarsocrural joint capsule and from distension of the intertendinous calcaneal bursa. Some horses develop an acquired or adventitious bursa between the DDFT and the Achilles tendon, and this can be difficult to differentiate clinically from true distension of the tarsal sheath without ultrasound or contrast radiography.

Chronic distension without associated lameness or obvious significant pathology is quite common and does not require treatment, but these cases must be distinguished from other causes of tenosynovitis that do cause lameness, including trauma, DDFT injury and infectious tenosynovitis (*q.v.*).

Diagnosis

Sudden onset lameness can coincide with **acute distension of the tarsal sheath** either symmetrically due to tenosynovitis or hemorrhage or asymmetrically associated with partial rupture of the sheath wall. Occasionally there is associated DDFT tendinitis (*q.v.*).

Diagnostic ultrasonography and contrast radiography help to elucidate which structure is involved and should be used to evaluate the integrity of the DDFT and sheath wall. Contrast radiography can also be useful. Standard radiographs including dorsomedial–plantarolateral oblique and flexed plantaroproximal–plantarodistal views of the calcaneus should routinely be obtained, particularly to assess the sustentaculum tali. Proliferative bone production and dystrophic mineralization of the sustentaculum tali are poor prognostic indicators.

Treatment

Sudden onset tenosynovitis is treated conservatively with stall rest, topical DMSO and NSAIDs, with or without intrathecal short-acting corticosteroids. More chronic cases and acquired adventitious bursae may require surgical intervention, but the prognosis in those cases is guarded. Tenoscopy may be useful to assess damage, treat infection, and facilitate treatment of lesions on the sustentaculum tali.

Carpal sheath distension

The carpal synovial sheath surrounds the DDFT and SDFT within the carpal canal and extends from approximately 10 cm proximal to the carpus to the proximal third of the metacarpus. The carpal canal encloses the sheath and is formed dorsally by the palmar ligament of the carpus, medially by the accessory ligament of the SDFT, laterally by the accessory carpal bone and associated ligaments, and palmarly by the flexor retinaculum, palmar metacarpal fascia and caudal antebrachial fascia.

Clinical signs

The distended sheath protrudes laterally along the distal antebrachium and both medially and laterally between the DDFT and the check ligament. Distension of the carpal sheath develops due to tearing of the accessory ligament of the SDFT, idiopathic synovitis, proximal tendinitis of the DDFT or SDFT, tearing of the flexor tendons at their myotendinous junctions, infection, trauma with intrathecal hemorrhage, fracture of the accessory carpal bone, exostosis of the caudal perimeter of the radial physis, or due to an osteochondroma on the caudal aspect of the radius.

Lameness is variable depending on the initiating cause and severity of the distension. Horses with **intrathecal hemorrhage** can show a very severe

lameness. Passive flexion of the carpus usually produces a painful response and can accentuate the lameness. Lameness is generally improved following intrathecal analgesia.

Diagnosis

Ultrasonographic, radiographic and endoscopic examinations help to determine if there is underlying pathology that will influence treatment and prognosis. Radiographs should be evaluated for evidence of exostoses of the caudal perimeter of the radial physis, or so-called "**physeal remnant spikes**".

Treatment

If no primary lesion can be identified then administration of short-acting corticosteroid and hyaluronan into the sheath, controlled hand walking for 4–6 wk, and **cryotherapy** is the treatment of choice. Prognosis is fair. Corticosteroids should not be used if a tendon lesion is identified, and tendon involvement warrants a more guarded prognosis.

Osteochondromas (*q.v.*) and radial exostoses are removed surgically, often using a tenoscopic approach, and prognosis is good. Distension of the carpal sheath secondary to an accessory carpal bone fracture (*q.v.*) may require transection of the palmar carpal retinaculum in order to relieve compression of the soft tissue structures in the canal.

With increasing use of endoscopic evaluation of the carpal sheath, exostoses of the caudal perimeter of the radial physis have been increasingly recognized as a cause of tenosynovitis and lameness. Lesions that penetrate the carpal synovial sheath and impinge on the DDFT can be managed by tenoscopic removal.

Horses with **complex tenosynovitis** involving chronic enlargement of the sheath and/or desmitis of the DDFT or SDFT may benefit from endoscopic evaluation of the sheath, surgical debridement and tenoscopic release of the carpal canal. Division of the carpal flexor retinaculum to decompress the carpal canal should also be performed when osteochondromas are removed, or if there is evidence of chronic flexor tendon compression in the canal.

Extensor carpi radialis, common digital extensor and lateral digital extensor tenosynovitis

The **tendon sheath** of the extensor carpi radialis starts approximately 10 cm proximal to the carpus and extends to the middle of the carpus. It is traversed by a dorsal annular ligament and extensor carpi obliquus. The tendon sheath of the common digital extensor begins approximately 8 cm proximal to the carpus and ends at the proximal metacarpus, and is crossed by two dorsal annular ligaments. The tendon sheath of the lateral digital extensor tendon starts approximately 8 cm proximal to the carpus and extends to the proximal metacarpus. It is traversed by an annular ligament.

Direct trauma (e.g. hitting a fence) is a common cause of tenosynovitis (*q.v.*), and the more dorsal tendon sheaths of extensor carpi radialis and the common digital extensor tendon are more commonly affected. Idiopathic and infectious tenosynovitis also occurs regularly.

Clinical signs

Tenosynovitis results in a **longitudinal soft swelling** that may be subdivided by the annular ligaments. The swelling should be differentiated from other soft tissue swellings including an acquired or false bursa, distension of the antebrachiocarpal or middle carpal joint capsules, joint capsule damage with secondary synovial membrane herniation, or diffuse soft tissue swelling. Ultrasound may be required to make this differentiation. The enclosed tendon may or may not be enlarged. Usually there is no associated lameness unless the distension is extreme or the result of septic tenosynovitis (*q.v.*).

Diagnosis

Additional information may be obtained from ultrasonographic evaluation. Usually this is a cosmetic rather than a functional problem.

Treatment

In most cases of idiopathic tendon sheath effusion treatment is unnecessary except for cosmetic reasons. With traumatic injury, topical DMSO and cold therapy may be beneficial in the acute stage. Intrasynovial corticosteroids, hyaluronan and/or atropine may be helpful in the absence of any concurrent tendinous pathology.

Occasionally, following a severe injury, there may be considerable synovial proliferation and adhesion formation requiring surgical intervention. Sepsis requires aggressive medical and surgical treatment.

Tendon sheath infections

Infection of a tendon sheath can occur as a result of a penetrating injury or hematogenous spread of infection; in some cases the etiology is unknown. Infection typically results in a sudden onset of severe lameness, associated with distension of the involved tendon sheath.

Diagnosis is confirmed by synovial fluid analysis using similar tests and interpretation to those used in the diagnosis of septic arthritis (*q.v.*). Specifically, fluid with an elevated total protein (>40 g/L), a leukocytosis ($>20 \times 10^9$ cells/L) and a neutrophilia (80% neutrophils) would be considered virtually pathognomonic for bacterial infection. Gram stain and bacterial culture, including anaerobic samples, should be performed.

Early aggressive therapy is essential but even then the prognosis is guarded. Treatment should include **aggressive lavage** of the sheath, on at least one and often several occasions. Effective lavage to remove bacteria-laden fibrin clots and debris can be performed via incisions in the proximal and distal aspects of the sheath and/or via tenoscopy. **Synovial resection** can be performed simultaneously, and is particularly valuable if the infection has been present for more than 2 or 3 days. Indwelling drains and continuous infusion antibiotic pump systems can be useful but require excellent nursing supervision.

Broad-spectrum systemic antimicrobial medication should be combined with local therapy including direct intrathecal instillation and/or distal limb

perfusion techniques. NSAIDs should be administered. Intrathecal hyaluronan can help to reduce adhesion formation if infection can be eliminated.

Tarsal sheath infections

In addition to the conventional routes of sheath infection outlined previously, **tarsal sheath infections** also develop as a sequel to **osteitis** of the sustentaculum tali or tuber calcanei. Osteitis (*q.v.*) has also been reported to occur secondary to infections of the tarsal sheath. The prognosis in these cases is guarded. Surgical management is warranted and may require endoscopic evaluation and lavage or cutting the thickened tarsal retinaculum to decompress the tarsal canal; even tenectomy/tenotomy of the DDFT has been reported.

BURSAE

Intertubercular (bicipital) bursitis

Due to its embryologic origins and function, the intertubercular bursa is more appropriately considered to be a tendon sheath. It is a large structure that surrounds the tendon of biceps brachii in the region of the intertubercular groove of the humerus, and extends from the level of the supraglenoid tubercle distal to the humeral tubercles. Occasionally there is communication between the tendon sheath and the joint capsule of the scapulohumeral joint, and this should be considered when interpreting responses to intrasynovial anesthesia.

Aseptic synovitis of the intertubercular bursa is comparatively rare (*q.v.*). There is usually pain induced by pressure applied over the bursa, or by retraction of the limb. Lameness is moderate to severe and generally improved following intrasynovial analgesia. The area should be examined ultrasonographically for evidence of concurrent biceps brachii, infraspinatus or supraspinatus tendon pathology. Intralesional corticosteroids and/or hyaluronan can be beneficial.

Mineralization within the intertubercular bursa can occur as a sequel to a fracture of the supraglenoid tubercle, and warrants a guarded prognosis for athletic function.

Septic intertubercular bursitis also occurs, either with or without history of a puncture wound. In foals the bursa can be infected hematogenously. Intertubercular bursal infection should be differentiated from septic infraspinatus bursitis. Aggressive treatment is essential for a successful outcome and should include thorough lavage and/or surgical debridement, systemic and local antimicrobial drugs and NSAIDs as required. Prognosis is guarded.

Calcaneal bursitis (capped hock)

A small subtendinous calcaneal bursa (or gastrocnemius bursa) is interposed between the tuber calcaneus and the insertion of gastrocnemius, and a large intertendinous calcaneal bursa is interposed between the tendons of the SDFT and the gastrocnemius, extending from approximately 10 cm proximal to the

hock to the mid-tarsal level. There is also a subcutaneous bursa over the point of the hock, and with slight repetitive trauma or a single more severe traumatic episode, horses also acquire an **adventitious** or false bursa subcutaneously over the tuber calcanei, resulting in a **capped hock** appearance.

Distension of the bursa interposed between the SDFT and gastrocnemius tendons is often associated with gastrocnemius tendinitis, but can result in a capped appearance to the hock. There is usually associated lameness in those cases.

Diagnosis is based on clinical signs, response to local analgesia and ultrasonographic evaluation. An acquired bursa is usually more localized and is usually only a **cosmetic defect** unassociated with lameness and no treatment is necessary. If the horse repetitively kicks the walls, consideration should be given to padding the walls. Protection of the hocks by **hock guards** may be useful when the horse is traveling.

Infection of any one of the bursal structures over the point of the hock can result in serious complications. Infection is usually caused by a penetrating injury or occurs as a complication of septic osteitis of the tuber calcanei (*q.v.*). Radiographs should be taken to determine bone involvement, and bone infection is associated with a poor prognosis. Aggressive medical and surgical management of the bursal infection is warranted. Endoscopic evaluation and lavage of the intertendinous calcaneal bursa has been reported for management of both infectious and non-infectious bursitis.

Olecranon bursitis (shoe boil, capped elbow)

As the result of repetitive trauma an acquired (false) bursa can develop over the point of the elbow resulting in a semi-firm to fluctuant soft tissue swelling. The bursa under the triceps brachii is not involved. This is usually merely a **cosmetic defect** and does not compromise function unless it becomes infected. It usually results from trauma from a shoe, either when the horse is lying down or when the shoe hits the elbow during exercise, and it is most common in draft breeds and gaited horses.

The use of a "**shoe boil ring/boot**" ("sausage boot") may help to prevent further trauma, and can resolve the problem in acute cases. In some cases draining the accumulated fluid and injecting corticosteroids and/or atropine can improve the cosmetic appearance, but strict asepsis is critical to avoid infection. Irritants including 7% iodine have been injected into the area in an effort to induce fibrosis, but can worsen the problem. Surgical resection has been reported, but is usually unnecessary.

Navicular bursitis

The navicular bursa (or **podotrochlear bursa**) is interposed between the palmar (plantar) aspect of the navicular bone and the dorsal aspect of the DDFT. In some cases lameness associated with caudal-heel syndrome can be alleviated with intrasynovial analgesia of that bursa despite the absence of detectable radiographic or CT abnormalities within the navicular bone. In those cases an isolated navicular bursitis may be the source of the lameness.

Soft-tissue-phase nuclear scintigraphy can support the diagnosis, and an ultrasound examination performed through a meticulously prepared frog may confirm synovitis and bursal distension. However, concurrent DDFT pathology should be excluded via MRI or contrast enhanced CT before this isolated diagnosis can be made definitively. In many cases intrabursal hyaluronan and corticosteroids will alleviate the lameness, although the problem will reoccur in some horses.

Atlantal bursitis (poll evil)

The atlantal bursa lies dorsal to the atlas on the midline between the nuchal ligament and the rectus capitis dorsalis. Occasionally synovial proliferation with or without mineralization has been seen in association with neck pain and/or an abnormal head carriage.

Infection of the bursa, so-called "**poll evil**", is now a rare condition. In the past it was seen, especially in draft breeds, in association with ill-fitting tack. Although any bacterium may be involved, ***Brucella* spp.** (*q.v.*) should always be considered and ruled out due to the risk for zoonotic infection. Treatment of either condition is surgical. Prognosis depends on the chronicity of infection and presence or absence of associated osteomyelitis (*q.v.*).

Supraspinous bursa infection (fistulous withers)

The supraspinous bursa lies dorsal to the dorsal spinous processes of the cranial thoracic vertebrae. Infection of the bursa results in localized swelling and pain. In advanced cases the bursa may rupture producing localized cellulitis and/or infectious osteitis of the dorsal spinous processes.

Determination of ***Brucella abortus*** serum titers and both aerobic and anaerobic bacterial culture should be performed. Radiographs should be taken of the dorsal spinous processes of the thoracic vertebrae. Horses that test seropositive for Brucella (*q.v.*) are more likely to have evidence of vertebral osteomyelitis.

In very early cases local and systemic antimicrobial drugs may be successful; in most advanced cases **surgical intervention** involving radical excision of the affected soft tissue and spinous processes of affected vertebrae will be required. Treatment with **strain 19 Brucella vaccine** and with **clofazimine** has also been reported. Prognosis is fair in lesions treated early, but guarded to poor in advanced cases.

Trochanteric bursitis (whorlbone disease)

The large trochanteric bursa is positioned between the tendon of the accessory head of the middle gluteal muscle and the cranial portion of the greater trochanter. Bursitis is usually diagnosed clinically (particularly in Standardbreds) in horses that respond painfully to pressure over the greater trochanter of the femur. Most horses develop **trochanteric bursitis** during racing or training, but it has also been reported to result from direct trauma. Confirmation of this diagnosis should entail reduced lameness and/or improved comfort following a bursal block as well as ultrasonography. In fact bursitis has

not been well documented since the advent of the routine use of diagnostic ultrasound.

When diagnosed, it is thought to be secondary to another cause of lameness in the lower hindlimb or in the forelimbs that has altered the horse's gait and produced strain on the gluteal muscles. Treatment traditionally involves injecting the soft tissues around the area with an iodine counterirritant. Alternatively, Sarapin and/or corticosteroids have been injected into and around the bursa. Rest and NSAID therapy are also appropriate.

Cunean bursitis

The cunean bursa is located between the cunean tendon (the medial tendon of the tibialis cranialis muscle) and the tarsal bones.

Lameness has been attributed to cunean bursitis as an isolated etiology, particularly in **Standardbred racehorses**, but many of these patients are also reported to have cunean tendinitis. Diagnosis requires confirmation that the lameness is improved following local anesthesia of the bursa alone. Radiographs must be taken to rule out associated osteoarthritis of the distal tarsal joints, and ultrasound can also be used to determine the degree of effusion and/or tendon involvement. It is difficult to confirm that joint disease is not contributing to the lameness without advanced imaging techniques such as scintigraphy and MRI.

A **syndrome** involving inflammation of the cunean tendon, bursa and other soft tissues over the medial hock has been described in Standardbreds in race training. No radiographic abnormalities are detected (often referred to as **blind** or **occult spavin**), and the inflammation appears to be the result of overwork particularly on hard surfaces. In these cases joint inflammation is likely to be the principal source of pain.

Treatment involves rest or reduced training, NSAIDs, cold therapy, local and/or intrabursal injection with corticosteroid, Sarapin and/or hyaluronan. Cunean tenectomy is often performed, particularly when tendon involvement or tarsitis is suspected.

Carpal hygroma

Hygroma is the name given to a fluid-filled swelling on the dorsal aspect of the carpus that develops as a result of direct trauma. It is a common injury resulting in a diffuse swelling that should be differentiated from enlargement of a tendon sheath, distension of the carpal joint capsules or a synovial herniation. Ultrasound and contrast radiography may be required to confirm the diagnosis and identify communication with other synovial structures.

Hygromas are a **cosmetic blemish** unless very large, and usually there is no functional compromise. In the acute stage topical anti-inflammatory agents and bandaging can help to reduce the swelling. Fluid drainage and injection of corticosteroids and/or atropine can reduce the effusion but the swelling often recurs. If the swelling is the result of repetitive low-grade trauma (e.g. hitting the stable door), preventative measures such as padding the door should be performed. En bloc surgical excision, injection of irritants (i.e. Lugol's iodine) or incisional drainage have been recommended for

unresponsive cases, but can result in a worse cosmetic appearance and complications.

DISEASES OF MUSCLE

Fibrotic or ossifying myopathy

Fibrotic or ossifying myopathy is a cause of mechanical hindlimb lameness. The condition usually involves injury to the semitendinosus, semimembranosus and/or gracilis muscles, and is thought to be a sequel to **muscle fiber damage** that inhibits the normal action of the muscles. It occurs most commonly in barrel racing horses and stock horses but can occur as a result of **repeated injections**, and an underlying **neuropathy** is suspected in some cases.

Fibrosis and/or mineralization within these muscles is usually palpable and results in a characteristic gait at the walk. The cranial phase of the stride is abnormally short, the foot of the affected limb being abruptly slapped to the ground (**goose stepping gait**). The lameness is very characteristic for the condition, tends to be most pronounced at a walk, and does not appear to be associated with any pain.

Diagnosis is based on clinical signs and can be confirmed ultrasonographically. Ultrasound also facilitates determination of the muscles that are involved. The condition should be differentiated from stringhalt (*q.v.*) and other types of neuromuscular dysfunction.

Surgical treatment involves resecting or transecting the affected tissue or cutting the tibial and/or tarsal insertions of semitendinosus tendon. Surgery is most effective in cases with primary semitendinosus involvement. In some cases the gait deficit recurs, but other horses are permanently improved.

Muscle strain

Muscle strain may be easy to diagnose acutely but can be a relatively difficult condition to diagnose when chronic. The most commonly affected muscles are the pectorals, biceps brachii, brachiocephalicus, gluteals, semimembranosus, semitendinosus, gracilis, biceps femoris, gastrocnemius and sartorius.

In the acute stage, there is usually **sudden onset lameness** associated with focal pain, with or without abnormal muscle tension and localized heat and swelling. Strain of the longissimus dorsi muscles also occurs relatively frequently and usually results in an overall shortness of gait. Ultrasound is valuable to evaluate the extent of muscle tearing and seroma or hematoma formation. Thermography can help to identify affected superficial muscle groups but should be performed under appropriate temperature controls. Scintigraphy can be useful for identifying muscle damage, and can identify areas of deep muscle injury.

Treatment includes rest combined with NSAIDs and physiotherapy, e.g. therapeutic ultrasound and massage. Both the duration of rest and the prognosis depend upon the severity of the injury. Only if muscle damage is severe or extensive are there significant elevations in serum muscle enzyme concentrations.

Post-anesthetic myopathy and neuropathy

Inappropriate positioning of a horse during general anesthesia (*q.v.*), inadequate padding beneath the horse and a persistently low blood pressure are contributing factors for the development of a **traumatic post-anesthetic myopathy** and/or **neuropathy**. Hypoperfusion due to pressure and/or hypotension is thought to be the primary cause.

Clinical signs

Clinical signs are generally not evident until the horse tries to stand up and can even be delayed for several hours after recovery. Myopathy results in **extreme pain** and the horse usually becomes very distressed and may sweat profusely. Affected muscle groups are usually hard.

The most commonly affected muscles are the triceps and the gluteals, but any muscles may be affected, whether or not they were under pressure during anesthesia, and bilateral involvement is common with hindlimb adductor myopathies. A generalized myopathy has also been recognized. If the triceps are affected the horse is usually reluctant to bear weight on the limb and stands with the elbow dropped, mimicking radial nerve paralysis. Radial nerve paralysis or neuropathy can also occur as a sequel to general anesthesia (*q.v.*); however, in those cases there will be much less evidence of pain. A **mixed syndrome** of myopathy and neuropathy is also seen.

Diagnosis

A diagnosis of myopathy can be confirmed by measurement of **serum muscle enzymes**. There is generally a moderate rise in creatine kinase (CK) and aspartate aminotransferase (AST) following general anesthesia.

In the very acute stages of myopathy there may be only a slight further elevation of these enzyme concentrations, since when the horse first stands the affected muscles may be relatively poorly perfused. In a normal, asymptomatic horse, 1 h after standing following general anesthesia, CK concentration is usually less than 2000 IU/L, whereas in a horse with clinical signs of myopathy, CK concentrations will usually exceed 10 000 IU/L. Characteristic ultrasound findings include increased echogenicity of the affected muscle with loss of the normal striations.

Treatment

Treatment aims to relieve pain and distress and to ensure adequate muscle and renal perfusion. It consists of **analgesics** usually in the form of NSAIDs (e.g. phenylbutazone 4 mg/kg IV, flunixin meglumine 1 mg/kg IV), sedatives (acepromazine 0.04 mg/kg IV, detomidine 0.01 mg/kg IV, butorphanol 0.02 mg/kg IV), corticosteroids (e.g. dexamethasone 0.1 mg/kg IV) and **balanced polyionic electrolyte solutions** administered IV. It may be helpful in severe cases to sling the horse. Fluids are indicated if there is severe muscle damage grossly, discolored urine or dehydration. Prognosis is fair to good in mild to moderate cases; prolonged recumbency is a very poor prognostic indicator.

Preventative measures include appropriate padding of the operating surface, positioning the horse to avoid pressure on susceptible muscle groups and to avoid rises in intracompartmental pressure, and **maintenance of adequate blood pressure**.

Compartment syndrome

Compartment syndrome is an unusual cause of acute severe lameness, usually the result of **direct trauma** to a muscle group contained within a closed non-compliant fascial compartment. Edema and hemorrhage can result in a marked elevation of pressure within the fascial compartment. If there are major vessels or nerves passing through the compartment the elevated pressure may result in occlusion of vessels and myonecrosis as well as a compromise in blood flow to the more distal limb, and/or neuropathy.

Provided that there is no compromise in blood flow the horse can respond adequately to analgesic and anti-inflammatory treatment; however, if blood flow is compromised then it may be necessary to perform a **fasciotomy**. This type of compartment-like syndrome can occur in the caudolateral muscles of the **antebrachium**.

Exertional rhabdomyolysis

Exertional rhabdomyolysis (*q.v.*) (also referred to as **tying-up**, **azoturia** and **Monday morning disease**) is a common muscle disorder in the exercising horse. The term covers a wide range of related diseases associated with exercise, and numerous causes have been proposed. Specific etiologies have been identified in some cases, for example polysaccharide storage myopathy, mitochondrial myopathy resulting from a deficiency in NADH coenzyme Q reductase, glycogen branching enzyme deficiency in Quarter Horse foals, and a defect in skeletal muscle excitation-contraction.

The condition can occur after strenuous exercise, e.g. endurance racing or after the steeplechase phase of a three-day event, particularly when there is a sudden increase in the duration or intensity of exercise (**sporadic exertional rhabdomyolysis**). Other horses are prone to repeated episodes of exertional rhabdomyolysis and may have an underlying muscle abnormality (**chronic exertional rhabdomyolysis**). Nervous horses, especially fillies, are predisposed. Episodes can occur after minimal exercise. Two heritable causes of chronic exertional rhabdomyolysis have been identified so far: **recurrent exertional rhabdomyolysis** and **polysaccharide storage myopathy**.

Clinical signs

Horses usually exhibit a stiff gait, muscle cramping, pain and reluctance to move. The **gluteal muscle mass** is the most commonly affected. Clinical signs vary depending on the degree of muscle damage. The horse takes progressively shorter strides and may be extremely reluctant to move. It becomes distressed and in pain. There may be patchy sweating. The horse may paw and look at its flanks. The affected muscle group(s) is usually firm. In severe cases the urine may be abnormally dark due to **myoglobinuria**.

Diagnosis

Diagnosis is confirmed by measuring raised serum concentrations of the muscle enzymes CK and AST (normal levels CK 35–125 IU/L, AST 80–400 IU/L). Following an attack of equine rhabdomyolysis, peak concentrations of CK are reached 2 h later and decline relatively rapidly within the next 2 days; peak concentrations of AST are reached approximately 24 h after the onset of clinical signs and decline more slowly over 7–10 days. However, peak concentrations of CK and AST are not always directly correlated with the severity of clinical signs. A horse with moderately severe clinical signs may have a CK concentration of 15 000 IU/L at 2 h, declining to 7000 IU/L at 24 h. Corresponding maximum AST concentration may be 4000 IU/L at 24 h.

The condition should be differentiated from colic and laminitis (*q.v.*). Muscle biopsies can be used effectively to differentiate between sporadic exertional rhabdomyolysis, recurrent exertional rhabdomyolysis, polysaccharide storage myopathy and various other myositis conditions (*q.v.*).

Treatment

The horse should not be moved since this may exacerbate muscle damage. Treatment consists of analgesics, NSAIDs, dantrolene sodium (2–4 mg/kg, PO) and sedation with acepromazine to reduce anxiety and improve circulation (but acepromazine should not be used until the horse is rehydrated). Intravenous or intragastric DMSO is commonly recommended, and in most cases IV fluid therapy is indicated to ensure adequate renal perfusion and excretion of myoglobin. Most horses are alkalotic, and bicarbonate therapy is not advised. The convalescent time is dependent on the severity of the attack.

Preventative measures include regular exercise, vitamin E, selenium and electrolyte supplements, and appropriate concentrate feeding for the amount of work being performed. In some horses the condition is recurrent, and a urinary fractional electrolyte excretion (FEE) (*q.v.*) should be performed. If abnormal FEE values are detected, the diet should be adjusted accordingly, usually by supplementation with sodium and/or potassium chloride and/or calcium carbonate. Affected horses should always be warmed up slowly, regularly exercised and turned out whenever possible.

Recurrent exertional rhabdomyolysis

Recurrent exertional rhabdomyolysis (*q.v.*) is an inherited, intermittent, stress-induced defect in the regulation of muscle contraction. This defect is responsible for a subset of the cases of chronic rhabdomyolysis that are diagnosed, and the condition primarily affects racing Thoroughbreds and Standardbreds. Apparent trigger factors include female gender, stress, high starch diets and heavy training. Often episodes are noted following a training session in which the horse was held to a slow gallop.

Affected horses have intermittent elevations in serum CK, episodes of muscle stiffness and a history of poor performance. Diagnosis can be based on exercise testing and muscle biopsies.

Treatment should **avoid prolonged stall rest**. Prevention includes avoiding stress-related trigger factors and appropriate dietary adjustments. Concentrate feeds that are low in starch and high in fat appear to be beneficial.

Polysaccharide storage myopathy

Another subset of horses with chronic exertional rhabdomyolysis have an inherited disorder in glycogen storage apparently resulting from enhanced insulin sensitivity. **Polysaccharide storage myopathy (PSSM)** is seen primarily in Quarter Horses, draft horses and related breeds. In contrast to horses with recurrent exertional rhabdomyolysis, horses with PSSM tend to be very calm and sedate.

The clinical signs are similar to those detected with any form of exertional rhabdomyolysis, but some horses develop rhabdomyolysis without any history of exercise. Muscle atrophy and an abnormal stiff gait are often detected with this condition, and diagnosis can be confirmed with biopsy. Replacing high carbohydrate grain in the diet with rice bran or other specially formulated diets with a high lipid content can minimize the clinical signs. **Regular, regulated exercise** regimens are critical for these patients.

Nutritional myodegeneration (nutritional myopathy, nutritional muscular dystrophy, white muscle disease)

This is a condition, detected primarily in foals, that is caused by a dietary deficiency of **selenium or vitamin E**. Both cardiac and skeletal muscle are affected. **Young foals** typically die acutely, but older foals may present with signs of lethargy and dysphagia. The skeletal muscle form of the disease is more responsive to treatment, which should include supplementation with selenium and vitamin E as well as appropriate supportive care.

Hyperkalemic periodic paralysis

Hyperkalemic periodic paralysis is an **autosomal dominant trait** affecting horses descending from the Quarter Horse sire, IMPRESSIVE. A DNA test to detect the point mutation from mane or tail samples is available, and horses that are homozygous for the mutation are most prone to serious clinical effect.

The defect prevents normal function of voltage dependent skeletal muscle sodium channels, and typically results in intermittent episodes of weakness and muscle fasciculations. The **defective sodium channels** fail to inactivate appropriately, allowing an excessive persistent depolarization, and elevations of serum potassium are typical during an episode. The severity of clinical signs varies widely and can be influenced by a number of external factors including stress, temperature, diet, exercise and anesthesia.

Treatment in acute episodes is directed toward lowering serum potassium levels by administering solutions containing 0.2–0.4 mL/kg of 23% calcium gluconate diluted in 1 L of 5% dextrose. Alternatively 5% dextrose alone or combined with sodium bicarbonate can be given. Long-term control involves management to reduce dietary potassium and regular exercise, and may require administration of acetazolamide (2–4 mg/kg, PO, q 8–12 h) or hydrochlorothiazide (0.5–1 mg/kg, PO, q 12 h).

Peroneus (fibularis) tertius—rupture or avulsion of the origin

In the horse, the peroneus (fibularis) tertius, along with the SDFT, is an integral part of the **reciprocal apparatus** of the hindlimb, mechanically flexing the

hock when the stifle is flexed. It originates in the extensor fossa of the distal femur, bifurcates distally and inserts on the proximal aspect of the third metatarsal bones, as well as the calcaneus and third and fourth tarsal bones.

Rupture is usually **traumatic** due to overextension of the hock joint (i.e. if the limb is trapped) or when a **full-limb cast** is applied to the hindlimb. Disruption can also occur with a **laceration**. It often initially results in lameness although the horse is able to bear full weight on the limb. The reciprocal apparatus is disrupted so that the hock can be passively extended while the stifle is flexed, and this maneuver creates a characteristic **dimple in the Achilles tendon** on the caudal aspect of the thigh. As the limb moves forward the stifle flexes, but the hock does not. The appearance is pathognomonic but the diagnosis can be confirmed ultrasonographically.

With **avulsion** of the origin of the muscle, which usually occurs in foals and also involves the long digital extensor muscle, lameness can be severe initially, and radiographs should be taken to confirm avulsion of the extensor fossa.

Treatment is prolonged stall rest and the prognosis is favorable for healing and for return to work. Over 70% of horses are reported to return to their previous level of exercise following an average of 8 mo of rehabilitation, but performance horses and horses with additional structures injured simultaneously are much less likely to return to work. Ultrasound should be used to monitor healing before returning affected horses to work.

Quadriceps femoris rupture

Quadriceps femoris has four heads that originate from the ilium and the femur and insert on the patella. **Rupture of quadriceps femoris** is an unusual catastrophic injury that prevents the horse from extending the stifle, and the horse will be unable to bear weight. The site of rupture is usually readily palpable. There is no viable treatment although the horse can be temporarily maintained in a sling, and the prognosis is poor.

Myotonia

Myotonia congenita is a rare skeletal muscle disease characterized by an extremely stiff hindlimb gait. Clinical signs are usually evident within the first few months of life. The hindquarters are often unusually well muscled. Percussion of the muscles results in characteristic dimpling due to prolonged contraction. The condition may be inherited but that has not been definitively demonstrated.

Characteristic histopathologic changes can be confirmed, but the diagnosis is best made with electromyography. There is no effective treatment, but in most cases the signs do not progress after a year of age.

Shoulder instability

Loss of stability of the shoulder (so-called "**shoulder slip**") is usually the result of a **collision** with another horse or a solid object, resulting in damage to elements of the brachial plexus. The horse tends to place the foot more axially than normal and as the limb starts to bear weight the shoulder appears to

bulge outward due to loss of collateral support. The development of muscle atrophy or areas of patchy sweating may help to elucidate which nerves are involved.

Prognosis depends on the nature of the nerve injury; speed of improvement is a helpful indicator.

Suprascapular nerve injury (sweeny)

Injury to the suprascapular nerve—usually resulting from direct trauma to the point of the shoulder, overstretching or a poorly fitting harness collar—can result in **profound atrophy** and **paralysis** of the infraspinatus and supraspinatus muscles. This condition is colloquially referred to as **sweeny**, and the horses classically present with a **withered appearance** of the upper forelimb and a prominent scapular spine.

While many reports have described lameness, lateral instability of the shoulder and abduction of the shoulder joint with weight bearing with this condition, the instability may be due to simultaneous damage to the brachial plexus. A presumptive diagnosis is made based on clinical evidence of muscle atrophy, and electromyography can detect denervation at about 7 days post injury.

Most cases respond to conservative management with **stall rest** and NSAIDs although improvement may take up to a year post injury. If the nerve has been transected no treatment is effective. Surgical management has been described, and originally entailed removing a notch from the scapula to decompress the nerve, but there were reports of serious complications including scapular fracture. Current modifications involve simple resection of the tendinous band that lies superficial to the suprascapular nerve. Timing of surgical intervention is complicated by the delayed improvement observed even in horses that respond well to conservative therapy, and the prognosis for return to athletic performance is good with both conservative and surgical management.

Serratus ventralis muscle rupture

The serratus ventralis is composed of cervical and thoracic portions that originate from the cervical vertebrae and ribs and converge to insert on the medial surface of the scapula to form the sling support that suspends the thorax between the forelimbs. **Rupture of the serratus ventralis** is a catastrophic but rare injury that occurs with dorsal impact over the withers and neck, or when a horse jumps off of an elevation. Usually both sides of the muscle sling are affected, the thorax is dropped so that the proximal borders of the scapula are prominent above the dorsal spinous processes of the withers, and the horse exhibits extreme pain.

Sling and intensive nursing support provide an alternative to euthanasia for managing these cases, but prognosis for athletic performance is poor.

DEVELOPMENTAL ORTHOPEDIC DISEASE

INTRODUCTION

Developmental orthopedic disease (DOD) (*q.v.*) is a comprehensive term that integrates a wide variety of conditions affecting the skeleton of **growing horses**.

These conditions are caused by a number of interrelated factors, many of which are poor defined. Developmental orthopedic diseases became a recognized entity in 1985 when a survey conducted by Ohio State University suggested that many of the orthopedic problems in young horses were the result of nutritional deficiencies or imbalances. Being multifactorial these diseases appear to have genetic, environmental and nutritional components.

Trauma can affect the relatively **weak growth centers** of the developing limb and result in developmental abnormalities (e.g. angular limb deformities). Similarly, nutrient excesses (e.g. excess mineral supplementation) and rapid growth (excessive protein and energy) often exacerbate musculoskeletal disorders. Of course **genetic factors** also regulate growth rate, and a lack of careful genetic monitoring can result in the introduction and propagation of disorders that become impossible to eliminate (e.g. osteochondrosis, *q.v.*).

The musculoskeletal system is in a **constant state of turnover** or change throughout life; the rate of turnover is greatest early in life, during the growth phase. Skeletal growth is most rapid in the first few months of life and slows through the first year until growth plate closure. Because the metabolic activity of the musculoskeletal system is so great early in life, the skeletal system is more susceptible to insult, both physical and metabolic.

This section covers the salient features of the pathogenesis of developmental orthopedic disease and provides a review of osteochondrosis, osseous cysts-like lesions, incomplete ossification of the cuboidal bones of the carpus and tarsus, physitis and angular and flexural limb deformities.

OSTEOCHONDROSIS

Osteochondrosis (*q.v.*) is a developmental orthopedic condition defined as a disturbance in **endochondral ossification**, a process that is responsible for the coordinated differentiation of cartilage-producing cells called chondrocytes. Any disruption in this sequence of events can result in the retention of poorly differentiated growth cartilage.

The structure of the joint surface is weakened by retention of this immature cartilage, resulting in necrosis and fissure formation extending to the articular surface. Damage to the articular surface causes inflammation, which is defined by the term **osteochondritis**.

In some horses, a cartilage flap will detach from the underlying bone, creating a lesion known as **osteochondritis dissecans** (**OCD**) (*q.v.*). A "dissecans" lesion commonly forms as a result of trauma acting on poorly developed cartilage and leads to the formation of a cleft extending from the articular surface to the subchondral bone. These cartilage flaps have been described as **type I lesions** and develop at or near the center of a convex joint surface. At some locations, such as the distal intermediate ridge of the distal tibia, abnormally developed cartilage may fracture along the cleft line resulting in the formation of an **osteochondral fragment**. The latter abnormality is defined as a **type II lesion**.

Pathogenesis

Epiphyseal cartilage is converted into bone through the process of **endochondral ossification**. The process through which cartilage is replaced by bone in the developing epiphysis is identical to that occurring in metaphyseal growth

plates. This process is accomplished as chondrocytes proliferate, mature and advance through four histologic zones to produce the extracellular matrix that defines this specialized tissue. Chondrocytes must progress through the **resting**, **proliferating**, **hypertrophic** and **calcification zones** in an orderly fashion to develop and function normally. The calcified layer is subsequently replaced by **bone**. If any of the events involved in endochondral ossification are altered to a significant degree, osteochondrosis can occur.

Histologically, an area of **necrotic cartilage** is typically the first identifiable sign of an osteochondrosis lesion. When the epiphyseal cartilage becomes necrotic, ossification cannot occur and the "cartilage template" ultimately is retained as a region of **thickened cartilage**. Because cartilage is avascular, its metabolic needs must be met by diffusion of nutrients from the synovial fluid. Consequently, chondrocytes in the deeper zones of abnormally thickened cartilage are deprived of nutritional support due to the increased distance between these cells and the synovial fluid. This further compromises normal cartilage development.

At the cellular level, important factors thought to be responsible for osteochondrosis include abnormal chondrocyte metabolism, abnormal coding for cartilage matrix production, and biomechanical forces leading to irregular articular loads. As it is likely that these factors participate concurrently in the etiology of the condition, osteochondrosis should be considered to be a **multifactorial disease**.

The metabolic requirements of cells involved in endochondral ossification are met by delivery of nutrients via the systemic circulation and by diffusion through the synovial fluid. Articular cartilage lacks a blood supply and must receive its nutrients by diffusion through the synovial fluid. In contrast, epiphyseal cartilage has a direct blood supply from vessels located in the perichondrium, a thin continuation of the periosteum over the extremities of bone. **Perichondrial blood vessels** penetrate and supply the epiphyseal cartilage through cartilage canals. This source of blood is vitally important during the early stages of cartilage development. If it is **disrupted** prior to the normal time frame required for epiphyseal development, ischemia and necrosis can result and produce lesions consistent with osteochondrosis.

Adequate production of normal **extracellular matrix** is essential to the development of the epiphyseal cartilage and the formation of bone. Chondrocytes are capable of producing many different types of matrix molecules, including collagen, proteogylcans and glycosaminoglycans. These molecules must be produced in the right order, location and arrangement to allow endochondral ossification to proceed normally. Disruption of this complex process due to **abnormal genetic makeup** or **cellular injury** may result in lesions consistent with osteochondrosis.

Because osteochondrosis lesions are noted to occur in consistent locations within each affected joint, **biomechanical influences** are presumed to play a role in their development. Some investigators hypothesize that physiologic trauma during development results in focal stresses on specific areas of developing articular cartilage, which leads to abnormal development of the tissue.

Etiology

Osteochondrosis has a **multifactorial etiology**. The proposed causative factors include **genetic factors** that affect **weight gain** and **growth rate**, **nutrition**,

heredity, **type and intensity of exercise** and **trauma**. A positive relationship has recently been identified in Standardbred and Warmblood horses between the occurrence of osteochondrosis in the tarsocrural joints and body weight at birth and during the growth phase. Furthermore, **rapid weight gain** has been noted to facilitate the development of osteochondrosis in the femoropatellar joints of Warmblood horses.

Diets that include appropriate amounts of **calcium**, **phosphorus**, **copper** and **zinc** tend to reduce the incidence of musculoskeletal problems. Feeding excessive amounts of calcium and phosphorus, however, is contraindicated as a combination of decreased exercise activity and excessive intake of calcium and phosphorus is associated with the development of multiple developmental orthopedic diseases, including osteochondrosis and irregular physeal closure. **Copper** participates in the function of the enzyme lysyl oxidase, which is essential in appropriately cross-linking pyridinoline in collagen. Collagen is a vital component of the cartilage matrix, and diets containing less than adequate amounts of copper result in reduced **collagen cross-linking** and, consequently, an increased incidence of osteochondrosis. Copper supplementation in mares during pregnancy and in foals after birth appears to reduce the incidence of osteochondrosis, especially involving the distal intermediate ridge of the tibia. Although copper is not the only important factor in the etiology of osteochondrosis, it is important to consider evaluating dietary copper in instances in which the incidence of osteochondrosis is excessive.

Other important dietary elements to take into account are **digestible energy** and **protein**. Diets containing high percentages of carbohydrate and protein have been associated with developmental abnormalities for many years. Excessive carbohydrate intake appears to disturb the balance between serum concentrations of **insulin** and **thyroid hormones** (T3 and T4) (*q.v.*) and disrupt their coordination of cartilage development leading to abnormal chondrocyte differentiation. In contrast, diets containing excessive amounts of protein do not appear to have similar detrimental effects on development; these diets cause only minor changes in the growth plates.

Although there is no conclusive evidence to support a role for **genetic factors** in the development of osteochondrosis, the role of genetic makeup has been suggested by heritability studies. These studies have shown that osteochondrosis of the tarsocrural joint may depend on genetic background and that the development of these lesions may in fact depend on progeny rather than environment.

The effect of **exercise** on development of osteochondrosis is controversial. The results of controlled studies do not support the hypothesis that increased exercise activity early in life is associated with development of osteochondrosis. Moreover, when low exercise and high exercise programs were compared in Thoroughbred foals, osteochondrosis lesions were significantly more common in the low exercising population of foals, indicating a possible protective effect of high-intensity short-duration exercise. Furthermore, in foals presumed to be genetically predisposed to develop osteochondrosis of the femoropatellar and femorotibial joints, exercise did not appear to influence the development of lesions, rather exercise altered the appearance and distribution of the lesions.

Trauma and **biomechanical loads** appear to play a role in the progression of an osteochondrosis lesion into a "dissecans" lesion (*q.v.*) or into an osseous

cyst-like lesion (*q.v.*). More convincingly, exercise-induced trauma may explain the consistent location of osteochondrosis lesions in the various joints, suggesting the influence of physical factors in the pathogenesis. It is generally accepted that physiologic loads applied to defective cartilage or abnormally high loads exerted on normal cartilage can lead to osteochondrosis.

Incidence

Osteochondrosis is estimated to affect **5–20%** of foals, although the occurrence rate may be much higher in certain breeds. All breeds of horses may be affected, however the majority of cases have been recognized in racing breeds. It was reported recently that 50% of horses undergoing surgery for osteochondrosis of the femoropatellar joint were Thoroughbreds. Osteochondrosis primarily affects diarthrodial joints and occurs more frequently in male than female horses.

It is important to remember that any articular surface may be affected, including vertebral articulations, with more than one joint frequently being involved. For this reason, evaluation for **any lameness** in young horses, particularly if bilateral, should include OCD as a differential diagnosis. The most common sites are the distal intermediate ridge of the tibia, the lateral and medial trochlear ridges of the talus, the lateral and medial trochlear ridges of the femur and, less commonly, the humeral head, the glenoid surface of the scapula, and the metacarpo/tarso-phalangeal and proximal interphalangeal joints.

Clinical signs and diagnosis

Generally, osteochondrosis lesions causing clinical **lameness** occur in horses <3 yr of age, although some horses remain asymptomatic until later in life. The latter presentation is particularly common when only mild lesions exist, and the horse has been allowed to mature before vigorous exercise has commenced. Older horses may present with degenerative arthritis, with the location and appearance of bony lesions being consistent with a diagnosis of long-standing osteochondrosis.

The most prominent clinical finding in horses with osteochondrosis is **effusion** in at least one affected joint. Effusion may not always be evident in the contralateral joint, even though radiographic evidence of disease exists. Lameness is variable, but is usually only mild to moderate. The lameness may be difficult to abolish completely with IA injection of local anesthetics. Muscle wasting is often evident in horses with long-standing osteochondrosis of the shoulder or stifle.

The age of the horse, its size and sex, and the presence of joint effusion are factors that can indicate a probable diagnosis of osteochondrosis. Confirmation of a diagnosis of osteochondrosis is usually made with **radiography**. In OCD, articular cartilage becomes thickened and usually does not mineralize, therefore it appears radiographically as a defect in the articular surface. Even when clinical signs are only apparent in one limb, the **contralateral** joint should always be radiographed. The horse should also be closely examined for abnormalities in other joints. A **neurologic examination** and cervical radiographs may be indicated to determine whether cervical vertebrae have been affected.

Common radiographic findings in horses with osteochondrosis include discrete osteochondral fragments, defects in the contour of the articular surface (flattening or depression), irregularly shaped lucent areas in the subchondral bone, subchondral bone sclerosis surrounding the lucent areas, and secondary osteoarthritis. Despite the presence of lameness and effusion, osteochondrosis lesions of the shoulder and stifle may not be readily identified radiographically. In these cases, the diagnosis can ultimately be made by investigating the joint via **arthroscopy**. It is important to note that lesions identified by radiography are not always clinically significant. Radiographic findings must be interpreted in light of the clinical signs.

Treatment

Conservative therapy consists of restricting the horse's exercise, slowing the growth rate, and ensuring that there are **no dietary vitamin or mineral deficiencies**. Excessive feeding of grain should be avoided. Conservative therapy is successful in 20–50% of cases, depending upon the site and severity of the lesion. Up to 1 yr of convalescence may be required, and joint effusion and lameness may be present for a considerable period of this time. Intra-articular injection of hyaluronan and systemic administration of polysulfated glycosaminoglycans do not appear to have any effect on the long-term outcome if combined with conservative treatment. Injection of corticosteroids into an affected joint is contraindicated.

Surgical treatment is usually recommended for horses with OCD and consists of removal and debridement of detached or abnormal cartilage to induce subchondral bone capillary bleeding. This facilitates the initiation of a repair process that, in the majority of cases, eventually leads to the formation of functional **fibrocartilage**. **Arthroscopic** surgery is preferred over arthrotomy, because of the ability to observe and operate on multiple sites within a joint, reduce surgical trauma and minimize postoperative complications. Approximately 70–80% of horses with OCD respond favorably to arthroscopic surgery. Improvement in clinical signs is often evident within weeks after surgery.

Postoperative care consists of 4 wk of stall confinement, then 4 wk of handwalking, followed by paddock rest for an additional 8–16 wk. This can be modified to suit the individual lesions and training program of the affected horse. If required, some horses, primarily those with small lesions of the distal intermediate ridge of the tibia, can resume exercise within 10–14 days of surgery.

Because osteochondrosis is often associated with some degree of **osteoarthritis**, clients need to be informed of the potential for the persistence of lameness and need for medical management after surgery. Early surgical management will help retard the development of osteoarthritis, thereby producing a less painful and more functional joint. The **prognosis** in appropriately managed patients is generally favorable.

Prevention

Measures designed to reduce the incidence of osteochondrosis and other developmental problems should be directed at the etiology as understood. However, considering the gaps in our understanding of the etiology of osteochondrosis, such measures cannot always be specific. Although the influence

of inheritance on the expression of osteochondrosis is unknown for most forms of OCD, in most cases it would be prudent to **avoid breeding** to horses that have shown the propensity to produce foals with osteochondrosis. Nevertheless, there are many highly productive lines of athletic horses that do have a high incidence of OCD, and it is not realistic or even rational to suggest that those genetic lines be eliminated.

Foals up to 1 yr of age should be allowed to exercise freely for at least 12 h/day and forced exercise should be avoided. Strict guidelines concerning diet are difficult because of the different types and quality of feed available and because individual foals respond differently to different diets. The best recommendation is to have a reliable laboratory analysis of feeds performed followed by consultation with a recognized equine nutritionist. Similar attention should be given to the diet of gestating mares. Moreover, it is important always to avoid over-supplementation of mineral/vitamin mixes.

OSSEOUS CYST-LIKE LESIONS

Osseous cysts (*q.v.*) occur most frequently in the **medial femoral condyle** within the stifle joint, but also occur in other sites, including the pastern and elbow (cubital) joints and carpal bones. Potentially cysts may occur in any joint. These lesions are characterized by infolding of articular cartilage into the underlying cancellous bone. The **infolded cartilage** then becomes **necrotic** and its matrix remains non-mineralized. Because the affected area lacks a blood supply, the normal repair processes cannot occur.

The etiology of bone cysts is uncertain but may be related to dietary abnormalities and may have a similar pathogenesis to OCD (*q.v.*). Several theories have been proposed to explain the origin of subchondral bone cysts, including a **disturbance** in the normal process of **endochondral ossification** similar to that in classical osteochondrosis. In support of this theory is the fact that osteochondral disease may lead to cyst formation. It also has been proposed that subchondral bone cysts are caused by **direct trauma** to the articular surface leading to full thickness cartilage degeneration. Experimentally, cysts can be induced by linear incision of the articular cartilage and penetration of the subchondral bone. In contrast, cysts do not form if only the articular cartilage is damaged. Because cysts are generally site specific, it is thought that certain joint surfaces are vulnerable to this disease due to the **biomechanical forces** acting at specific sites.

Bone cysts may or may not be associated with clinical **lameness**. Cyst-like lesions close to the articular surface are more likely to cause lameness than those deep within the bone. The treatment of choice is surgical evacuation where access to the cyst is feasible. Conservative therapy may be successful in some cases, but many horses treated conservatively develop long-term degenerative joint disease.

INCOMPLETE OR DEFECTIVE OSSIFICATION OF THE CARPAL AND TARSAL BONES

Delayed ossification of the carpal and tarsal bones in newborn foals may be a result of **prematurity/dysmaturity**, hypothyroidism (*q.v.*) or a variation of

normal ossification rates. Lack of ossification of the cuboidal bones in these joints results in collapse and deformation, and subsequent development of joint abnormalities. In the carpus an angular limb deformity occurs, whereas a flexural deformity appears in the hock.

When the tarsal bones are involved, the most prominent clinical sign is the development of a characteristic **"bunny hopping" gait** that is usually present at, or soon after, birth. Radiographic examination will reveal the presence of one or more abnormal bones in these joints. The cuboidal bones are usually collapsed, incompletely ossified and may show varying degrees of fragmentation. If a diagnosis is made early and the deformity is not severe, effective treatment can be as simple as exercise restriction and application of full limb bandages to provide support. In more advanced cases, straightening the leg with the foal under general anesthesia and applying a full limb or tube fiberglass cast (*q.v.*) should be considered.

In young foals, the cast will need to be changed initially every 7–10 days or more often to accommodate the rapid growth occurring at this time. This treatment will only be successful if instituted prior to degenerative changes occurring in the joint. When the diagnosis is delayed or the angulation of the limb is severe, surgical treatment is recommended. Surgical correction of the resulting angulation deformities includes growth acceleration and retardation procedures that are more thoroughly discussed elsewhere in the text. The prognosis is somewhat guarded, as some horses become sound, but many are left with a chronic lameness.

PHYSITIS

Physitis is traditionally defined as a generalized inflammatory response of a **growth plate**. The disease occurs with biphasic age peaks, typically detected between 3 and 6 mo in the distal metacarpus/metatarsus, and between 8 mo and 2 yr of age in the distal radius and occasionally in the distal tibia.

There is still controversy regarding whether to classify physitis as an inflammatory process or a disturbance of endochondral ossification. Regardless, in its acquired form, physitis is most likely to result from compressive forces producing **Salter–Harris type V physeal fractures**, and can be classified as a developmental orthopedic disease. Because of the higher load applied to the medial aspect of the forelimb, these fractures tend to propagate in a medial to lateral direction.

During the delicate phase of active growth, **nutritional imbalances** associated with heavy feeding programs that include diets rich in concentrate feed can predispose to excessive weight gain and weakening of the epiphyseal cartilage template. The growth plates enlarge in response to inflammation and excessive load bearing, which cause subperiosteal osteogenic cells (osteoblasts) to initiate new bone formation. Horse owners will often complain of physeal enlargement without any other clinical signs. These mildly affected cases are usually transient and can be effectively managed with rest and a balanced **low energy** diet. In more severe forms, enlargement of the physis may be accompanied by local heat, pain and variable degrees of lameness.

The diagnosis is usually clinical, but lateral and dorsopalmar/plantar radiographs show characteristic changes: the physis is thicker and more irregularly undulating than normal, and the metaphysis may show sclerosis and flaring. The disease is usually self-limiting but treatment includes retardation of growth, low doses of phenylbutazone, and restricted exercise.

It is particularly important to reduce energy intake and body weight, but the **nutritional balance** of the diet (*q.v.*) must be maintained. Feed analysis and consultation with a nutrition specialist are advised. Several feed companies are developing diets specifically designed to manage foals with this type of developmental problem. The prognosis is usually good. Foals with this disease should be monitored for development of flexural and angular limb deformities.

ANGULAR LIMB DEFORMITIES

The term angular limb deformity refers to limb deviations that occur in a frontal plane and are lateral or medial deviations along the long axis of the limb. The deformities can be **congenital** or **acquired**, and they most commonly involve the carpus, tarsus and metacarpo/metatarsophalangeal joints. Foals may develop these problems after birth because of the interplay of the aforementioned factors involved in the pathogenesis of developmental orthopedic disease.

Valgus deformities are those in which the limb deviates laterally, distal to a reference point (in other words, the angulation distal to the reference point is away from the midline of the body). In **varus** deformities the limb deviates medially distal to the reference point (in other words, the angulation distal to the reference point is towards the midline of the body). The terms valgus and varus are adjectives and should precede the nouns they describe; however, in common usage they are usually applied following the noun that they modify (i.e. "carpus valgus").

Deformities of the **carpus** and **tarsus** are most often valgus, with a lateral deviation of the limb below the carpus or tarsus, and less commonly varus. A combination of valgus and varus deformities will produce a so-called "**wind swept**" appearance. Deviations associated with the **metacarpo/metatarsophalangeal** joints can be either valgus or varus. Angular deformities arising from curvature of the diaphysis of the metacarpus and metatarsus also have been reported.

Most foals are born with a slight **bilateral carpus valgus** and outward rotation of the forelimbs. This is considered **normal** and should correct within 7–10 days of birth. Should this fail to occur the foal needs to be critically observed since correction of angular limb deformities must be implemented within the period of active growth. The majority of growth in the distal radial and tibial physes occurs within the first 6–8 mo of life, whereas the distal metacarpal/metatarsal physes are active from birth to 3 mo of age.

As a general rule, each of the following differentials should be considered in any foal that presents with an angular limb deformity:

1. Laxity of periarticular soft tissues
2. Incomplete ossification of the cuboidal bones and collapse

3. Disproportionate growth at the level of the physis
4. Metacarpal/tarsal bone displacement
5. Diaphyseal curvature (MC3, MT3).

The pivot points of **acquired angular deviations** are usually in either the epiphyses or physes on either side of the joint. The deviation can also be centered over the cuboidal bones when hypoplasia is present. Angular deviation due to ligamentous laxity is usually congenital, although it also can occur following prolonged limb immobilization.

Visual inspection may demonstrate both rotational and angular deformities. For this reason the clinician should examine the foal by standing directly in front of the dorsal aspect of the limbs and positioning the hooves directly under the proximal aspect of the limb. The same principles apply for hindlimb evaluations except that the examiner views the foal from the rear. Gait assessment is aimed at evaluating hoof breakover in order to implement the most appropriate corrective trimming or shoeing measures. Manipulation of the limb may induce complete or partial correction of the deformity in cases of ligamentous laxity or cuboidal bone hypoplasia.

Dorsopalmar/plantar radiographs are valuable to determine the pivot point(s) and deviation angle of the deformity. In addition, hypoplasia of the cuboidal bones, usually the ulnar, third and fourth carpal bones and the central and third tarsal bones, can be identified from radiographs. In long-standing cases there may be radiographic evidence of **degenerative joint disease**, which influences prognosis. Sufficient length of the appendicular skeleton must be included on the radiographs proximal and distal to the clinical site of the deformity so that lines can be drawn along the axis of the long bones on either side of the joint. For this purpose, long narrow cassettes (18×43 cm) are commonly used. The lines will intersect at the site of angulation in deviations caused by a single deformity. However, perfect radiographic positioning of bones proximal and distal to the pivot point is frequently impossible because of rotation of the distal limb. In addition, appropriate positioning of the two intersecting lines is often very subjective. An alternative technique for determining the pivot point has been described using lines drawn through the physes and the joint spaces. In a normal limb these lines will be parallel, but in an affected foal the lines will deviate at the level of the deformity. Again, accurate positioning of these lines is very subjective.

In most cases, **conservative** management is successful in treating angular limb deformities. Stall rest or limited small paddock turnout and corrective shoeing and trimming will resolve the deformity by altering weight-bearing patterns. To address **carpus valgus** problems, the clinician can elect either to apply commercially available glue-on shoes with dorsomedial hoof extensions or to over-trim the lateral hoof wall. Although trimming has been used successfully for many years, glue-on shoes are preferred because they do not affect **hoof balance**. Deformities that can be improved by manipulation (i.e. those deformities due to ligamentous laxity or cuboidal bone hypoplasia) may benefit from splints or tube casts (*q.v.*). **Pressure sores** are a common complication of external support when applied to irreducible deformities and are extremely difficult to treat or manage.

External coaptation will not resolve angular deformities due to disparity in growth rates at the physis. Angular deformities associated with epiphyseal or physeal dysplasia or ligamentous laxity can resolve spontaneously.

Surgical correction should be attempted if the deformity is severe, if the degree of angulation is increasing rapidly, if conservative therapy has failed, or if inadequate time is left for conservative therapy to be effective before closure of the physis occurs. Surgical correction of deformities arising from the epiphysis or physis involves **growth retardation** by **transphyseal bridging** or **growth enhancement** by **hemicircumferential periosteal transection and elevation** (periosteal stripping). Diaphyseal curvature of the metacarpus or metatarsus that is identified before 1 mo of age can be treated with periosteal transection and stripping of the distal metacarpal/tarsal physis and the entire concave surface of the bone. In older foals, an osteotomy will be required.

There is some evidence that **periosteal stripping** may not be as effective as originally purported. However, additional research needs to be performed to determine accurately the effectiveness of this technique. The difficulty has been identifying an appropriate model to represent naturally occurring angular limb deformities in order to allow accurate comparisons between treated foals and untreated controls.

Regardless, surgery needs to be performed well before cessation of metaphyseal growth to be of benefit. This requires intervention before approximately 6 wk of age for metacarpo/metatarsophalangeal joint deformities and 4–6 mo of age for deformities of the carpus and tarsus. Therefore, once deemed necessary, the surgery should be performed promptly. Occasionally, however, surgical correction has been achieved at the metacarpus/metatarsus and carpus/tarsus as late as 3–4 mo of age and 9–14 mo of age, respectively.

Correction of >20° has been reported for carpal valgus but 8–15° is a more reasonable expectation; anticipated correction at the metacarpo/metatarsophalangeal joints should be more modest, approximately 5–8°. The rotational deformity usually corrects with the angular limb deformity, although if left too long part or all of the rotation may become permanent. Correction of angular and rotational deformities following physeal closure can achieved by an **ostectomy** or **osteotomy** and a variety of different derotational, step (frontal and sagittal plane), and wedge ostectomy/osteotomy techniques have been described for use in horses. These are generally considered to be salvage procedures.

FLEXURAL DEFORMITIES (CONTRACTED TENDONS)

A flexural deformity represents a deviation in the sagittal plane and is detected as a **persistent hyperflexion** of a joint region. Flexural deformities are most commonly encountered in the distal interphalangeal joint, the metacarpo/metatarsophalangeal joint and the carpus. These deformities are commonly referred to as **contracted tendons**, even though true tendon contracture is unlikely to be the cause of the problem.

With flexural deformities, the soft tissue structures of the palmar and plantar limb are affected such that the limb is held in varying degrees of flexion. The forelimbs are more frequently affected, and the problem can involve one or more limbs at the same time. The true cause and method of development of

flexural deformities remain unknown, although horses with acquired deformities (those that develop after birth) often share similar factors to those associated with the **developmental orthopedic disease** complex (*q.v.*).

Many foals are born with mild **digital hyperextension** characterized by flaccidity of the flexor tendons, which causes the toes of the front hooves to elevate off the ground during weight bearing. Most of these deformities are **self-limiting**, and correction occurs during the first two weeks of life as muscle and tendon tone improves. Tendon laxity may be more severe and excessive toe elevation causes load bearing to occur on the bulbs of the heel or pastern leading to soft tissue abrasion. This condition can be successfully treated by applying **heel extensions** until muscle and tendon tone improves.

Congenital flexural deformities

Multiple factors have been implicated in the **congenital form** of the disease including intrauterine positioning, ingestion by the mare of certain toxins such as locoweed, collagen cross-linking defects, equine hypothyroidism/goiter and unidentified predisposing genetic factors. Congenital flexural deformities can be due to hyperflexion or, less commonly, hyperextension due to flaccid or relaxed flexor muscles and tendons. Some of these deformities can cause dystocia or difficult foaling.

The most common congenital flexural deformity occurs at the level of the **distal interphalangeal joint and fetlock**. These deformities are appropriately classified according to the joint involved. The contracture associated with the DDFT involves the distal interphalangeal joint (coffin joint) and the contracture associated with the SDFT affects the metacarpophalangeal joint. The two need to be carefully differentiated since the prognosis for the latter is generally worse. Careful palpation of the flexor tendons should be completed with the foal in a weight-bearing and non-weight-bearing position to determine which of the flexor tendons is most involved. Involvement of both SDFT and DDFT to a similar degree can occur. Congenital flexural deformity of the **carpus** is also fairly common, and can occur as part of a generalized limb contracture involving several joints.

If the foal can stand, and the limbs can be manually extended into a normal position, the prognosis is favorable for resolution with temporary **splinting** with stiff PVC splints or splints constructed from synthetic casting material applied to the back of the leg over a heavy wrap. Splints can cause **pressure sores** (*q.v.*), thus they require careful application for only a few hours each time, maintaining an accurate schedule. Analgesia is also important, but **NSAID use** should be monitored carefully to avoid complications such as gastric ulceration or renal papillary necrosis. More severe forms may require **surgical correction**, which is described below in the section on acquired flexural deformities (*q.v.*).

The empirical use of **IV oxytetracycline** has been reported to cause laxity of tendons and ligaments and can be used for the early treatment of these conditions. The mechanism of action is unknown, but is thought to relate to receptor binding or calcium chelating properties of the antibiotic. Two different courses of therapy have been used: 1 g IV repeated for 3 consecutive days, or 3 g once followed by a second identical dose if correction is not observed. The

lower dose is advocated by some because of decreased risks of reported renal toxicity, diarrhea and excessive laxity of the other normal joints.

Flexural deformities occurring at the level of the **carpus** usually carry a poor prognosis. Foals born with this condition hold the carpus in permanent flexion and are often unable to stand. **Careful evaluation** of these cases should be undertaken to determine whether surgical correction is even feasible. Commonly, contracture of the carpal joint capsule and associated ligaments accompanies that of the carpal flexor tendons, eliminating the chance for successful surgical treatment even after complete carpal flexor tendon transection.

Rupture of the common digital extensor tendon (*q.v.*) can be congenital or acquired, unilateral or bilateral; the cause is unknown but it has been observed to develop in foals with congenital flexural deformity of the carpus (*q.v.*). A characteristic swelling will be located over the tendon sheath at the dorsolateral aspect of the carpus. Foals knuckle over at the fetlock when walking, and appear "over at the knee" when standing. **Temporary full limb splint application** prevents knuckling over and allows the tendon ends to fibrose and eventually return to complete function. Surgery is not required.

Acquired flexural deformities

Acquired flexural deformities are included in the classification of developmental orthopedic disease and share many pathogenetic factors with osteochondrosis (*q.v.*) and other growth related abnormalities. Fast-growing horses on a **high plane of nutrition** are often affected. Furthermore, foals on a poor plane of nutrition that are subsequently introduced to good quality feed often develop flexural deformities. Other important factors include pain caused by osteochondrosis, septic arthritis, physitis and trauma. Pain in one limb will cause abnormal weight bearing on the contralateral limb, resulting in a flexural deformity.

Foals typically develop evidence of **distal interphalangeal joint deformities** between 1 and 4 mo of age. This is in contrast to deformities of the metacarpophalangeal joint that usually occur around 1 yr of age. This difference is thought to be associated with the disparity in growth between the distal and proximal portions of the forelimbs. Distal limb growth is nearly complete by 3 mo of age, whereas distal radius growth continues for much longer. During the rapid growth phase, bone lengthening is not paralleled by passive elongation of the DDFT and SDFT, which are thought to be restricted by their respective accessory (check) ligaments.

The DDFT inserts on the flexor surface of the third phalanx, therefore a decrease in its length will lead to dorsiflexion of the distal interphalangeal joint. Conversely, the superficial flexor tendon bifurcates into medial and lateral branches just distal to the metacarpophalangeal joint. These branches insert on the palmarodistal aspect of the proximal phalanx and the palmaroproximal aspect of the middle phalanx. A shortened superficial flexor unit, therefore, causes the pastern area to be drawn palmarly and the metacarpophalangeal joint to dorsiflex creating the "knuckled forward" appearance. It is believed that this problem mainly relates to the SDFT, but the DDFT and suspensory ligament can concurrently be involved.

Flexural deformity of the distal interphalangeal joint (club foot syndrome)

Increased angulation and shortening of the dorsal wall and elongation of the heels give a typical conformation termed "**club foot**". The disease may progress so that the angle of the dorsal wall with the ground exceeds 90°, with the heels and frog no longer touching the ground and the dorsal wall becoming concave.

Very severely affected foals will walk on their dorsal hoof wall. These foals are classified as having a **type II deformity**, whereas when the dorsal hoof wall is less than perpendicular to the ground, foals are said to have a **type I deformity**. This classification may aid the clinician in formulating a prognosis because type II problems have a poorer treatment outcome even with aggressive treatment such as surgery.

The diagnosis is based on appearance and palpation of a taut DDFT with the limb in extension. Radiographs of the distal interphalangeal joint will identify abnormal joint angulation, and in chronic cases remodeling of the distal phalanx and secondary changes in the distal interphalangeal joint.

Appropriate **dietary management** should be implemented. This needs to begin with the mare's diet so that milk production is limited. **Exercise** should be controlled so that some exercise is given but excessive exercise at pasture is eliminated. Mildly affected animals respond to gradually lowering the heels and systemic non-steroidal analgesics (where necessary) to control pain and enhance weight bearing.

Non-steroidal analgesics must be used with caution in foals because they can cause gastrointestinal ulceration. The risk of gastrointestinal ulceration (*q.v.*) should be minimized by using the non-steroidal analgesic at the lowest dose required for the shortest duration possible to achieve the desired clinical effect (1–2 mg/kg **phenylbutazone** q 12–24 h, but up to 4 mg/kg has been recommended); anti-ulcer medication, e.g. omeprazole paste (GastroGard) 4 mg/kg s.i.d., can be used concurrently to reduce the likelihood of gastrointestinal symptoms related to non-steroidal analgesics.

Moderately affected animals (i.e. those with angulation approaching or slightly greater than 90°) and mild cases that fail to respond to non-invasive therapy usually require **desmotomy** of the accessory ligament of the DDFT (inferior check ligament) possibly supplemented by an extended toe shoe. Severely affected animals may require **DDFT tenotomy** performed in the mid-metacarpus or mid-pastern as a salvage procedure.

The prognosis for return to athletic function is usually good for animals that do not need a DDFT tenotomy, but may vary with the intended use of the horse and age at which surgery is performed; in Standardbreds the prognosis for racing after an inferior check ligament desmotomy is reportedly poor for foals operated on >5–8 mo of age.

Flexural deformity of the metacarpophalangeal/ metatarsophalangeal joint

The prognosis for this deformity is generally poorer than that associated with the distal interphalangeal joint. Severity may be classified as mild if the

metacarpo/metatarsophalangeal joint is more upright than normal but dorsiflexion is not present; moderate if intermittent dorsiflexion is present; and severe if the joint is in permanent dorsiflexion.

As with conditions involving the distal interphalangeal joint, the diagnosis is principally based on appearance. **Palpation** of flexor tendons and suspensory ligament with the limb in maximal extension should assist in defining the principal structures involved. Radiography of the fetlock joint should be performed prior to treatment to detect the presence of secondary changes that may affect the prognosis.

Mildly affected animals respond to treatment involving **dietary management** to decrease growth rate, **phenylbutazone** to control pain, and **shoeing** with elevated heels with or without a toe extension. Exercise should be restricted and controlled but should not be eliminated. Moderately affected horses respond to similar conservative therapy in combination with surgery. There is considerable debate as to the relative efficacy of desmotomy of the superior and inferior check ligaments in the treatment of this condition. Determining which structure is involved by palpation may assist the surgeon in deciding which surgery to perform, but the use of the *inferior* check ligament desmotomy is generally recommended in mildly affected animals. Horses with more pronounced deformities may or may not respond to corrective shoeing together with both superior and inferior check ligament desmotomies. Superior check ligament desmotomy can be associated with seroma formation (*q.v.*) and infection if postoperative management is not careful, and tenoscopic techniques have been developed to minimize these complications.

The prognosis for return to athletic function in mild and moderately affected animals is favorable, but it is poor when the deformity is severe.

Chapter 16

Performance-related problems and exercise physiology

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Chapter contents

INTRODUCTION

There have been many developments in the science of training and fitness testing of horses over the last 40–50 years. Many of the research findings on blood lactate, heart rate and hematology in the exercising horse are of clinical relevance to veterinarians. The following sections provide an overview of the normal physiology and biochemistry of the equine athlete, both at rest and during exercise.

Veterinarians are frequently asked to examine horses that are either destined to be athletes or are not performing well. The main factors that contribute to good athletic performance include the structure and function of the respiratory, cardiovascular and musculoskeletal systems. It is not the purpose of this chapter to give details of all abnormalities of these or other body systems that affect performance, such as lameness and respiratory disease. The emphasis is rather on those **techniques** that are routinely used to assess performance, such as hematology and electrocardiography, and some new techniques based on the application of measurements made during or after standardized exercise tests. Some of these techniques are now routinely performed in large and successful racing stables. Unfortunately, veterinarians have been slow to apply many of the practical aspects of recent findings on exercise and performance in horses. This may be due to a lack of information on applied aspects of the many research findings in this area. One aim of the following sections is to review the research and present aspects of its practical application.

There are three principal aims of the application of science to training horses.

1. To develop techniques for **testing fitness** of horses for competition. Exercise testing may contribute to the financial success of training establishments in several ways. These include:
   (a) Early identification of horses with **inferior stamina**. This information can hasten their removal from the stables, or identify limitations to performance in young horses even before they have commenced racing.
   (b) Repeated tests evaluate **improvement or deterioration** in fitness during training. Information gained in one preparation can be used to assess the fitness attained in subsequent preparations.
2. To design training programs that **maximize fitness**, reduce the incidence of injury and improve results in competition. Heart rate measurements during exercise and blood lactate concentrations after exercise can provide a guide to ideal training speed for development of stamina. This enables adjustments to the training routine in order to increase fitness without overtraining the horse.
3. To evaluate horses with **poor performance**.

Many of the techniques referred to in this chapter have been validated both in the laboratory and on the racetrack in Europe, USA and Australia. Moreover, similar techniques have been used by human athletes and sports science laboratories for decades and are now part of the daily routine of human athletic training. It has taken time to adapt and develop suitable protocols for horses.

It is hoped that this chapter increases veterinarians' understanding of the normal physiology and biochemistry of exercise in equine athletes and illustrates the limitations of some of the traditional methods of assessment of equine performance. This chapter also points the way ahead to the application of new techniques for monitoring fitness in horses.

BIOCHEMISTRY OF EXERCISE AND FATIGUE

ENERGY SOURCES

The processes of muscular contraction and relaxation require **adenosine triphosphate (ATP)** as an energy source. Hydrolysis of ATP to adenosine diphosphate (ADP) and a phosphate molecule liberates heat and energy. The energy is used in the process of actin–myosin crossbridge cycling in skeletal muscle cells, and muscular contraction and relaxation. The nature of the myosin ATPase enzyme in the muscle cell determines the twitch characteristics of a muscle fiber, and characterization of muscle fibers according to their actin–myosin ATPase activity forms the basis of **muscle fiber typing**.

The horse has very **small stores of ATP** within its muscles. These stores are quickly exhausted at the onset of exercise. In order for a horse to sustain exercise, it must be able to replenish ATP at a rate compatible with usage. The ability to utilize and regenerate ATP is a major factor limiting performance. There are several metabolic pathways that have the potential to contribute to ATP resynthesis. The relative importance of each pathway to overall ATP production is determined by the **intensity and duration** of exercise.

The immediate sources of substrate for **ATP resynthesis** are high energy phosphate molecules stored within the cell. These substrates are most important at the onset of exercise, and during times of extreme energy demand, such as the sprint at the end of a race. **Creatine phosphate (CP)** represents the largest pool of high energy phosphate in the muscle. CP can donate a phosphate group directly to ADP. Thus, ATP regeneration is rapid, but CP stores are too small to support more than a few seconds of exercise. During times of **extreme energy demands**, a high energy phosphate group may be transferred from one molecule of ADP to another. One molecule of ATP is produced with one molecule of adenosine monophosphate (AMP), which is metabolized to inosine monophosphate and eventually ammonia.

Sustained exercise demands an energy supply beyond that available in stored phosphate bonds. This demand is met by the energy available in fuel stores derived originally from feeds. There are two primary energy sources: carbohydrate and fat. **Carbohydrate can be metabolized aerobically (using oxygen) or anaerobically (without oxygen). Fats are metabolized aerobically**. Proteins have a minor contribution as an energy source during exercise.

AEROBIC METABOLISM

When the demands for energy are low, aerobic metabolism is capable of meeting the requirements for ATP resynthesis. Aerobic metabolism is the primary

pathway by which ATP is regenerated during **endurance-type exercise**. Aerobic metabolism also contributes greatly to the energy supply during high intensity exercise such as galloping. Anaerobic metabolism makes up the deficit in total energy resynthesis during high intensity exercise.

Aerobic metabolism is the process by which fats and carbohydrates are oxidized, culminating in the production of ATP, carbon dioxide and water. The oxidation of substrates produces hydrogen ions. Pairs of hydrogen ions are accepted by coenzymes **nicotinamide adenine dinucleotide (NAD)** and **flavin adenine dinucleotide (FAD)**, which are reduced to NADH and FADH. These coenzymes transport the hydrogen atoms to the enzymes of the respiratory chain, which are located within the **mitochondria**. These enzymes, the cytochromes, have electron transport functions and are capable of delivering electrons derived from oxidizable substrates to oxygen. In the process, derived energy is stored as ATP. Three moles of ATP are formed from each mole of NADH entering the respiratory chain, and two moles of ATP from each mole of FADH.

Fat is stored in **depots** around the body and as **triglycerides** within muscle cells. Mobilization of fat from the depots occurs under hormonal influence. Non-esterified fatty acids (NEFA) are transported to the muscle by the circulation, and move into cells along a concentration gradient.

Carbohydrates are stored in the muscle and liver in the form of glycogen. Glycogenolysis is activated by **epinephrine (adrenaline)**. Glucose, transported to the cell by the bloodstream, can also be oxidized to produce energy.

Fatty acids enter the mitochondria and undergo a process known as **beta-oxidation**, which results in the production of hydrogen and acetyl coenzyme A (acetyl CoA). Acetyl CoA enters the tricarboxylic acid (TCA) cycle, where it is metabolized to produce four pairs of hydrogen atoms and CO_2. Acetyl CoA is also the entry point of amino acids to the TCA cycle.

Glycogen and glucose are metabolized to pyruvate in the **Embden–Meyerhof pathway** by a process known as **glycolysis** that results in the production of hydrogen ions that can be accepted by NAD and FAD. Pyruvate may be metabolized to acetyl CoA, and enter the TCA cycle when sufficient oxygen is available. The oxidation of 1 mole of NEFA of average composition yields approximately 138 moles of ATP. One mole of glycogen is oxidized to produce 37 moles of ATP. The oxygen cost of oxidation of NEFA is approximately 10% higher than the cost of glycogen oxidation.

Glycogen and blood glucose are the substrates **immediately available** for aerobic metabolism. Mobilization of NEFA requires a considerable time, and their contribution as a substrate for aerobic metabolism increases as the duration of exercise increases.

The capacity of the horse to generate energy aerobically is primarily limited by the **availability of oxygen** in the working muscle. Potential limitations include the function of the upper airways, lungs and cardiovascular system, erythrocyte numbers, and capillarity and fiber diameter within the muscle. The concentration of enzymes in the muscles appears to be in excess of the levels required to fully metabolize the oxygen delivered by the blood.

Training enhances the capacity for oxygen delivery to the muscle, therefore increasing the capacity of the animal to generate energy aerobically. Mitochondrial density and enzyme concentrations also increase.

ANAEROBIC METABOLISM

At the onset of exercise, the delivery of oxygen to the muscles does not instantaneously reach the level required to support aerobic metabolism. Approximately 30 s of exercise is required before **maximal aerobic activity** is achieved. During this time, there is an increase in heart rate and ventilation, an increase in the oxygen carrying capacity of the blood as the splenic erythrocyte reserve is mobilized, and redirection of blood flow to the skeletal muscles. Increases in body temperature may enhance enzyme activity. During this period, the **deficit** in energy production is met by **anaerobic metabolism**. During intense exercise, the maximal accumulated oxygen deficit can be measured, and this measure reflects the anaerobic capacity.

When **insufficient oxygen** is available to support the activity of the TCA cycle and respiratory chain, or when the rate of pyruvate production is very high, pyruvate may act as a recipient of hydrogen atoms from NADH, resulting in the production of ATP and lactate. No oxygen is required in this reaction.

One mole of glycogen yields three moles of ATP when metabolized anaerobically. When glucose is the substrate, two moles of ATP are produced, as one mole of ATP is used to phosphorylate the glucose on its entry to the cell. In contrast to the reactions of aerobic metabolism, which occur in the mitochondria, the processes of anaerobic metabolism occur in the cytoplasm.

Lactate diffuses from muscle cells to the bloodstream and is transported to the liver where it is oxidized to pyruvate by NAD in the cytoplasm. The pyruvate is converted to glycogen and stored in the liver in an energetically expensive series of reactions. Fatty acid oxidation may provide the energy used in these reactions. During exercise, mobilization of liver glycogen stores helps to maintain blood glucose concentrations. Lactate ions are also metabolized aerobically in slow twitch muscle fibers during and after exercise.

Anaerobic metabolism reaches its peak capacity within 20–30 s of the onset of exercise. It is best viewed as a **supplement to aerobic metabolism** that enables the total demands for energy to be met. The balance between aerobic and anaerobic metabolism depends on the rate at which NADH can be oxidized. For carbohydrate metabolism to continue, a supply of NAD is required. Resynthesis of NAD can be viewed therefore as a key step in ATP generation. As the duration of exercise increases, or as speed falls, the contribution of anaerobic metabolism to the overall energy equation becomes smaller.

In a horse galloping over 1200 m, aerobic metabolism accounts for approximately 65% of the ATP generated. Demands for ATP resynthesis during exercise at a velocity slower than 18 s/200 m (11 m/s, or 650 m/min) can be almost fully met by aerobic metabolism in most horses. Post-competition measurements of blood lactate concentrations in **showjumpers** have shown that anaerobic metabolism is significant in that form of exercise.

FATIGUE

Fatigue can be defined as the failure to maintain a desired power output during exercise. Many factors contribute to the development of fatigue, and the importance of individual contributors depends on the intensity and duration of the exercise. At a biochemical level, the most important factors are **depletion**

of high energy phosphate reserves, changes in metabolite concentrations, and the depletion of glycogen stores. Depletion of intracellular ATP will also inhibit the cell membrane sodium–potassium pump, so there is accumulation of potassium in the extracellular fluid. Cycling of calcium between the cytosol and the sarcoplasmic reticulum will also be compromised, and fatigue is associated with **increased calcium ion concentration** in the cytoplasm.

During endurance exercise, the biochemical cause of fatigue is **depletion of glycogen reserves** in the muscle. Muscle biopsy studies have shown that muscle fibers are recruited progressively as glycogen stores in other fibers are exhausted and their power output decreases. When all fibers have depleted their glycogen reserves, exercise must stop. The oxidation of fatty acids alone is not sufficient to maintain the required power output, although the energy held in fat stores would support many days of continuous slow exercise. However, increased use of fatty acids as a substrate for aerobic metabolism has the effect of sparing glycogen reserves and increasing the potential duration of exercise. Aerobic training **enhances fat utilization** by increasing the concentrations of enzymes involved in fat metabolism and increasing mitochondrial volume.

Appropriate training will increase the capacity of the horse to use fatty acids as a substrate. The value of **glycogen loading**, of proven benefit to human endurance athletes, remains unclear in the horse. It is possible that the very large glycogen stores that are found in equine muscle may approach the limit of storage capacity. Hyperthermia, dehydration and electrolyte imbalances (*q.v.*) also contribute to fatigue and the **"exhausted horse" syndrome** during prolonged exercise.

The **accumulation of lactate** in the cytoplasm is a characteristic of cells generating energy **anaerobically**. Traditionally, the development of **intracellular acidosis** resulting from the production of lactic acid by anaerobic metabolism has been believed to be a major factor contributing to fatigue. However, at physiologic temperatures, reduced intracellular pH has little direct effect on muscle contraction and fatigue. Glycolysis may provide a high and sustainable supply of ATP without causing muscle fatigue.

The development of fatigue during high intensity exercise is related to **oxygen delivery** to the muscles. Oxygen modulates intracellular metabolism to influence the rate of change of metabolites—mainly inorganic phosphate (P_i) — and may affect fatigue by influencing the rate of P_i accumulation. In muscle cells, an increase in P_i may reduce crossbridge force production and myofibrillar Ca^{2+} sensitivity, and inhibit Ca^{2+} release and/or reuptake. When oxygen delivery is limited, there is greater reliance on substrate-level phosphorylation for ATP resynthesis, resulting in disruption of metabolic homeostasis and a decline in developed tension. Studies in humans have found that hypoxic conditions that decreased aerobic capacity had no effect on performance for sprints of up to 60 s, and had very little effect on sprints of up to 120 s, indicating that maximal human running speeds for short- and intermediate-length sprints are relatively unaffected by large reductions in aerobic power. The ability to maintain power output at a time when aerobic capacity was decreased suggests that additional metabolic energy must have been derived from anaerobic sources during exercise in hypoxic conditions, that maximal metabolic power outputs during sprinting under normoxic conditions are not

limited by rates of anaerobic metabolism, and that human running speed is largely independent of aerobic power during all-out sprints lasting less than one minute.

PRINCIPLES OF TRAINING

INTRODUCTION

Successful performance of a horse in an athletic event will depend on its **adaptation to the physical demands** of the event. The degree of adaptation will depend on inherited characteristics of heart size (*q.v.*), muscle fiber types and other factors. It will also depend on adaptations that occur in response to the stimulus of regular exercise, or training. A key aim of training the horse is **increasing fitness** in order to **delay the onset of fatigue during exercise**. In some events, such as dressage and showjumping, **skill** is also likely to be a very significant factor influencing performance.

The development of fatigue during exercise is likely to be multifactorial. The body of research in exercise physiology encompasses five general models to explain the processes affecting performance:

1. The **cardiovascular/aerobic model** of fatigue is based on the idea that increasing the ability of the muscles to utilize oxygen, thus delaying the onset of lactate accumulation in the blood, will delay the onset of fatigue.
2. The **energy supply/energy depletion model** is based on the idea that fatigue during high intensity exercise may be due to the inability to supply ATP at a sufficient rate to support exercise.
3. The **muscle recruitment (central fatigue)/muscle power model** holds that brain concentrations of serotonin (and perhaps dopamine, acetylcholine and other neurotransmitters), alter the neural drive to exercising muscles, or that reflexes generated in the exercising muscles reduce recruitment of alpha motor neurons at the level of the spinal cord.
4. The **biomechanical model** states that biomechanical characteristics of the muscle (such as the capacity to act as a spring), affect the demands for force production, and therefore limit metabolite accumulation and heat production.
5. According to the **psychological model**, the ability to sustain exercise results from a conscious effort.

Physical fitness is associated with the capacity of the horse to do work. Therefore, in order to achieve fitness, it is necessary to enhance the function of all systems that may limit work capacity. Physical training that increases the work capacity of the horse must impact on one or more of the factors that contribute to fatigue. As **the ability of the horse to use and regenerate ATP is a vital factor limiting performance**, achieving an increase in the capacity of the horse to generate and utilize ATP is a key aim of training. In addition to enhancing energy generation capacity, training should increase the strength of the muscles, tendons and skeleton, enabling the horse to generate higher work outputs without succumbing to injury.

Other factors that limit performance, in particular skills and psychology, are beyond the scope of this chapter. **Skills training** may result in improvements in **gait** that result in increased efficiency of movement and a decrease in energy demands. In addition, training of this type may improve the **psychological condition** of a horse, making it more willing to work. The benefits of physical training can easily be undone by **inadequate provision of rest** periods before competition, so that the horse becomes tired and disinterested in competing.

AEROBIC TRAINING

In order to design a **training program** aimed at improving energy economy, it is necessary to know the contribution of the various metabolic pathways to ATP resynthesis in the athletic endeavor for which the horse is being trained.

Aerobic metabolism makes a significant contribution to ATP resynthesis during exercise of any intensity. **All horses** being trained for any purpose require aerobic training as part of their program. In events that require relatively low rates of energy turnover, such as dressage or endurance riding, aerobic metabolism can satisfy the demands for ATP resynthesis. As exercise intensity increases, the contribution of anaerobic metabolism becomes relatively more important, supplementing the energy produced aerobically to meet the total energy requirements for exercise.

When anaerobic metabolism makes a significant contribution to energy generation, a horse will be unable to sustain exercise as **metabolic changes in the muscle will result** in the onset of fatigue. If the capacity of a horse to generate energy aerobically is increased, its reliance on anaerobic metabolism to generate energy during exercise at a given intensity will be decreased. Therefore, the onset of fatigue will be delayed.

The **maximum work capacity** is determined by the sum of the aerobic and anaerobic capacities. Therefore, training that enhances anaerobic capacity will enhance performance in horses working at maximal intensities.

There are several **basic principles** that apply to training. Training will produce changes in the function of all parts of the body, but most importantly in the musculoskeletal and cardiovascular systems. In order to produce changes in a specific system, that system must be stressed in the training process. This has been described as the **overload principle**. However, it is important to avoid fatiguing the animal during training. It is therefore beneficial to have a method of measuring **training intensity**.

The changes produced by training are influenced by how often the horse is trained, the duration of training and the training intensity. Training-induced changes will be **lost** if a horse ceases regular exercise, although **maintenance training** programs will preserve the adaptations.

Aerobic training results in increases in circulating **blood volume** and **stroke volume**, which produce an increase in the amount of oxygen transported to the muscle. Within the muscle, there is an increase in the capillary distribution to individual muscle fibers, and fiber cross-sectional area. Mitochondrial volume, enzyme concentrations and myoglobin concentration increase within the cell. Training also appears to increase intracellular **glycogen stores**.

The metabolic cost of exercise is largely unaffected by training. A horse working at a given submaximal speed has a set requirement for oxygen delivery. As stroke volume increases during training, heart rate will fall. **Heart rate provides the best indicator of the intensity of aerobic training**, and heart rate changes can be used to monitor aerobic fitness.

The **aerobic capacity of a horse can be increased** by training at a relatively low intensity. Exercise at a heart rate approximately 50% of maximum appears to be sufficiently intense to maximize gains in aerobic power (maximum heart rate in the horse is in the range 195–240 bpm). Regular monitoring of the heart rate allows the training intensity to be increased as the horse becomes fitter. Exercise that results in heart rates in the range of approximately 70–90% of maximum is likely to be associated with **metabolic changes** in the muscle. These changes promote development of buffering capacity in muscle cells.

Training sessions aimed at enhancing aerobic power should last for at least 30 min. Where horses are being trained for endurance riding, at least one session per week should be in excess of 1 h in duration, in order to ensure that mobilization of NEFA has occurred in the fat depots of the body.

Skeletal remodeling is an important factor contributing to the maintenance of soundness through training and competition, and should be considered an important goal in this stage of training. Because the intensity of work is low during aerobic training, the skeleton is not exposed to extreme stresses. Only a minimal increase in the exercise intensity is required to promote bone remodeling. Although increases in aerobic capacity are rapid, morphologic changes in the skeleton and muscle occur more slowly. This must be considered when planning the **duration of the aerobic component** of the training program.

Once a horse has achieved a high aerobic capacity, specific training is not required to maintain it. The higher intensity work given to train the anaerobic system will maintain aerobic power. If a horse is not undertaking high intensity work, relatively low intensity exercise such as trotting will enable it to maintain considerable aerobic capacity.

ANAEROBIC TRAINING

Anaerobic training is often the most neglected aspect of training. During this phase, the aim is to increase the **capacity of the anaerobic pathways to generate ATP**, and to increase the capacity of the muscle to cope with changes in metabolite concentrations and intracellular acidosis.

The point at which anaerobic work should be introduced to the training program is debatable. At least 4–6 wk of aerobic work appears to be necessary to provide an appropriate level of background fitness. However, many human athletes include an anaerobic component from the onset of training. As they become fitter, the anaerobic proportion of the total training load is increased. Some horse trainers believe that excessive low intensity training of racehorses results in a loss of speed.

An appropriate **training load** to stress the anaerobic system is one that results in post-exercise blood lactate concentrations in the range 4–10 mmol/L. Heart rates in the range of 85–95% of maximal are also appropriate. At this exercise

intensity, anaerobic metabolism is making a significant contribution to energy generation. The resulting metabolic changes cause an increase in sprint capacity and an increase in intramuscular buffering capacity, which enables the horse to sustain intense exercise for longer periods.

It has been suggested that exercise eliciting a heart rate of 200 bpm should be sufficient to generate lactate concentrations in the range 4–10 mmol/L. However, some horses working at this speed will have lactates either higher or lower than this range. In some horses, the target heart rate will be appropriate and may be used as an approximate guide when lactate measurement facilities are not available. New technology that combines simultaneous measurement of heart rate and velocity with a global positioning system (GPS) has great potential for improving the monitoring of exercise intensity during horse training.

During anaerobic training, the horse can quickly become fatigued. Measuring blood lactate concentrations to monitor workload enables the trainer to avoid fatiguing the horse. **Training-related anorexia** is generally seen in horses working frequently at an intensity that generates blood lactate concentrations greater than 10–15 mmol/L. In addition, an excessive anaerobic training load may result in glycogen depletion in the muscles, and a "tired" horse. Regular **light training days** should be provided to enable the horse to replenish its glycogen stores.

The optimal amount of anaerobic exercise in each training session and the optimal frequency of training sessions have not been determined. When the exercise intensity is closely controlled by regular blood lactate analysis, horses can cope with an exercise volume far in excess of the amount that has traditionally been considered the limit. However, in general, it would be unwise to regularly use very high intensity exercise training on more than two days per week.

Speed is an important factor contributing to the occurrence of injuries. Working horses uphill increases the intensity of exercise at a given speed, enabling an appropriate training stimulus to be generated at lower speeds, and minimizing the risk of injury. However, there has been a report that uphill treadmill exercise also increases the severity of exercise-induced pulmonary hemorrhage after intense exercise. Excessive use of training at speeds >900 m/min in Thoroughbred horses increases the risk of injury.

For horses involved in events where maximal exercise intensities are reached, **speed training** is the final component of the training program. The aim of this phase is to increase maximum speed and strength, and to increase stores of high energy phosphates. In order to achieve this, high speeds, generally higher than mean race speed, are required. Traditionally, sprint training of racehorses has been limited to a few maximal sprints at the end of training gallops. In human athletics, interval training techniques with up to six repetitions in each session have been used.

During the sprints, the horse should not reach the point of fatigue. A **fatigued horse** is unable to work at maximum speed, and therefore does not receive the appropriate training stimulus. In addition, the **risk of injury** is increased in a fatigued horse because gait becomes abnormal. The amount of sprint training required to achieve the maximum performance benefit in the horse is unknown. The distance over which the horse is sprinted

should equal, or slightly exceed, the distance over which it will sprint during competition.

TRAINING FOR SPECIFIC PURPOSES

Racehorses

The discussion of training above provides general guidelines to **racehorse training**. The duration of each phase of training must be balanced between the time required to optimize performance and the costs of keeping a horse in training. As a general rule, a program consisting of 4 wk slow aerobic training, 4 wk medium pace and 2 wk sprint training can be considered as a bare minimum. The sprint training component includes skills work such as practice starts from stalls. Approximately 4 days before the race, the workload should be decreased to enable the horse to **replenish intramuscular glycogen** stores.

Horses that have achieved race fitness do not require intensive training in order to maintain fitness. Low intensity exercise with weekly gallops appears to be sufficient. In Standardbreds, which may race at intervals of <7 days, racing may be the only high intensity exercise required.

Endurance horses

As a general rule, **training volume** is the key to success in preparing endurance horses. The more training exercise given to a horse, the greater the improvements in performance. Some training sessions must be long enough to ensure that mobilization of fatty acids occurs (at least 1 h). Initially, low intensity exercise should be given to increase aerobic capacity and stimulate bone remodeling. Once preliminary aerobic training is completed, an appropriate training speed is 80–100% of speeds in endurance races.

A characteristic of **elite endurance** athletes is that lactate does not begin to accumulate in the blood until the intensity approaches that generating maximal heart rates. Training intensities that generate lactate can shift the lactate accumulation point closer to the maximum heart rate. All endurance horses should receive some anaerobic training. Many endurance riders are reluctant to allow their horses to canter or gallop, as they believe this may teach them bad habits for the race. If the trainer is reluctant to increase the speed of exercise, beneficial results may be obtained by working the horses at lower speeds up hills or on inclined treadmills. Treadmill training is a regular feature of many top class human athletes.

One to two weeks before an event, the horse should be given one training session where at least half the distance of each race leg is covered. The greater the distance covered in this session, the greater the benefits to performance. During the week prior to the event, **training should be tapered** to ensure that intramuscular glycogen stores are maximized.

Dressage

Skill training is far more significant in **dressage horses** than fitness training. The skill training to which the dressage horse is subjected should result in the development of adequate fitness.

Showjumpers

Post-competition blood lactate concentrations in **showjumpers** approach 10 mmol/L, indicating that anaerobic metabolism makes a significant contribution to energy generation. Training sessions are generally limited to 20–30 min of jumping or other work.

Eventers

Horses involved in **cross-country events** generate high lactate concentrations in the blood. In the steeplechase stages, the work intensity is similar to that of racing. Therefore eventers should benefit from programs designed to increase aerobic and anaerobic capacity. A highly successful training program involves 60–90 min of conditioning 6 days per week. Most of the work is given at a hard trot or steady canter, with two to three easy gallops over approximately 1000 m. In the final weeks before the event, the horses are given several steeplechase sessions at approximately 800 m/min.

INTERVAL TRAINING

Interval training has achieved widespread acceptance with Standardbred trainers, and is commonly used by human athletes. The aim of interval training is to **increase the volume of work** done in an individual training session. In order to achieve this, **exercise is provided in bouts, with a recovery period** between each bout.

There are five factors to be considered in designing an interval training program. These are:

1. The intensity and duration of each interval
2. The number of repetitions
3. The rest interval between bouts
4. The type of activity during the rest period
5. The frequency of training.

The final program depends on the goal of training. Where the **anaerobic system** is the target, intervals are generally conducted at 10% below race speed. Recovery between bouts does not need to be complete. **Heart rate monitors** are commonly used to measure recovery, with a heart rate of approximately 120 bpm the goal. The distance of each interval does not appear to be particularly important. Where enhancement of **sprint capacity** is the aim of training, the horse must be fully recovered before a heat is commenced. Trotting a horse between exercise bouts will result in a more rapid fall in blood lactate concentration than walking or cantering.

Flexible interval training programs tailored to meet individual requirements can produce good results. However, repeated high intensity interval training can also cause overtraining in racehorses, with weight loss and loss of performance.

OVERTRAINING

Overtraining can be defined as an **imbalance between training and recovery**. Overtrained animals appear fatigued and stale. Their performance

deteriorates and they may lose weight. Short-term overtraining can be corrected by rest for a period of days to weeks. Where the severity of the overtraining is greater, a recovery period of several months is required.

Overtraining appears to be associated with dysfunction in the neuroendocrine system. The **blood cortisol response** to intense exercise is reduced in overtrained horses. The syndrome is not associated with exhaustion of the adrenal glands (*q.v.*). Rather, there is a downregulation of the hypothalamic response (*q.v.*) to the exercise stimulus. The syndrome cannot be diagnosed by routine hematology or biochemistry in resting horses.

HEMATOLOGY OF HORSES IN TRAINING

INTRODUCTION

Routine blood testing is used by trainers in a variety of ways. Many of the claims of the usefulness of blood tests have been overrated. Blood testing can be used routinely to check the health status of the animals in a stable. However, this becomes expensive where large numbers of horses are involved, and the costs of such a program may well exceed any benefits that are gained.

Blood tests should be considered as a **diagnostic aid** in evaluating loss of performance, as they can be used to identify horses suffering from subacute diseases that may impair performance. In addition to the direct loss of performance, the stresses associated with racing may exacerbate a pre-existing condition, with the result that far more severe problems develop. This is particularly true of horses with respiratory disease.

Many trainers use routine blood testing in the belief that it will enable them to assess the fitness of their horses and estimate their performance in competitive events. Although certain hematologic changes do occur as a result of training, **hematologic evaluation cannot be used as a guide to fitness**, or to identify horses that will win races. In a comprehensive study of Thoroughbred horses conducted in Australia in the late 1970s, attempts were made to correlate the pre-race hemogram with subsequent performance. From the results it was apparent that no relationship existed between the hemogram and subsequent racing performance. Similar results have been found in a subsequent study of Standardbreds.

The usefulness of hematologic evaluation as an indicator of fitness is limited by the variability in the results obtained. The sources of variability are: the state of the horse; the handling of the sample; variation in the normal values recorded in different laboratories; and individual variations between horses. Erythrocytes, as a step in the oxygen transport chain, represent a potential limitation to performance. However, many other factors affect performance in a healthy horse, and the blood cannot be considered the key limiting factor. **Transport of horses** can have a significant effect on their blood indices.

RED BLOOD CELLS

The horse holds a large store of erythrocytes in its spleen. Under stimulation of the sympathetic nervous system, the spleen contracts, injecting the stored cells

into the circulation and resulting in an increase in the hematocrit. Splenic contraction occurs in anticipation of or during exercise. However, changes in the hematocrit (*q.v.*) are minimal following endurance exercise unless dehydration has occurred. Hematocrit values >0.55 L/L, and plasma protein concentrations >90 g/L in endurance horses are signs of **potentially dangerous fluid loss**.

The **act of blood sampling** may be sufficient to cause mobilization of the splenic erythrocyte pool in some nervous horses. This can result in large increases in the hematocrit. Because the temperament of the animal is a variable that cannot be controlled, comparison between horses becomes meaningless.

In order to minimize the variation in results obtained in multiple tests conducted on the one animal, **conditions of sample collection should be standardized**. Minimal restraint should be used, and the same person should collect the sample on each occasion. The sample should be collected **before** the horse is fed or exercised. Feeding is associated with an increase in hematocrit and plasma protein concentration, and a fall in serum potassium concentrations.

Stallions tend to have a higher hematocrit than geldings or mares. The hematocrit in Thoroughbreds is usually higher than in other breeds. Red cell numbers increase as a horse becomes fitter, and as it ages. In general, training results in an increase in erythrocyte numbers and total blood volume. However, changes in horses undergoing endurance training are minimal. Species and state of training must be considered when analyzing erythrocyte values.

Poor performance has been reported in racehorses with a resting hematocrit <0.36 L/L. If abnormally low red cell indices or hemoglobin concentration are suspected, collection of a blood sample within 5 min of a fast gallop should be used to confirm the condition. Normal hematocrit after a fast gallop is in the range 55–70 L/L.

In horses used for endurance exercise, the lower limit of normality may be considered to be 0.30 L/L. Resting hemograms are a useful aid in the detection of **anemic horses**. In such animals, the hematocrit is lower than the lower limit of normality at the laboratory conducting the analysis. In addition to poor performance, signs include pale mucous membranes and a rough coat.

Two common causes of **anemia** (*q.v.*) in horses are **chronic inflammation**, which causes bone marrow suppression, and a **heavy parasitic burden** (*q.v.*), which causes increased blood loss. **Subclinical infections**, which have the potential to impair performance, may cause bone marrow suppression. Because reticulocytes do not appear in the bloodstream, a **bone marrow biopsy** (*q.v.*) is required to determine whether anemia is regenerative or non-regenerative. Anemia is rarely due to a primary iron deficiency, and **iron supplements should not be considered** a treatment for the condition. The animal must be examined to determine the underlying cause. Iron supplementation has been associated with severe **phlebitis** when injections are incorrectly administered. Fatalities have also been reported to occur following iron injections. Erythrocytes require 5–7 days to mature. It is therefore very optimistic to expect that any treatment for anemia is going to help the performance of the horse in a race two days later.

It has long been argued that **polycythemia** (*q.v.*) is the mechanism or hallmark of overtraining syndrome in Swedish Standardbred trotters. However,

a longitudinal study of overtraining that included a control group failed to confirm that overtraining causes red cell hypervolemia.

If the resting hematocrit is in the normal range, no further interpretation can be made from the results. There is no relationship between resting hematocrit and the post-exercise hematocrit, which can be 55–70 L/L.

WHITE BLOOD CELLS

Increases in leukocyte numbers may be indicative of the presence of a variety of conditions that may decrease performance. **Increases in neutrophil numbers are generally associated with bacterial infection**.

Lymphopenia is a common finding in any animal with chronic disease. Monocyte numbers generally decrease during acute inflammation, but may increase when inflammation becomes chronic. Lymphopenia may also be associated with **corticosteroid administration** (*q.v.*).

Leukocyte numbers also increase **following exercise**. An increase in neutrophils, persisting for 4 h following a vigorous training gallop, has been reported. A **post-exercise lymphocytosis** also occurs due to the release of lymphocytes from the spleen during mobilization of the erythrocyte store. These factors should be considered when interpreting the results of tests performed on samples collected soon after exercise.

Stress in endurance horses during an event is associated with a progressive neutrophilia and lymphopenia. A neutrophilia with a significant left shift and lymphopenia are signs of exhaustion in endurance horses. Stress of training is often diagnosed if a "high" ratio of neutrophils to lymphocytes is measured. **There is no basis for this diagnosis**. Moreover, the extreme stress of overtraining syndrome is not associated with any abnormality of the red or white blood cell counts.

PLASMA PROTEINS

Maximal exercise causes an **increase in total plasma protein** concentration due to fluid redistribution that decreases plasma volume. This change in plasma volume also contributes to the high hematocrit found in horses after maximal exercise.

Plasma **fibrinogen** may be elevated in animals with mild to moderate inflammation that is not associated with a leukocytosis or neutrophilia.

ELECTROLYTES

Alterations in electrolyte concentrations can seriously affect performance, but these are unlikely in healthy horses in training if appropriate supplements of sodium chloride are used in the diet. **There is no indication for any need for potassium supplementation** in racehorses. **Hypochloremia** will be found in endurance horses during and after competition because of the high chloride concentration in equine sweat.

Calcium supplementation of diets has been advocated on the basis of low blood calcium concentrations. However, blood calcium is carefully controlled by the body. In addition, calcium concentrations are affected by plasma

protein concentrations, as approximately 50% of blood calcium is bound to plasma protein. Calcium levels will be lower in hypoproteinemic horses.

Training appears to have little effect on plasma electrolyte values. However, **during high intensity exercise**, there are large increases in plasma sodium and potassium concentrations, with smaller increases in calcium and phosphate. Bicarbonate concentration decreases. These changes persist for approximately 1 h after exercise, and are normal expectations.

During exercise, electrolytes are lost in the **sweat**. However, these changes may not be reflected in plasma electrolyte concentrations until significant losses have occurred. Therefore, **use of 50–100 g salt (NaCl) supplementation** (*q.v.*) in the feed is recommended for the exercising animal, with greater supplementation in horses undertaking long distances of training exercise in hot environments.

Electrolyte supplements are commonly used to replace losses in sweat. A horse that is sweating heavily will lose large amounts of chloride. In order to maintain electrical neutrality, the horse will retain bicarbonate, and metabolic alkalosis may develop. **Electrolyte supplements** for endurance horses should be **high in chloride and low in bicarbonate**.

Bicarbonate supplements for horses following high intensity exercise are of dubious value as the horse is physiologically well adapted to neutralizing post-exercise acidosis. There is no evidence that supplements with high bicarbonate buffer prevent **tying up** (*q.v.*), and their inappropriate use could contribute to high plasma bicarbonate concentrations in horses presented for pre-race testing.

ENZYMES

Enzymology can provide useful information regarding tissue damage. Serum creatine kinase (CK) and aspartate aminotransferase (AST, SGOT) are elevated in horses with exertional rhabdomyolysis. However, they are often elevated following exercise, although signs of muscle damage may not be evident on examination. CK peaks 3–5 h after exercise, then declines over 24 h. AST peaks at around 24 h, and declines more slowly. Very high serum CK concentrations have been found in normal horses, and horses may have myopathy without elevated serum enzymes.

Gamma-glutamyltransferase may increase as a result of training. Overtraining or training stress is not associated with abnormalities of serum enzymes.

ELECTROCARDIOGRAPHY

Electrocardiography (*q.v.*) is frequently used by veterinarians involved in assessment of performance horses. The most common reasons for examining the electrocardiogram (ECG) of an equine athlete are to **investigate arrhythmias and poor racing performance**. ECG has also been used to estimate heart size by calculation of the heart score. The ECG is also used in horses to measure heart rate and investigate the cardiac rhythm during and after exercise as part of examinations for poor athletic performance. The popularity of the ECG as a tool for diagnosis of poor racing performance and estimation of heart size

varies in different countries. Detailed discussions on cardiology can be found elsewhere (*q.v.*).

TECHNIQUE

The **limb lead system**, based on Einthoven's triangle (*q.v.*), is usually employed. Most normal values for equine ECGs have been produced with this system. Electrodes are placed on the skin in standard limb positions. On the forelegs, the electrodes are placed on the posterior aspect of the radius. On the hindlegs, the electrodes are placed on the anterior aspect of the tibia. Other lead systems have been described, such as the XYZ leads, which attempt to create an orthogonal lead system that can be used for vectorcardiography. Unfortunately there is little information available on XYZ vectorcardiography in normal horses and horses with heart disease. The limb lead system has been used for vectorcardiography in the horse, although there are criticisms of this technique in quadrupeds.

For investigation of **arrhythmias**, a simple alternative to the bipolar limb leads is the **Y lead, or base to apex lead**. This lead places a positive electrode (e.g. the LA lead) on the skin over the xiphoid process of the sternum, and the negative electrode (e.g. the RA lead) on the ventral chest in front of the manubrium or at the right jugular furrow. This lead gives a high amplitude signal, and the record is less likely to be disturbed by movement of the horse. This lead is ideal for the routine examination of arrhythmias.

The skin does not need to be clipped. Alligator clips can be attached directly to the skin after application of a suitable **electrode gel**. Horses usually tolerate this technique if the points of the teeth on the alligator clips are filed down. Alternatively the leads can be connected to tin plates held against the skin with clips or elastic straps.

Recordings are made at 25 mm/s, with the horse standing quietly. The heart rate of the resting horse can increase from 30–40 bpm to $\geqslant$100 bpm very quickly due to excitement or fear. High heart rates abbreviate the PQ and QT intervals, and P waves also lose their notching.

A good technique for examining the ECG is to identify the **P waves** first. The P wave of the equine ECG can vary greatly from beat to beat, but this variation is normal. Notching is frequent, so that the P wave is divided into two components, P1 and P2. P2 is frequently of higher amplitude than P1. It is thought that P2 is due to activation of the atrial septum. Changes in heart rate also dramatically affect the shape of the P waves, due to alterations in vagal tone. Normal P wave duration is $<$0.16 s.

Absence of the P waves may indicate hyperkalemia (serum $K^+ > 6$ mmol/L), atrial fibrillation (*q.v.*), sinus arrest or junctional rhythm. **Sinus arrest** (*q.v.*) is rare in horses. Junctional rhythm refers to a rhythm originating at the atrioventricular node, with P waves buried in the QRS complex, which is traveling toward the base of the heart as well as to the bundle branches in the ventricular septum.

COMMON ARRHYTHMIAS IN HORSES

Second degree atrioventricular block and **sinoatrial block** (*q.v.*) are characterized by dropped beats. Both arrhythmias are regarded as normal in the resting horse. This has been attributed to a high vagal tone, and the arrhythmias

disappear during exercise. The presence of **dropped beats** immediately after exercise may also be associated with vagal dominance during cardiac deceleration, and are probably not significant.

Sinus bradycardia, a resting heart rate of ⩽24 bpm, has been described as abnormal in racehorses and as a cause of poor performance. The resting heart rate in horses is greatly dependent on the degree of relaxation of the subject. However, some horses with sinus bradycardia (*q.v.*) have a history of **collapse**, possibly due to cerebral anoxia. The prognosis for this condition is poor if it is accompanied by an arrhythmia.

Third degree atrioventricular (AV) block (complete heart block) occurs occasionally in racehorses. This arrhythmia is associated with organic heart disease or severe drug toxicity, and rarely is caused by very high vagal activity. It is usually associated with poor race performance.

Atrial fibrillation, recognized by the absence of P waves or the presence of "flutter" (f) waves, and irregular R–R intervals, is probably the most common arrhythmia causing poor race performance. It is important to differentiate atrial fibrillation from the ECG affected by muscle twitching. Normal P waves can be identified on the tracing affected by muscle twitching. Atrial fibrillation (*q.v.*) can often be successfully converted to sinus rhythm with **quinidine sulfate**, with many affected horses returning to racing. It has been suggested that a P wave duration >0.16 s after conversion may indicate atrial disease.

Ventricular premature contractions (VPC), or ectopic beats, are generally described as being evidence of myocardial disease. The QRS wave is widened and bizarre in comparison to the normal wave. If the ectopic beat occurs before the sinus impulse, there is often a following compensatory pause. Alternatively, the ectopic beat may occur between two normal beats in resting horses, and sinus rhythm remains undisturbed. An extra beat is inserted in the rhythm.

Ectopic beats generally become more frequent during exercise and also become more frequent during heart rate slowing after exercise. It has been suggested that if ectopic beats (*q.v.*) occur infrequently, the prognosis may not be poor. The prognosis is poor if they occur frequently. VPC is one of the few arrhythmias in which a period of rest may be beneficial, and re-examination some months later is therefore justified.

Ventricular tachycardia (VT) refers to four or more ventricular extrasystoles at a rapid rate with regular rhythm. The QRS complexes in VT are normal in appearance. They are usually associated with myocardial disease (*q.v.*). Both VPC and VT can be found in horses with sepsis, hypoxia, viral disease, electrolyte imbalance and metabolic disease, and can be due to drugs such as digitalis and halothane.

ASSESSMENT OF HEART SIZE

Horses with severe heart disease may develop chamber hypertrophy, as in other species. Vectorcardiography and echocardiography can be used to investigate the presence of **ventricular hypertrophy**.

Measurement of **heart size** by ECG in healthy horses is popular with some veterinarians and horse trainers. This technique involves calculation of the heart score. **Heart score** is the mean of the QRS durations in the three bipolar limb leads, expressed in milliseconds. Proponents of the technique emphasize

that heart rates must be ⩽42 bpm, consistency of the horse's stance, and a standardized approach to measurement of the duration of the QRS complex. The form of the QRS wave can differ between horses and leads. Guides for the measurement of QRS duration in the different QRS wave forms have been published. The original study on this subject reported a correlation of 0.89 between heart score and the weight of the heart at post mortem. Unfortunately there have been no other published studies that confirm this finding. A recent study found **no significant correlation** between heart score and left ventricular wall measurements obtained echocardiographically.

The results of several investigations into the relationship between **heart score** and **race performance** are contradictory. Some studies have shown weak correlations between heart score and racing performance. Coefficients of determination in those studies indicated that 16–23% of the variability of racing performance was attributable to variability of heart score. However, other studies have shown no significant correlation between heart score and racing performance. An electrocardiographic and echocardiographic study of Thoroughbred yearlings in Ireland found no relationship between heart score and ECG measures of heart size and later racing performance in 125 2-yr-olds and 127 3-yr-olds. The study concluded that selection of young racehorses on the basis of heart score is unlikely to be successful. It seems that assessment of heart size by ECG is an inappropriate technique for prediction of athletic performance.

Assessment of young racehorses by echocardiography is now commonplace. Detection of **cardiac defects that could limit performance** is an important role for this examination. As well, indices of ventricular size are correlated with maximal oxygen uptake.

Measurement of the **whole-body oxygen transport** by measurement of maximal rate of oxygen consumption, or measurement of blood lactate variables during standard exercise tests, offers greater chances of success when trying to identify limitations to performance. In human sports science, these measurements frequently have coefficients of determination ⩾50% for running performance in events that are energetically similar to horse races. In Standardbred racehorses in Sweden, exercise tests with measurement of total red cell volume, heart rate and blood lactate after exercise have yielded encouraging results. Maximal trotting velocity was significantly correlated with several variables. Running speed and racing performance of Thoroughbreds has also been significantly associated with blood lactate response to exercise, with coefficients of determination of 40–50%.

T WAVES IN THE PERFORMANCE HORSE

The nature of the T wave in the ECG of the resting racehorse has been proposed as a means of assessment of horses with poor race performance. The presence of certain abnormal T wave forms has been suggested as a diagnosis of **myocarditis** (*q.v.*), or "heart strain". Normal and abnormal T waves have been described, based on the shape and direction of the T wave in six selected leads. However, recent studies have confirmed that abnormal T waves are not associated with poor performance. T waves do change in some horses during training, but this development does not reflect heart disease.

HEART RATE DURING EXERCISE

MEASUREMENT OF HEART RATE

The resting heart rate in the horse is generally in the range 25–50 bpm. In human athletes, the resting heart rate taken first thing in the morning is used as a guide to fitness and health. Highly trained human athletes, especially endurance athletes, have very low resting heart rates. If the resting heart rate is abnormally elevated, this could indicate loss of fitness, illness or "overtraining". Unfortunately it is difficult to use resting heart rate in horses as a measure of increasing fitness because the resting heart rate is subject to great fluctuation due to excitement. For example, **resting heart rate can fluctuate** between 25 and 120 bpm over a 30 s period, depending on the degree of excitement, fear or alarm.

It is therefore necessary to evaluate **heart rates during exercise** to assess fitness in racehorses. Heart rate measurements during exercise are important because there is a very close relationship between heart rate and metabolic rate. Many **heart rate meters** designed for use in exercising horses are now available. These meters use electrodes that are placed under the girth. Some meters have leads connecting directly to the receiver, which is designed to strap on to the saddle or jockey's leg. Others have remote receivers that can be worn on the wrist. A jockey can then keep an eye on the horse's heart rate while the horse is working. The meters also have a memory function, enabling later evaluation of the heart rates. Telemetric ECG can also be used to measure heart rates during exercise. This technique has the advantage of enabling simultaneous evaluation of the ECG during and after exercise.

HEART RATE AND SPEED

There is a **linear relationship between heart rate and speed** of submaximal exercise. This pattern is common to all horses during exercise. However, the actual heart rates that any horse records at the trot or slow canter can vary greatly, depending on age, fitness and health of the horse. The heart rate during slow work can also be elevated in horses with lameness or illness.

For all horses there is a work speed that does not result in an increase in heart rate. A plateau occurs, and no further increases in heart rate occur, regardless of increases in speed. The highest heart rate that can be recorded in such a test is called the **maximum heart rate** (HR_{max}). Maximum heart rates in horses are generally in the range 195–240 bpm. Each horse has its own individual HR_{max}, and the HR_{max} is not influenced by training. There does not seem to be any relationship between a horse's maximal heart rate and its fitness. However, it would be expected that racehorses with the higher velocities at which maximal heart rate is attained would have superior performance.

HEART RATE AND METABOLIC RATE

Heart rate is a good estimate of the relative amount of oxygen that is being used by the horse during exercise at slow and moderate work speeds. The relationship between relative heart rate and oxygen consumption during

submaximal exercise on an inclined treadmill is very close. The relative oxygen consumption (% of maximal) is equal to 1.6 times the percentage of maximal heart rate, minus 65. For example, a horse exercising at 75% of maximal heart rate is exercising at approximately 55% of maximal oxygen consumption. The speeds at which 100% of maximal heart rate and maximal oxygen consumption are attained are similar. Therefore improvements in maximal oxygen uptake will be reflected in lower heart rates during submaximal exercise, and a higher velocity at which the maximal heart rate and oxygen uptake are achieved.

EFFECTS OF EXERCISE

During **swimming**, heart rates may be as high as 180–200 bpm when horses are forced to work hard in the pool. Heart rates as low as 120–130 bpm have also been recorded.

Heart rates at **onset of slow exercise** can be erratic, taking several minutes to achieve a steady rate. This may reflect excitement, or can be related to a physiologic phenomenon in horses whereby the heart rate increases quickly at the start of exercise and then decreases after this initial "overshoot" to a lower rate over the next few minutes.

At the **start of fast exercise**, the increase in heart rate is very rapid. Within 30 s, the heart rate can be greater than 200 bpm. The rate of increase in heart rate at the commencement of exercise depends on the use of a "warm-up" period. With inadequate or absent warm-up, heart rates increase more slowly after the commencement of exercise. Such slow kinetics of heart rate would limit oxygen transport during the first 30 s of intense exercise. This causes a higher accumulated oxygen deficit during a race at maximal speeds, and would limit performance because the relative dependence on anaerobic ATP resynthesis would be greater.

RECOVERY PERIOD

After exercise, heart rates decrease rapidly in the first minute, and then continue to decline at a slower rate. Results of several studies demonstrate that **recovery heart rates** are lower after a standard exercise test as a result of training. However, routine use of recovery heart rates to assess fitness is not advised. The results can be easily influenced by excitement, and unless the exercise is carefully controlled on a treadmill, differences in intensity of exercise performed will make the results very difficult to interpret. Lack of standardization of the horse's activity both during exercise and during the recovery period makes useful interpretation of recovery heart rates very difficult.

Some advocates of interval training also contend that recovery heart rates are a guide to whether or not horses should continue with further workouts. A recovery heart rate of 120 bpm or less has been suggested as indicating that the horse is sufficiently recovered for more fast work. However, this approach must be used with caution, as heart rates less than 120 bpm can be found in horses 5 min after racing. There is no evidence that 5–10 min recovery heart rates after fast exercise are a good guide to recovery of body temperature or acid-base status.

Post-race heart rates can be used as a guide to inadequate recovery, as heart rates that remain elevated post exercise are a warning sign. Veterinarians who are requested to check horses that may have performed poorly in races should **routinely check** the heart rate and rhythm. Heart rates that remain >130 bpm for 5–10 min after exercise suggest a poor recovery. Such a result could indicate that the horse is not fit enough, or that the horse may have clinical problems such as atrial fibrillation, respiratory infection or lameness (*q.v.*). Dysrhythmias should be identified, and followed up with ECG for accurate diagnosis.

Evaluation of heart rate recovery is a vital part of the assessment of horses during **endurance rides**. Horses with abnormally elevated heart rates at checkpoints are not allowed to continue. Specific rules differ nationally, but generally require that heart rates are <55–60 bpm 30 min after arriving at the checkpoint. Endurance riders should ensure that their horses are accustomed to the approach of strangers to measure heart rates, so as to eliminate the **effect of excitement** on recovery heart rates during competition.

WARM-UP EXERCISE

Warm-up prior to strenuous exercise, such as 5 min trotting, ensures a more rapid increase in heart rate and oxygen uptake at commencement of strenuous exercise. This is beneficial for horse performance, as the horse is more rapidly able to mobilize the transport of oxygen to the skeletal muscles, so minimizing the accumulated oxygen deficit. All horses should undergo a trot and canter warm-up before gallops and racing. Many Standardbred horses in Australia are now given two warm-ups prior to racing. Horses are often jogged for 2400 m 30–60 min before racing, and again 5–10 min before racing. Some trainers also let the horse exercise at near racing speeds for 200–300 m 5 min before the race.

Unfortunately, Thoroughbred horses do not always have the opportunity for adequate warm-up prior to racing. This omission probably contributes to premature fatigue and so **limits performance**. Fatigue causes inefficient locomotion, and therefore gait abnormalities may occur, possibly contributing to soft tissue trauma during races. Obviously it can be very difficult to give an adequate warm-up before some Thoroughbred races, especially when the start is near the saddling enclosure. There is still much to learn about the best intensity and duration of warm-up exercise for horses, and the ideal interval between the warm-up and the subsequent exercise.

TRAINING

There is a predictable effect of training on heart rate during slow exercise, but little change in either maximal heart rate or resting heart rate. During submaximal exercise, heart rate falls by approximately 20–30 bpm. This means that, at a set speed of exercise resulting in heart rate less than HR_{max}, training will decrease the heart rate at that speed by approximately 20–30 bpm, or more. Therefore the horse can work at faster speeds at the same heart rate. The increase in blood volume is thought to contribute to this physiologic response to training. Stroke volume increases, and so the same cardiac output can be maintained with a lower heart rate.

Several other factors can influence heart rate during submaximal exercise. If the horse developed lameness, muscle soreness, respiratory infection or another illness, the heart rates at the same speed could increase. Likewise, if the horse stopped training, the loss of fitness during detraining would be reflected in a higher heart rate during slow exercise.

FITNESS TESTS

The heart rate of Thoroughbred horses during slow exercise on a racetrack can vary enormously due to excitement. It is therefore very difficult to conduct a standard exercise test in that environment. The results of exercise tests are more reliable when the tests are conducted on treadmills, and then only in horses which have been adequately accustomed to treadmill exercise, so reducing the effect of excitement.

Heart rate measurement during **treadmill fitness tests** usually employs a stepwise exercise test. These tests involve measurements at several slow work speeds. The treadmill speed is increased every 1–2 min, and heart rate is recorded in the last 10–15 s of the exercise at each speed. Graphs of treadmill speed versus heart rate are then plotted. Several indices of performance have been suggested. Most popular is ***V_{200}*, the treadmill velocity that results in a heart rate of 200 bpm**. Other workers use similar indices, such as V_{140} and V_{160}. If the fitness of different horses is to be compared, the velocity at which the horse reaches a speed corresponding to maximal heart rate should be measured (V_{HRmax}).

V_{200} has also been calculated using **racetrack exercise tests** in trotters. The horses were exercised over 1000 m at four increasing submaximal speeds, with the driver maintaining a constant speed during each run. The fastest speed was chosen so that it would result in a heart rate of just >200 bpm.

An alternative index of fitness based on heart rate measurement during exercise is calculation of HR_{10}, the heart rate at a constant speed of 10 m/s. This index is suitable for trotters, pacers and other horses that can be exercised at a set speed (10 m/s) for 3000–4000 m. Both this index and V_{200} calculated from a racetrack exercise test are negatively correlated with maximal trotting speed over 1000 m. A low heart rate response to the exercise tests was associated with faster 1000 m times, with coefficients of determination of 55% and 36%, respectively.

Several studies have described simple field tests for galloping horses. Exercise testing on a treadmill allows strict control over environmental conditions and test protocol, as well as permitting a large range of testing procedures. However, it cannot take into account many factors in the normal competition environment, such as the effect of rider and tack, terrain, surface and wind resistance. Treadmill exercise testing also requires expensive, sophisticated equipment. The major advantage of field-based exercise testing over treadmill testing is that the measurement can take place in the horse's usual competition or training environment. In addition, field-testing precludes the need to transport a horse to a specialist laboratory and obviates the need for periods of acclimation to treadmill exercise.

Typically an exercise test involves a series of exercise steps at predetermined speeds and durations, with constant velocity of exercise during each step. Inability to standardize exercise and track surface conditions often limits the interpretation of results from field tests. Comparison of results obtained from

different tracks is also difficult, because variations in track geometry, surface and condition can significantly affect the responses to exercise. Furthermore, gait and physiologic variables are significantly affected by differences in track conditions.

The following field exercise test was used to assess **fitness in 3-day event horses**. Each horse was given dressage work 20–30 min before the test. The exercise test was performed after a uniform warm-up of 5 min trotting, and consisted of four bouts of exercise on a 450 m undulating grass track at progressively increasing speeds, with a recovery of 400 m at the trot between each repetition. Target speeds for each step were 250 m/min (trot), 350 m/min (slow canter), 450 m/min and 600–650 m/min. Horses were timed with a stopwatch over each step to determine average velocity, and riders were asked to maintain a consistent speed if possible during each step of the exercise test. Heart rates were recorded, and then related to velocity for each step of the test in order to calculate V_{200}.

It has been suggested that heart rate meters should be used as a guide to the intensity of exercise during training. At heart rates of 130–150 bpm, horses can undertake prolonged exercise without fatigue due to the accumulation of lactate and hydrogen ions in the skeletal muscle. However, prolonged exercise at such heart rates is likely to be limited by dehydration, electrolyte disturbances and hyperthermia.

Some workers recommend that medium intensity work should be carried out at exercise speeds that produce heart rates of 200 bpm. This is based on work that implies that HR_{200} is the work rate at the "anaerobic threshold". It has been demonstrated that training horses at exercise intensities that result in blood lactate concentrations of 6–12 mmol/L results in an increase in muscle buffering capacity. This response will help limit fatigue during intense exercise.

BLOOD LACTATE MEASUREMENT

LACTATE PRODUCTION

Accumulation of lactate in muscle cells and in the blood is a **normal consequence of fast exercise** in the horse. At low speeds, the horse is able to generate sufficient energy by catabolism of glycogen, glucose and fat. This metabolic process uses oxygen to generate ATP and is referred to as **aerobic**. At higher speeds, aerobic metabolism does not regenerate ATP quickly enough.

Exercise at speeds greater than approximately 700–800 m/min recruits fast twitch skeletal muscle fibers. These fibers can be classified as being highly oxidative or highly glycolytic in nature. At fast speeds, recruitment of fast twitch, highly glycolytic muscle fibers results in accumulation of **lactate anions and hydrogen** ions in the muscle cells, due to the contribution of **anaerobic** glycolysis to ATP resynthesis. Both these ions diffuse into the extracellular fluid. It is generally thought that the stimulus for anaerobic glycolysis in skeletal muscle fibers during fast exercise is a limitation to the supply of oxygen at the cellular level.

The production of many molecules of lactate and hydrogen ions results in **acidosis** of both the muscle cell and the blood. The increasing acidity of

muscle cells is implicated in fatigue during intense exercise. In any horse at top speed for approximately 800 m, the accumulation of lactate and the concomitant cellular acidosis has a negative effect on energy production by anaerobic glycolysis. The rate of ATP production is decreased, and the animal reduces speed.

NORMAL BLOOD LACTATE CONCENTRATIONS AT REST AND AFTER EXERCISE

Resting blood lactate concentration in the horse is approximately 1–1.5 mmol/L. At low speeds this value does not change greatly from the resting value. At moderate speeds lactate begins to accumulate in the blood. Accumulation of lactate in blood occurs most quickly when the work speed is faster than that at which blood lactate is approximately 4 mmol/L. This work speed at which blood lactate is 4 mmol/L is often referred to as the **anaerobic threshold**, or the speed at onset of accumulation of blood lactate (OBLA). It is also frequently referred to as $V\text{La}_4$. $V\text{La}_4$ is therefore the work velocity which results in a blood lactate of approximately 4 mmol/L. This value is derived from inspection of graphs of exercise speed (on the *X* axis) plotted against blood lactate concentration (on the *Y* axis).

At speeds greater than $V\text{La}_4$, **lactate accumulates rapidly** in the blood. The general relationship between velocity and blood lactate is therefore usually described as exponential. However, if sufficient steps are used in the exercise test, the relationship is described by two straight lines, with an obvious velocity at which the blood lactate begins to accumulate in blood.

LACTATE CLEARANCE

After a race, blood lactate concentrations are usually >20 mmol/L. It is normal for the blood and muscle lactate concentration to gradually decrease over a 1–2 h period after a race or fast work. Acidosis of muscle and blood is a normal result of fast work, and this **acidosis is rapidly reversed** by the horse's own metabolism. It is not necessary to medicate horses with salts such as sodium bicarbonate and citrate, which are marketed to prevent acidosis in racehorses. Horses do not become chronically acidotic in training. Any acidosis is due to a temporary accumulation of lactate and protons, a **normal physiologic response** to fast exercise. Acidosis is not a cause of tying up (*q.v.*).

The rate of decrease in blood lactate after exercise is affected by the activity during this period. For example, blood lactate decreases more quickly after strenuous exercise if the horse is trotted, rather than walked. The slowest rates of blood lactate clearance are found in horses that do not walk or trot at all after the exercise. However, prolonged slow exercise after racing or other fast exercise is likely to compromise recovery of normal body temperature, and is not normally recommended.

LACTATE AS AN ENERGY FUEL

Lactate can be used as a fuel for energy in muscle fibers with high oxidative capacities. These fibers are found in the skeletal muscle and in the heart,

where lactate can be used as a fuel aerobically. Some lactate can be used as a fuel during exercise. The role of lactate as an energy substrate at various speeds in horses is not known, although it is probably not an important fuel source during slow work.

LACTATE AND FITNESS

Many studies of horses trained on both treadmills and on racetracks consistently demonstrate that **training results in lower blood lactate concentrations** at the same work speed. The speed at which blood lactate begins to accumulate rapidly, $V\text{La}_4$, also increases. The horse is able to work at a higher speed without accumulating lactate and without becoming acidotic.

$V\text{La}_4$ (*q.v.*) is a common measurement in human athletes to estimate **endurance fitness**. $V\text{La}_4$ tests are also suitable for any athletic horse as a means of measuring increasing stamina with training. If more than one horse is tested, measurements of $V\text{La}_4$ enable comparisons of the relative stamina in each horse. $V\text{La}_4$ measurements every 2–3 wk also enable measurement of changes in fitness through the training program. However, $V\text{La}_4$ measurements have the disadvantage of requiring several blood collections and analyses. A simple, one-step exercise test can be designed to give the same information (see Box 16.2). Details of the design and conduct of such tests for horses are outlined below (*q.v.*).

LACTATE ASSAYS

When blood is collected for lactate assays, it should be added to tubes containing a suitable anticoagulant and inhibitor of glycolysis. **Fluoride and oxalate combinations** are suitable, as the blood stores well at room temperature for at least 2 days in those chemicals. However, if possible, blood should be stored in a **refrigerator or on ice** until analysis. Individual laboratories should be consulted concerning ideal storage conditions, as different centers use different techniques to conduct the analysis.

Lactate assays can also be conducted on plasma. However, plasma and whole blood lactate concentrations in blood collected after exercise are not equivalent. Plasma lactate concentrations are 140–150% of concentrations found in whole blood, due to **unequal distribution** of lactate between plasma and erythrocytes in horse blood after exercise. Plasma and whole blood lactate concentrations should therefore **not be directly compared**.

In the past, lactate assays have been complicated and not readily available. The analysis of plasma or serum for lactate concentration has been greatly simplified by the development of rapid analyzers.

LACTATE AND TRAINING

Blood lactate measurements are a common feature of the normal training routine of many human athletes. The rationale is that training should be very efficient, neither too strenuous nor too low in intensity. Many human athletes are constantly subjected to blood lactate measurements in their training

for this purpose. This helps to maximize fitness and minimize the risk of overtraining.

This technology has not been widely applied to the training of horses. However, the technique does offer advantages. Since horse racing is an exercise that depends on anaerobic and aerobic capacities, it is important to train the muscles to metabolize glycogen anaerobically (for speed) and to resist fatigue. It has been suggested that if horses are trained at speeds that constantly produce high concentrations of lactate in muscle during training, there is a risk of overtraining and associated loss of performance and interest in racing. This risk may be reduced by giving racehorses more exercise that produces only moderate increases in blood lactate concentrations, in the range 4–10 mmol/L.

EXERCISE TESTS

INTRODUCTION

There is no better test of racing ability than **performance** on the racetrack. However, some owners and trainers of racehorses appreciate having an approximate guide to their horse's ability based on scientific measurements. Also, veterinarians are often requested to assess racehorses with poor race performance. In the past, tests such as blood analysis in resting horses and ECGs for heart score measurement were popular in some countries. Unfortunately, these approaches are of limited use. In one study of 131 racehorses presented to a university clinic for poor performance, all hematologic and plasma biochemical results were within the laboratory's normal ranges.

A superior approach is to assess changes in **physiologic variables during and after exercise**, using techniques commonly employed in human exercise laboratories. This approach may well be applicable to racehorses as well as to human athletes.

The basis of these tests is usually measurement of **blood lactate and/or heart rate response to a standard exercise test**. Exercise tests conducted at treadmill facilities may also incorporate measurements of body temperature, respiratory gas exchange (oxygen consumption and carbon dioxide output), blood volume, arterial blood gas tensions, hematology and serum biochemistry. Such tests may greatly assist the diagnosis of poor performance problems in horses, when combined with the usual complete clinical examination in the resting horse. Recently, the **endoscopic assessment of upper airway function** during gallop exercise on a treadmill has become part of the assessment of horses with suspected upper airway problems (*q.v.*), and for assessment of responses to upper airway surgery.

Exercise tests may consist of assessment of the physiologic response to a single bout of exercise, or may involve tests in which the horse undertakes a series of steps at gradually increasing speeds. The one-step approach to exercise testing has also been validated in human athletes. Multi-step tests are standardized so that results can be compared. The tests can be continued until the horse cannot keep pace with the treadmill, so that the responses to exercise at submaximal and maximal intensities are assessed.

STANDARDBRED RACEHORSES

A simple, **multi-step exercise test** for Standardbred racehorses (Box 16.1) enables measurement of $V\text{La}_4$ (*q.v.*).

It is also possible to measure fitness with a **one-step exercise test** (Box 16.2). In this test, the horse must work over a set distance at an even, set speed. In fit

Box 16.1 The multi-step exercise test for Standardbred racehorses

1. Suitable, standardized warm-up routine
2. Four workouts over 1000 m (5 furlongs). Suitable velocities for these four steps are 550, 650, 700 and 750 m/min. The time for each 1000 m is recorded, ensuring that the pace is even throughout the work
3. Collect blood 3 min after each step.

The driver should attempt always to use the same speeds in each exercise test. A speedometer can be used to help standardize this important aspect of the test. Bicycle speedometers can be fitted to the sulky. Horses should walk for a set period of time between each of the four steps. Three to 5 min would be suitable. It is important that the time period between each heat is kept constant for all horses in all tests.

When the results have been returned from the laboratory, a plot of speed versus lactate is drawn. By drawing a line horizontal to the 4 mmol/L level, the $V\text{La}_4$ can be calculated directly from the graph. In trained Standardbred pacers, $V\text{La}_4$ ranged from 615 to 705 m/min in a similar exercise test.

The blood lactate response to a four-step exercise test described above will depend on many factors. These include:

1. The inherent ability of the horse
2. Stage of training: the blood lactate response to the exercise test will gradually decrease as the horse gets fitter; the $V\text{La}_4$ therefore increases
3. Type of training used: endurance training is more likely to more rapidly lower the lactate values than is pure sprint training
4. Length of the track on which the test is conducted
5. Type of track, e.g. undulations and track surface
6. The velocities of the four steps of the exercise test, and constancy of the horse's pace during the test
7. Time after exercise that the blood sample is collected: this factor should be kept constant in each test
8. Warm-up and warm-down procedure used
9. Correct storage of blood sample.

It is important that an attempt be made to **standardize** points 4, 5, 6, 7, 8 and 9 in particular, so that the procedure is the same each time an exercise test is performed.

Veterinarians interested in using these tests in Standardbred horses should develop their own exercise test routine on the client's racetrack, as the results will differ on tracks of different surface and length.

Box 16.1 continues on page 1087

Box 16.1 The multi-step exercise test for Standardbred racehorses [continued]

In general, the horses with the best **stamina** (lowest lactates during exercise, or highest $V\text{La}_4$) in an unfit state are also the horses with the best stamina after training. It is therefore possible to test young horses, or horses just entering training, to get some idea of which horses in a group are likely to be poor performers. However, until a trainer has the results from many exercise tests on many different horses, and is confident in the results, no horse should be retired from the stable on the basis of the exercise test results.

Box 16.2 The one-step exercise test for Standardbred racehorses

1. Standard warm-up procedure, for example jogging for 5 min
2. Standard mile (1600 m) time, for example 2 min 16 s, at an even pace (4×34 s quarters)
3. Standard warm-down procedure before taking blood sample at 3 min after exercise
4. Store blood in refrigerator or in ice

The obvious disadvantage of this one-step test is that minor variations in the time for the mile (1600 m) will affect the results. For example, if the horse works at 2 min 12 s or 2 min 20 s, the results are not valid for that test, and the test has to be repeated. In a four-step test, the speed of each step is not so crucial.

The blood lactate response to this exercise test will vary considerably. The fittest horses will generate lower lactates at this speed than less fit horses.

or nearly fit Standardbred racehorses, it is suggested that the guidelines are followed closely for best results. The one-step test in Box 16.2 is too difficult for unfit horses. They should be tested using a mile rate of 2 min 40 s (40 s quarters).

THOROUGHBRED RACEHORSES

Thoroughbreds can also be tested on the racetrack, following the principles outlined above for Standardbred horses. However, one-step testing of Thoroughbreds is a much more difficult task. The exercise test requires the horse to work at a set speed (approximately 15 s per furlong [200 m]) over a set distance. This is harder to achieve in Thoroughbreds than in Standardbreds.

Thoroughbreds have been tested by conducting a **two- to three-step test** (Box 16.3). This test can be repeated on successive days, or over a 7-day period. A graph of blood lactate concentration versus time for the 1000 m (5 furlongs) is then drawn, using at least three data points. Horses with **superior race performance** have **lower blood lactate concentrations** at work speeds in the range tested. Horses with consistently high blood lactate responses in this test are generally poor performers, despite the best of training. Their poor performance may be due to their inherent structure of heart, lung and muscle.

Box 16.3 The two- to three-step exercise test for Thoroughbreds

1. Suitable warm-up trot and canter, as per normal training routine
2. The horses work on firm ground over 1200 m (6 furlongs). The jockeys are asked to accelerate to a speed of 14–16 s per furlong from the 6 furlong mark, and then maintain that speed for 5 furlongs
3. The time for the last 1000 m (5 furlongs) is recorded
4. A blood sample for lactate analysis is collected 3–5 min after exercise

The results of this track test sometimes produce blood lactate values that do not fit the expected pattern. The inability to have strict control of the rate of acceleration at the start of the gallop can contribute to this problem. Horses that accelerate more quickly at the start of the gallop will have unusually high lactates. Likewise, horses that vary their speed of galloping or pull against restraint by the jockey during the 5 furlong workout will also have unusually high lactate values, which should be ignored.

Any decision on the results of a track exercise test should be based on results from at least three or four separate tests, eliminating any high lactates that do not lie close to a line of best fit for at least three data points.

It may also be due to disease of the respiratory tract or heart (*q.v.*). If there is no evidence of any disease causing poor oxygen transport to the muscles, then it must be concluded that the horse does not have the optimal physiologic make-up for racing.

EXERCISE TESTS AND THE HEMOGRAM

Exercise tests can be used to help diagnose anemia (*q.v.*) in racehorses. The resting hemogram can be **highly variable** in an individual horse, and there is no predictable relationship between hematologic findings in resting horses and the hematologic findings after maximal exercise. In English Thoroughbred racehorses, the mean hematocrit 3–14 min after 6 furlong (approximately 1200 m) races averaged 59% (SD 3%). After longer races, mean hematocrit values were 63% with 95% confidence limits of approximately 54–70%. There is no relationship between race performance and post-maximal exercise hemogram in the Thoroughbred. A correlation has been demonstrated between total red cell volume (RCV) and performance of Swedish trotters. Measurement of RCV necessitates measurement of plasma volume and post-exercise hematocrit.

Collection of blood 5–10 min after fast exercise at or near racing speeds can help with the diagnosis of anemia in those horses with low hemograms at rest. Published data suggest that horses with a 10 min post-race hematocrit $<50\%$ are probably anemic. Veterinarians should establish their own **standardized protocol** for checking post-exercise hemograms, and establish their own normal values in a range of horses. The hematocrit gradually decreases after exercise, so a constant time of blood collection post exercise must be used.

TREADMILL EXERCISE TESTS

Treadmill exercise tests are usually employed to assess **stamina**, or endurance fitness, by measuring heart rate, blood lactate and oxygen consumption (maximal aerobic capacity) during exercise. There has only been one report of measurement of anaerobic capacity in horses. Obviously **anaerobic capacity** will be a major contributor to the **strength and sprinting ability** of a horse. The best test of sprinting ability and acceleration is a time trial on a racetrack.

Stamina is an important component of successful racing over all distances, but it is of course particularly relevant to middle and longer distance racing. Performance in Quarter Horse racing is unlikely to be greatly dependent on stamina however, as the events are completed in less than 24 s.

Exercise tolerance tests are conducted by exercising horses at set treadmill speeds and angles, and measuring the body's physiologic responses to that exercise. Superior horses cope with the exercise more easily, and the response to a set amount of exercise changes with training. In general, the horse that is able to maintain a high work rate **without reliance on anaerobic energy production** has superior stamina.

A simple exercise test for **race-fit horses** is as follows. The treadmill angle is set at 6° (or a 1 in 10 slope). The horse is trotted for 2 min (at 4 m/s), followed immediately by 2 min slow cantering (6 m/s). The horse is then walked on the treadmill for 4 min, and then given 2 min exercise at 10 m/s.

Blood is collected into fluoride oxalate tubes 3 min after the finish of the exercise test, and is analyzed for whole blood lactate concentration. As horses get fitter, they produce less blood lactate in response to a standardized exercise test. Race-trained Thoroughbred horses with blood lactates >8 mmol/L after the test described above have definite limitations to stamina, and are unlikely to be good racehorses. Racehorses with superior stamina, or endurance fitness, have blood lactate concentrations of <4 mmol/L after the test.

Incremental treadmill exercise tests, with measurements of heart rate and blood lactate at various speeds, can also be conducted. Such tests enable calculation of indices of fitness such as V_{200} and $V\text{La}_4$ (*q.v.*). Collection of blood at each speed necessitates stopping the treadmill after each step, or placement of an IV catheter. Sterile heparinized saline solutions can be used to maintain catheter patency during the tests. Such tests are now common at research centers with treadmills for assessment of poor performance. Measurements of heart rate, blood lactate and oxygen consumption are usually conducted during submaximal exercise and during exercise at maximal intensities.

LIMITATIONS OF TREADMILL TESTS

It should be remembered that all tests of fitness using blood lactate analysis during or after submaximal exercise are an assessment of the **endurance fitness**, or stamina, of the horse. The results have little relevance to the ability of a horse to accelerate quickly at the start of a race, or to the top speed of a horse over 2 furlongs (400 m). These factors are, of course, of great importance to the ability of racehorses in events lasting 2–8 furlongs.

Stamina is a vital component of all racehorses except the Quarter Horse. Stamina, or "staying" ability, is obviously more important in the longer distance events. Performance in Standardbred and Thoroughbred races depends on many factors, but **both stamina and sprinting ability** are paramount. A horse with superior speed, strength and acceleration but only moderate stamina may still win races, especially over the sprint distances. Likewise, at the other end of the spectrum some horses have superior stamina, but poor speed over 2–3 furlongs. These horses cannot be expected to perform very well in Thoroughbred or Standardbred races.

It should not be expected that results of treadmill tests will detect very small differences in fitness between horses. For example, it would not be possible to distinguish between 20 horses of similar grading, even though there might be several lengths between them at the end of a race. Fitness tests that try to classify horses on the basis of their stamina should be restricted to rating a horse as having good, average or poor stamina, dividing populations of racehorses into large subsections.

The blood lactate response is therefore a **guide to ability**, and the other factors that contribute to racing success must not be ignored. However, a treadmill study of 12 English Thoroughbred racehorses indicated that 47% of the variability in *Timeform* rating (a handicap rating system) was due to variability in their blood lactate response to treadmill exercise, using a test similar to that described above. The better horses had a lower blood lactate after treadmill exercise at 10 m/s on a treadmill inclined at 10%. Similar results have been reported in trotting horses. The **blood lactate response to exercise** is a very important determinant of likely success or failure on the racetrack.

MEASUREMENT OF MAXIMAL OXYGEN CONSUMPTION

Measurement of the maximal rate of oxygen consumption is performed as part of exercise tests at many clinics. The **maximal rate of oxygen consumption (VO_2max)** is expressed as mL O_2/min/kg. In fit racehorses, the range is approximately 125–190 mL/min/kg. This value expresses the ability of the horse to **transport oxygen from the atmosphere to the skeletal muscle mitochondria and use it to regenerate ATP**.

The value of VO_2max for any horse depends on the product of **maximal cardiac output** and the **amount of oxygen** extracted from the arterial blood supplying all tissues during exercise. Of course, during exercise the majority of the arterial blood is directed to the active skeletal muscle. Rates of maximal oxygen consumption increase by 15–20% with training, mainly due to increases in **stroke volume**.

In human athletes, VO_2max is highly correlated with performance in many running events. Running ability of Thoroughbred horses racing over 2000 m on an 800 m track was moderately correlated with VO_2max ($r = 0.45$) in one study. It is highly unlikely that horses with VO_2max values in the lowest three deciles are destined for good performances on the racetrack in events lasting more than 60 s. Standardbreds with superior performance also had higher maximal oxygen uptakes than values in a group of horses with inferior performance.

CONCLUSIONS

In conclusion, exercise tests on racetracks are more suitable for pacers and trotters, but are difficult to apply in Thoroughbreds. Treadmill exercise tests are generally superior to track tests, as the test conditions are easily standardized. Most horses become accustomed to treadmill exercise after 3–5 exposures to the routine. Treadmill exercise tests facilitate examination of metabolic, cardiovascular, hematologic and respiratory responses to exercise. As well as being a useful research tool for the study of equine exercise, such tests can be used routinely to monitor fitness and assess performance potential in equine athletes. Field tests can be used to assess fitness, but standardization of the exercise test protocol can be more difficult. However, field tests have the advantage of being conducted in the horse's own environment, and veterinarians should explore ways of using field fitness tests to assess equine athletes, using measurements of heart rate and/or blood lactate concentration.

EFFECTS OF TRAINING ON BONE

INTRODUCTION

It is over 200 years since the relationship between mechanical stress and bone structure was first appreciated. In 1892, the German anatomist Julius Wolff reported that "every change in the function of a bone is followed not only by certain definite changes in its internal architecture, but in its external conformation as well, in accordance with mathematical laws". Since then some elegant studies have been carried out in both humans and animals to investigate the response of bone to a variety of biomechanical situations. However, it is only more recently that any investigations on racehorses have been undertaken to try and monitor the effects of training.

The specific effects of exercise on bone have been shown to depend not only on the animal's age but also on the duration and intensity of training. This section deals with some of the specific responses that take place in cortical bone of young Thoroughbreds following maximal exercise (galloping) and in their practical application to problems of exercise-induced lameness (e.g. shin soreness).

BONE BIOMECHANICS

Bone has a dual role, to support the body (**skeletal homeostasis**) and act as a source of calcium (**mineral homeostasis**). It is a dynamic tissue in which changes continue to take place throughout life to maintain optimal strength and to adapt to external forces. This involves a continual and coordinated activity of forming (by osteoblasts) and removing (by osteoclasts) bone, which is termed remodeling. The actual structure of bone is very complex, but its basic make-up is a collagen framework hardened by hydroxyapatite mineralization to give it strength.

The skeleton of the horse reflects the load-bearing competence of its individual components; in other words bones are capable of adapting to the prevailing biomechanical stresses (**load bearing**). In racehorses, the extent of load

bearing is essentially determined by the training regimen to which they are subjected. The objective of training is to increase skeletal strength while limiting the possibilities of exercise-induced injury.

Although the actual mechanisms of response to loading are poorly understood, it is clear that bone readily adapts either to imposed stress or to the lack of any stress by forming or losing tissue. **Bone hypertrophy (modeling)** occurs when stress is applied. Lack of exercise has been shown, particularly in humans, to be one of the most significant factors in stimulating bone turnover, initially seen as remodeling but leading eventually to osteoporosis. The withdrawal of any functional loading of the bone also results in rapid loss, although this can be reversed by exposure to short daily periods of suitable dynamic loading.

The effects of loading and unloading of bone are well known, but the means by which the specific signals are recognized at the cellular level are not yet understood. It is now believed that there is a limiting strain range called the **minimum effective strain (MES)** that turns these mechanically controlled responses "on" and "off". It has been suggested that, to switch on a modeling response, ~1500–3000 μ strain (microstrain) is required. However, a much smaller threshold strain range (~100–300 μ strain) is necessary for the mechanical control of remodeling.

It has also been shown that bone requires stimulation by appropriate strain rates for optimal maintenance of strength. Bones resist compression twisting and bending in many directions and can be trained to resist these forces. A dose–response curve has been produced that shows strains below a certain peak magnitude are associated with bone loss while those above that level not only protect the existing bone tissue from resorption, but also provide an **osteogenic stimulus** resulting in deposition of an amount of new bone proportional to the degree of "overstrain" engendered. Once a loading regimen has been repeated so that it is recognized by the bone, subsequent repetitions apparently do not affect the nature or magnitude of the adaptive response. This, of course, has important connotations for training of racehorses in trying to reduce exercise-induced lameness by limiting excessive amounts of fast work.

POOR SKELETAL CONDITIONING AS A CAUSE OF "WASTAGE"

The principal aim of any training program is to condition all the systems of the body to maximal athletic performance while achieving the minimum of damage. Knowledge of the effects of training and the ability to maximize potential in relation to the muscular and cardiorespiratory systems is now quite extensive. However, while appreciating the importance of training effects on bone and joints, there is very little published information available. This is regrettable when one considers that surveys of "wastage" by insurance companies and in the racing industry have highlighted lameness and orthopedic conditions as being the most important cause of losses.

The most serious cause of exercise-induced lameness in young Thoroughbred horses in training is associated with **sore shins** (bucked shins, dorsal metacarpal disease) (*q.v.*). This condition is particularly common in 2-yr-olds during their first year of training. It has been recognized for over a hundred years as being

associated with uni- or bilateral lameness after fast work on hard ground. The pathogenesis is not completely understood, but it involves both damage to the periosteum of the dorsal cortex and microdamage to the underlying cortex.

Despite its frequency, little seems to have been done to reduce the incidence of **sore shins** (*q.v.*). The condition is particularly common in the USA, Canada and Australia, but is less commonly seen in the UK. Surveys in the USA indicate a 65–70% incidence; in Australia the incidence is at least 70%; while in the UK two surveys estimated the incidence at ⩽17%. Shin soreness causes wastage through lost time during training and therefore appearances on the racetrack. Periods of absence from training vary greatly, but range from 1 to 6 mo, and a small percentage of horses are lost to racing completely. Although many horses only go shin sore once, the problem can recur both in 2- and 3-yr-olds. In the more chronic form of the condition **stress fractures** (*q.v.*) of the dorsal cortex occur that significantly prolong recovery and predispose to further bouts of lameness.

There is no single answer or therapeutic panacea for shin soreness, but research is being carried out to identify the specific conditions and intensity of exercise required to trigger the condition, so that training programs can be adjusted to reduce susceptibility.

METHODS FOR ASSESSING BONE QUALITY

It is necessary objectively to assess and sequentially to monitor changes in bone strength in order to follow the effects of training on cortical bone in racehorses. The non-invasive measurement of **bone quality** in the horse has traditionally involved the use of **radiography**. There are now some other modalities available to evaluate cortical bone quality and strength. These include **ultrasound speed** in bone, which gives an estimate of its stiffness and elasticity, and **radiation-based assessment**, which gives a direct measurement of **bone mineral content (BMC)** or **bone mineral density (BMD)**.

Quantitative ultrasound (QUS)

The speed of an ultrasonic wave (speed of sound) through bone is related to the modulus of elasticity and the specific gravity of the bone. There is now a simple method for determining ultrasound speed in cortical bone by passing a longitudinal beam of ultrasound between two transducers along the cortex of the third metacarpus. The speed of ultrasound is calculated from the time of flight and the distance between the two transducers in m/s. The precision of this method is <3.0% and normal values for young racehorses range from approximately 3700 to 4200 m/s.

Radiation-based assessment of bone

An accurate measurement of bone mineral mass by single photon absorptiometry was developed in the USA in the early 1960s. The principle of the technique is to scan the bone with a narrow beam of low energy photons from a monoenergetic radionuclide source and measure the reduction in attenuation

using a scintillation detector. A direct relationship exists between the number of photons absorbed by the bone and its mineral content. The radionuclide source used for horses is americium-241, which has the photon energy required (60 keV) to penetrate the dense cortical bone of the equine metacarpus. The precision of this technique in the live horse is around 2%. The method takes a little longer than that for ultrasound speed and the limb is required to be surrounded by a soft tissue equivalent material. Normal values for BMC in adult horses range from 8.0 to 10.0 g/cm.

Dual energy X-ray absorptiometry employs two beams of photons: one of higher energy and one of lower energy. This is the most widely used technique for measurement of BMD in man. A portable system is now available for use in the horse.

Invasive methods

There are a number of important invasive methods used to assess bone strength and quality in the horse.

1. Mechanical testing in vivo using rosette strain gauges, or on excised bones to measure Young's modulus and ultimate strength
2. Microradiographic and histomorphometric examination of bone to study the static changes in bone due to exercise, and by using intravital bone labeling to appreciate the dynamic effects of bone turnover
3. In vitro studies of the orientation of collagen in cortical bone using polarization microscopy, which has an important connotation with functional loading.

EFFECTS OF EXERCISE ON BONE

The effects of exercise on cortical bone have been examined in growing (1–2-yr-old) and adult horses at both submaximal and maximal intensities. These studies reveal that submaximal exercise even for prolonged periods ($\leqslant$6 mo) in young and adult horses does not dramatically alter the mass or density of cortical bone in the metacarpus. In contrast, training at high speeds results in significant increases of ultrasound speed in both adult Thoroughbred and Standardbred horses. This increase in ultrasound speed is only approximately 1.5% ($\sim$50 m/s) and is thought to reflect a small increase in bone density due to a reduction in bone porosity.

Maximal exercise in young Thoroughbreds (15 mo old) at speeds $>$12 m/s results in a rise in ultrasound speed, but also more substantial increases in bone mass. This intense type of exercise causes a decrease in **intracortical porosity** that is reflected in high ultrasound speed readings. However, the increase in ultrasound speed is never greater than 1–2% and differs from the non-exercised horses only by 3–4% ($\leqslant$120 m/s). These small changes may have an important effect on bone strength since bone strength is proportional to the density cubed.

A more dramatic change in response to fast exercise is the alteration in **distribution of compact bone** that occurs in young horses. Histomorphometric examination of bone samples from these horses reveals that both modeling

and remodeling of bone have been substantially changed. First, intracortical bone remodeling is significantly reduced by decreasing bone porosity. Second, the cross-sectional morphology of the metacarpal shaft is altered, resulting in greater bone formation on the dorsal periosteal and endosteal surfaces.

It appears that increase in bone formation on the dorsal periosteal surface does not occur at any appreciable rate until speeds greater than 12 m/s are achieved. It has been postulated that the signals that regulate intracortical bone density may be different than the signals that cause the enlargement of the cortex. There is now increasing evidence that important changes in the density of subchondral bone also occur as a result of high speed exercise.

The change in the **shape of the metacarpal bone** due to high speed exercise is important in the adaptation of the bone to the rigors of fast galloping and also helps to reduce the risk of bone damage (shin soreness). The adult Thoroughbred's third metacarpal bone has a thick dorsal cortex compared with that of Standardbreds. This difference between the two breeds is not necessarily genetically related, as there is evidence that the normal growth pattern of the Thoroughbred does not always involve specific enlargement of the dorsal cortex. However, it is clear that intense exercise of young Thoroughbreds will dramatically enlarge the size and shape of the dorsal cortex, compared with non-exercised age-matched controls.

The response of the metacarpus to the forces of compression is to enlarge the cross-sectional area. This reduces local **bone stress**, since stress is equal to the force (load) divided by the area over which the force acts. If the horse's metacarpus were subjected simply to axial compressive forces (no bending) during galloping, then the alteration in cross-sectional area would be uniform. This, however, is not the case, since substantially more bone is laid down on the dorsal cortex than at other sites. We can assume therefore that some bending forces on the metacarpus must occur during galloping in addition to compression. Bending increases the local strain on the dorsal cortex and leads to the preferential enlargement of the bone in this axis. This bending is thought to occur only at the fast gallop, since it has not been possible to measure at slower speeds. The Standardbred's cannon bone does not have an enlarged dorsal cortex, which indicates that the bending forces probably do not occur at the fast trot or pace.

There are a number of other structural factors in bone, which have not yet been investigated, that may be influenced by training. For example, the alignment of collagen fibers within the bone contributes significantly to the compressive strength of the cannon bone. It is feasible that the **collagen formed in trained horses** is better aligned than in untrained horses, thus contributing to the structural strength of the bone. The collagen cross-linkage of bone is also an important factor that can regulate bone mineralization and bone strength. Increases in the number of collagen cross-links may also contribute to the bone strengthening effect of training.

It is clear therefore that **controlled fast work over short distances** will improve the biomechanical strength of the metacarpus of young horses. Further studies are required to determine the minimum amount of fast work that will result in an improvement in the strength of the metacarpus, and also the duration and speed of fast exercise that provides an unacceptable risk of causing bone damage.

SHIN SORENESS—AN EXERCISE-INDUCED INJURY

The cause of shin soreness (*q.v.*) was originally attributed to the tearing of the periosteum and subsequent subperiosteal hematoma. More recently **biomechanical injury** has been proposed as a more likely cause of shin soreness involving a fatigue failure of the bone on the dorsal aspect of the metacarpus. **Microfracturing** in the outer layer of the dorsal cortex is now proposed as the instigating factor leading to local inflammation and pain.

The major risk factors involved in shin soreness in order of precedence are high speed work, immaturity, too much work too soon and low bone strength/density. Over 90% of shin soreness cases exhibit the first signs during the fast work stages of their preparation.

Bone that is repetitively loaded will suffer **fatigue** during which the bone loses strength and will ultimately **fracture**. Bone that is under very large loads will fatigue quickly, whereas bone under smaller loads will take longer to fatigue (the greater the load or strain, the fewer cycles required to cause fatigue). On the other hand the fatigue life of bone is positively related to its density (the denser the bone the more cycles required to cause fatigue).

However, the situation in young racehorses is more complex. We have already seen that the metacarpus of young horses responds to intense exercise by producing **more bone** on its dorsal surface. This bone is of low density initially, as mineralization of the newly formed bone is fairly slow. This bone therefore will have a much **lower fatigue life** than that of fully mineralized bone. For a given load, this bone will deform more than fully mineralized bone, thus setting up large shear forces between areas of new low mineralized bone and older fully mineralized bone. These larger shear forces may result in more rapid fatigue of the bone, which leads to microfracturing. This is followed by an inflammatory reaction resulting in **periostitis** (*q.v.*) with serum oozing underneath the periosteum. The inflammation and damage to the bone matrix stimulates the formation of periosteal new bone (generally woven bone).

TRAINING TO MAXIMIZE BONE QUALITY AND MINIMIZE LAMENESS

Although it is possible to train a horse without the horse going shin sore, it is unlikely that horses can be trained without **some degree of shin soreness** occurring. Alteration of current training and racing practices could result in a reduction of the occurrence of shin soreness, as well as a reduction in many other orthopedic injuries such as carpal chips, traumatic arthritis, etc. (*q.v.*). These, together with improvements in track structure and design, are thought to be the important factors that will affect the incidence of shin soreness in the future.

An **incremental training program** that increases the length, speed and repetition of galloping has been proposed as an alternative training program. It has been shown in other species that small numbers of high intensity loads per day can result in enhanced bone growth. Therefore, the distance over which horses gallop needs only be short (200–400 m). We know that the faster the speed at which this work is done, the greater the bone's response.

In order to control this response and not promote excessive risk of shin soreness, the horses should be started at a slow gallop and the speed progressively increased after periods of 4–5 wk. As galloping speed increases, so does the risk of shin soreness, so close surveillance is required. This type of training program involves a trade off between maximizing the bone response and minimizing the incidence of shin soreness. Acute shin soreness occurs from excessive strain in a bone that is relatively small. As a result of training the bone enlarges, which means for a given load (speed) there will be less strain. The strain in an adult Thoroughbred at full gallop is around 3500 μ strain, whereas it may be ⩾5000 μ strain in a 2-yr-old. If the bone strain is kept at 3000–3500 μ strain during a gallop then the risk of shin soreness should be low.

The proposed advantages of such a training program include a reduction in the amount of shin soreness, and as a result an **improvement in welfare** for the horse. It is envisaged that other types of exercise-induced bone and joint problems may occur less often, which could add substantial benefits. The other factor is that reductions in these orthopedic conditions may greatly enhance the horse's useful racing life and thereby reduce the substantial wastage that occurs in the racing industry.

CONCLUSIONS

In summary, galloping exercise at maximum speeds results in important adaptational changes in the size and shape of the metacarpus to provide extra bone strength. The extent of these changes will vary between individual horses and in some instances the end result will be exercise-induced injury such as shin soreness. Enlargement of the dorsal cortex will also result from shin soreness because the acute inflammation produced activates the periosteum and results in a rapid production of bone. This bone is often a type that will gradually need to be modified to provide suitably strong (organized) bone by the process of remodeling.

SORE BACK IN THE PERFORMANCE HORSE

INTRODUCTION

Sore backs are a common and often underrated problem in performance horses. The conditions involved may be primary or arise secondarily as the result of lameness, faulty tack or inadequate schooling. It is worth remembering that the most common reason for presentation of a back problem is **poor performance** rather than overt back pain.

Diagnosis of back problems is notoriously difficult and always requires a **thorough and systematic examination**. Despite this attention to detail and the application of sophisticated clinical aids, a definitive diagnosis is often only made by elimination of all other conditions.

PATHOPHYSIOLOGY

Specific pathogenesis of many back problems is unknown. However, a thorough knowledge of **functional anatomy** of the spine is the basis of pathophysiology.

It is important to remember that the horse keeps its back almost **rigid** to act as a bridge between the fore- and hindquarters. It then transmits the power or impulsion from the hindquarters to enable increased stride length and performance. The equine spine has been likened to a "**string and bow**" arrangement where the "bow" is the rigid vertebral column and the "string" keeps it under constant tension.

The conformation, type and use to which horses are put can have an important bearing on the injury. For example, specific spinal malformations (e.g. lordosis and scoliosis) tend to predispose to injury through the inherent weakness of the back or "bow" arrangement of the thoracolumbar spine. These conditions place extra strain on the "string" or epaxial muscles of the back, which can lead to recurrent soft tissue injuries. The majority of horses do not have this type of gross deformity, but **mild conformational defects** are common. Those horses that are short-backed with restricted flexibility of the spine tend to exhibit more vertebral lesions than longer-backed animals, which have relatively more suppleness and seem to be more prone to muscular or ligamentous strain. Large-framed animals with comparatively weak-looking quarters appear to be more susceptible to sacroiliac problems (*q.v.*).

There also seems to be an association between the type of back injury and the **sort of work** the horse is involved in. Acute sacroiliac strain or subluxation is more prevalent in horses jumping at speed, whereas overriding of the dorsal spinous process is most common in showjumpers. The incidence of soft tissue damage is much the same in both of these groups and age is not nearly such an important factor in equine back disorders as it is in humans. **Spondylosis deformans** appears more frequently in mares, and overriding of the dorsal spinous processes is most often seen in short-backed Thoroughbred geldings.

Another feature that seems to have a bearing on pathophysiology is the **seat of the injury** itself. Bone damage tends to be centered on the mid-point of the back, while soft tissue injuries are more often seen in the cranial and caudal parts of the thoracolumbar spine. This point can be helpful if no special radiographic facilities are available to differentiate soft tissue from skeletal damage. For example, a common scenario is acute onset of **noticeable discomfort** in the animal's back behind the saddle region (cranial lumbar spine). This would most likely be due to soft tissue damage and could be treated accordingly. In general practice it should be possible therefore to facilitate diagnosis of spinal disorders by carrying out a **thorough clinical examination** and using the ancillary aids available (assessment of muscle-derived enzyme levels, a short course of a non-steroidal anti-inflammatory drug [NSAID] and local anesthesia of the interspinous spaces).

DIAGNOSIS OF BACK PROBLEMS

One of the most difficult aspects of examining horses with potential back problems is being able to assess objectively the site and degree of pain involved. This is further complicated by the marked variation of individuals in their response to pain even on a day-to-day basis (**pain threshold**). As in human patients there is also the involvement of **temperament** as a contributory factor.

It is suggested that impaired performance is sometimes due to a horse trying to "save its back" even though the clinical signs of pain have apparently abated. Horses that keep their backs stiff for any reason are not going to perform satisfactorily as they will lose hindlimb impulsion. Some credence to this idea has been given by inducing stiffness of the back with small injections of concentrated lactic acid into the longissimus dorsi muscles under experimental conditions. The effect of local pain and associated back stiffness produced a noticeable reduction in performance capacity as analyzed by high speed cinematography on a treadmill.

A practical scheme for examining a horse with a potential back injury is given in Table 16.1.

Palpation of the spine

Clinical examination of the horse should be carried out **in stocks or in the box** with the horse in as relaxed a state as possible. To begin with, a test of the horse's reaction to **running a hand gently** along its back from the withers to the base of the tail is made. It is very difficult to palpate more than the tips of the dorsal spinous processes, although in most horses the interspinous spaces can be identified. It should be possible to detect **spasm of the longissimus dorsi** muscles as well as any protrusion or thickening around the summits of the dorsal spinous processes. Thin-skinned or hypersensitive horses will cringe when this is done, but unless there is a really dramatic response

Table 16.1 A practical scheme for examination of horses with a potential back injury (the examination should be standardized as much as possible)

Case history	Assessment of management factors Experience of owners: animal's temperament and ability to perform Time of onset and duration of clinical signs Response to any treatment given, particularly manipulation and NSAIDs
Clinical examination	At rest—visual inspection, palpation, manipulation Rectal palpation At exercise—in hand, lunged, ridden or driven
Radiologic examination	Lateral views of thoracolumbar (T2–L3/4) and sacrococcygeal (S2–Cy4) regions performed in standing position Radiography of lumbosacral (L4–S5) spine carried out under general anesthetic in ventrodorsal plane Linear tomography for sacroiliac lesions
Laboratory examination	Hematologic analysis—whole blood count Biochemical analysis, including muscle-derived enzymes (AST and CK), before and after exercise test
Other aids	Local anesthesia of interspinous spaces Faradic stimulation of muscles for confirmation of soreness Short-term effect of NSAID on performance "Slap test" for evidence of cervical vertebral stenosis causing mild to severe hindlimb incoordination Nuclear medicine (scintigraphy) for bone lesions Thermography for "hot spots" in back muscles Ultrasonography of soft tissue structures of the back

(e.g. kicking out, rearing, grunting) this should not be considered of clinical significance.

Palpation of the tips of the sacral spinous processes in the croup should also be carried out, particularly in horses used for harness racing. Pain may be palpable over the tendinous insertion of longissimus dorsi on the spines of S2 and S3 and in the sacrosciatic ligament. The tail and croup region should be examined for any flaccidity or perineal paralysis, which may be a sign of **neuritis of the cauda equina** (*q.v.*).

When there has been a history of trauma, a **rectal examination** should be carried out to determine the presence of damage to the pelvic canal, sublumbar group of muscles and/or sacroiliac region. If there is active damage to the muscles or ligaments in the sacroiliac region, then pressure exerted above each tuber coxae and on the midline at L4–5 usually produces pain or discomfort.

The next part of the procedure involves alternate **pinching** of the midline of the caudal thoracic and sacral region, in order to make the animal flex (ventroflex or arch) and extend (dorsiflex or dip) its spine. Reluctance to perform this maneuver and **rigidity of the back** are often significant findings, as they may reflect some underlying pain due to soft tissue or lesions of the thoracolumbar spine. Pain or discomfort produced by carrying out these tests is often accompanied by spasm of longissimus dorsi on one or both sides of the back. Areas of pain need to be located as precisely as possible for comparison with the results of any bony abnormalities noted on radiographic examination.

Skin sensitivity over the back and loins has proved an unreliable test as it seems to be so variable between individuals. However, **firm stroking** of longissimus dorsi with a pencil to produce muscular contraction and lateral flexion of the thoracic and lumbar spine is a very useful technique. There should normally be no marked resentment to this test unless there is some painful muscle involvement. If some chronic bony or muscular problem is present in the mid-back, then a reluctance or difficulty in lateral flexion in one or both directions is often seen.

Examination at exercise

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 moderate to severe pain is present a wide straddling hindlimb is usually seen, but in the horse with a low grade, less painful problem the action behind will be very close (**plaiting**).

The animal should be turned as short as possible in both directions with the intention of making it **flex the spine laterally**. 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 is 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. Severe lameness in one or both hindlimbs is not usually a feature of a back problem and diagnostic nerve blocks should be used to differentiate this from a genuine thoracolumbar condition. Mild shifting lameness or simply an **unlevel action** of one hindlimb is much more commonly seen.

Flexion tests rarely have any effect on the gait, but can be useful in distinguishing hock or stifle problems.

A session of 10–15 min exercise on the **lunge rein in a sand ring** is useful to assess critically the horse's gait. This also provides an opportunity to see any improvement or deterioration in the action as the horse warms up. Animals with restricted hindlimb gait often show poor tracking of the hindfeet (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 animal looks uncomfortable in its work. A poor action is usually best seen at the trot. Some difficulty is often seen when changing pace along with an inability to lead on the correct leg (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.

Finally **the horse should be ridden**, if possible by its regular rider, and with its regular harness, and an assessment made of the action at the walk, trot and canter. If the horse is a showjumper it should also jump over the type of fences that usually cause the most trouble (e.g. combination-type fences). For harness racing horses it is of great benefit to have the animal driven to assess the performance and trotting or pacing gait at fast exercise.

After a period to allow the animal to cool down, it should be exercised in hand again to see if there is any change in action. This is particularly useful in horses with low grade **exertional rhabdomyolysis** (*q.v.*) as they show increased stiffness of the hindquarters.

Differential diagnosis

The list of conditions that may be confused with a genuine back injury (Table 16.2) is deliberately presented *before* the section on conditions affecting

Table 16.2 Conditions to be considered in differential diagnosis of a thoracolumbar disorder

General category	Specific lesions/problems
Temperamental problems	Apparent hypersensitivity of back or "cold back"
Management problems	Poor schooling and equitation Badly fitting tack (saddle, bridle, bit)
Lameness	Forelimb lameness: Bilateral carpal or fetlock damage Navicular disease (e.g. laminitis) Hindlimb lameness: Originating from pelvic region Stifle problem (e.g. partial fixation of the patella) Hock lesion (e.g. spavin)
Hindlimb incoordination	Spinal cord damage in cervical or thoracolumbar regions
Miscellaneous conditions	Head-shaking and dental problems General debility and stiffness Traumatic cervical damage with neck stiffness

Table 16.3 Conditions of the thoracolumbar spine that may directly cause back problems in the horse

General category	Specific lesions
Deformities of vertebral column	Congenital or acquired curvature of the spine (scoliosis, lordosis and kyphosis) Synostosis (congenital vertebral fusion) Sacralization of L5/L6 vertebrae
Soft tissue injuries	Muscle strain of longissimus dorsi and/or sublumbar muscles Strain or damage to supraspinous and sacroiliac ligaments of the back Exertional or cramping of back muscles
Fractures	Dorsal spinous processes—single or multiple overriding fractures Vertebral bodies and neural arch
Other vertebral and articular lesions	Spondylosis deformans Crowding and overriding of the dorsal spinous processes ("kissing spines") Osteoarthritis and fusion of the dorsal spinous, transverse and articular processes Chronic sacroiliac problems (instability and spine formation)

the horse's spine. It is not uncommon for owners to blame poor competitive ability on a condition of the thoracolumbar spine when it is simply due to problems of schooling, rider equitation or poor track. The signs of a "cold back" on tightening the girth or mounting are not necessarily an indication of an underlying spinal problem.

Hindlimb lameness (e.g. a bilateral hock problem) is probably the most common differential diagnosis. Both fore- and hindlimb lameness can result in secondary back soreness and stiffness.

CONDITIONS AFFECTING THE HORSE'S BACK

Specific conditions of the spine

The size and complexity of the thoracolumbar spine of the horse predispose it to a wide range of problems that may lead to locomotor dysfunction. A list of the specific lesions that have been reported to cause directly back pain and discomfort in horses is given in Table 16.3.

Injuries to the **soft tissues** (muscles, ligaments and tendon insertions) are the most common causes of back injuries in horses. These conditions are usually traumatic in origin and carry a hopeful prognosis.

Alleged back problems

There is another category of so-called "back problems", which, despite lay opinions that they are important, have limited anatomic or pathophysiologic evidence to support their occurrence (Table 16.4). It is this latter group that forms the basis of **much controversy** between veterinarians, physical therapists and horse owners. These difficulties are exacerbated by the fact that many horses suffer **low grade and chronic lesions**. The major clinical sign is always

Table 16.4 Conditions alleged to cause back problems in horses for which there is currently no definitive scientific evidence

General category	Specific problems
Vertebral subluxation	Subluxation of thoracic or lumbar vertebral bodies and articular processes Malalignment of dorsal spinous processes in thoracic or lumbar region
Disk injuries	Intervertebral disk prolapse and herniation
Peripheral nerve injuries	Pinching of peripheral nerves to epaxial structures of the thoracolumbar spine

Table 16.5 Techniques known to be used to treat back problems in horses

General category	Individual methods
Rest	Box rest followed by period at pasture
Management	Replace saddle and/or use sheepskin numnah Change stable and work routine Attempt reschooling Attention to rider's equitation
Medical treatment	NSAIDs by oral, parenteral or local injection Muscle relaxants Sclerosing agents injected locally
Physiotherapy	Heat therapy: Infra-red or heat lamp Poultice, charges or counter irritation Shortwave diathermy Light therapy Lasers Solarium Ultrasonic therapy; muscle stimulation; Faradism; cyclotherapy; magnetic field therapy; swimming and hydrotherapy; graduated exercise program often combined with other forms of physiotherapy
Manipulative therapy	Osteopathy/chiropractic in the standing animal or under general anesthetic
"Natural medicine"	Acupuncture Conventional Laser beam therapy Radionics ("black box") Homeopathy Iridology Faith healing
Surgical removal	Compound fracture of withers Overriding dorsal spinous processes

a loss or reduction in performance whatever the underlying pathogenesis; other clinical signs may be more difficult to precisely define.

MANAGEMENT OF BACK INJURIES

The list of treatments for thoracolumbar disorders in horses is extensive (Table 16.5) and many of these methods will be given in combination, either at

the same time or concurrently (e.g. rest, medical treatment plus some form of physiotherapy). As yet there are few lines of therapy that have been objectively assessed for efficacy and there is also no doubt that some of the methods listed are used simply as placebos.

This lack of precise data results in some therapies becoming fashionable with owners and trainers: a few years ago surgery was often requested for back problems, then swimming became very popular, followed by manipulative procedures. It looks now as if the trend for the future may be in natural medicine (e.g. acupuncture). It should also be noted that many of these types of treatment are performed by non-veterinarians; some are qualified physiotherapists, but a considerable proportion are not. However, there appears to be an encouraging trend to set up rehabilitation centers for performance horses where physiotherapy is being used properly and to good advantage.

Much is talked about **manipulation** for treatment of equine back disorders. This line of therapy, which includes chiropractic and osteopathy, is now routinely performed throughout the world. It is reported to give immediate, but transient, relief to horses with back injuries. It does not always address the underlying pathogenesis of the thoracolumbar condition, which may be why recurrence of signs is common. However, it is encouraging to note that in recent times some real science has gone into investigating the potential of chiropractic for therapy and its mode of action, although no critical or controlled trials of its efficacy or the exact mode of its action have yet been published. The technique is performed either in the standing animal or under general anesthesia.

CONCLUSIONS

Back problems are an **occupational hazard** in racing and performance horses. The conditions that may result are often difficult to diagnose accurately, but it is worth remembering that some horses can perform badly without suffering from a back problem, some horses can perform adequately in spite of having a back problem, and spontaneous recovery from many types of back problem is quite common.

Finally, the simple recourse to a period of **rest** followed by a **graduated program of exercise** is all that is required in many cases. This can often be supplemented by various techniques of physiotherapy. Surgery is limited to resection of overriding spinous processes in selected cases where the diagnosis has been confirmed by radiologic examination and local anesthesia of interspinous spaces. Further studies on the biomechanics of the vertebral column and pathology of thoracolumbar injuries are essential to better understand pathogenesis, and from this sounder principles for therapy can be established.

Chapter 17

The nervous system

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Chapter contents

INTRODUCTION

With the advent of **equine protozoal myeloencephalitis** (*q.v.*) and **West Nile virus** (*q.v.*), neurologic diseases of horses have become increasingly significant worldwide. Since the laboratory diagnosis of those two diseases is not straightforward, and other diseases need disparate treatments and offer a different prognosis, there is increasing pressure on clinicians to make the correct clinical diagnosis.

In the neurologic examination of the equine patient, it is important to remember that the objective is to make an "**anatomic diagnosis**", i.e. establish in which neurologic structures the lesion(s) are likely to be in order to result in the observed neurologic signs.

Mentation, cranial nerve reflexes, cutaneous reflexes, tail and anus function and gait should be carefully examined. Is the lesion **central** (i.e. brain or spinal cord) or in the **lower motor neuron unit** (lower motor neuron cell body, peripheral nerve, neuromuscular junction or muscle)? Can the signs be explained by a **focal lesion** or are they likely to be due to a **multifocal or diffuse disease**? The answer to those questions will dramatically narrow down the possible differential diagnoses and will determine the choice of diagnostic tests.

This chapter aims to provide the equine practitioner with a synopsis of the clinical findings, diagnostic tests, treatment and prognoses for common neurologic disorders.

CONGENITAL AND DEVELOPMENTAL PROBLEMS

HYDROCEPHALUS

The congenital form of hydrocephalus is rare in newborn foals. When it does occur, it is usually due to **cerebral malformation** and accumulation of fluid in the **ventricles**. The head may or may not be grossly enlarged or dome shaped. Most foals with **congenital hydrocephalus** die shortly after birth but cases can be diagnosed later as incidental findings. **Severe dystocia** (*q.v.*) may be associated with the condition if the head is grossly deformed.

Acquired hydrocephalus is also occasionally observed and is usually due to **adhesions** secondary to bacterial meningitis or intracranial hemorrhage. Adhesions obstruct the normal outflow of **cerebrospinal fluid** (CSF). The head is sometimes, but not always, grossly enlarged. Foals with acquired hydrocephalus may be obtunded. As intracranial CSF pressures increase, **seizures** (*q.v.*) may ensue.

CSF analysis in congenital hydrocephalus is usually normal. In acquired cases, it may reflect the primary disease. In foals, the fontanelles of the cranium are not open, thus ultrasonography is not useful. Computed tomography or magnetic resonance imaging is potentially the best means to obtain an **ante mortem diagnosis**.

There is no practical form of treatment with congenital or acquired hydrocephalus. The prognosis for long-term survival is poor.

CEREBELLAR ABIOTROPHY

Cerebellar abiotrophy is suspected to be an inherited disorder with an 8% incidence in some **Arabian** family lines. It is also considered an inherited disorder in Oldenburg light-breed horses and in Eriskay and Gotland ponies. Either gender can be affected. The diagnosis is based on breed, history and clinical signs. The signs may be present at birth, but can be difficult to recognize in foals <1 mo of age. The clinical signs are characterized by **jerky head movements** and **hypermetria/dysmetria**. Affected foals assume a **wide-based stance** at rest and may fall over backwards if asked to back up or elevate the head. As the foal ages, it will appear **strong but ataxic** and continue to exhibit a **rhythmic head bobbing** or head tremors, characteristic of cerebellar disease (*q.v.*). Blindness and gait paresis are not features of this disease.

There are no ante mortem tests. The CSF is normal. There is no treatment and affected foals should be euthanased because they may injure themselves or their handlers. Cerebellar abiotrophy is confirmed at post mortem by a cerebellum that weighs <10% of the weight of the whole brain, histologic evidence of thinning of the granular and molecular layers of the cerebellar cortex and degeneration of the Purkinje cells.

JUVENILE EPILEPSY OF FOALS

Juvenile epilepsy in foals is probably not a form of true inherited epilepsy. It is speculated to be a type of **pediatric seizure** that reflects the neonate's low seizure threshold in response to **temporary derangements**. The temporary derangements can be caused by toxic, metabolic, physical, infectious or circulatory disorders.

A form of **idiopathic epilepsy** is occasionally reported in suckling and weanling foals, in particular those of the **Arabian** breed. Seizures begin between 1 and 12 mo of age. Several seizures may occur immediately prior to presentation. The seizures are characterized by episodes of **sudden loss of consciousness** with or without tonic-clonic activity. Affected foals can experience **temporary central blindness** (which can last a few hours to a few days). **Head trauma** due to thrashing is a common complication. Seizures do not usually persist into adulthood.

Once other causes for seizures have been ruled out, a diagnosis of idiopathic epilepsy can be given. Although the disease is **self-limiting with age**, seizures must be kept under control (Table 17.1) to avoid permanent brain damage or head trauma. Initial anticonvulsant therapy with **diazepam** (5–20 mg IV) repeated two or three times will usually control the seizures. For maintenance anticonvulsant therapy, affected foals should be kept on **phenobarbital** (100–500 mg PO s.i.d. or b.i.d.) for a minimum of 10–14 days, or as long as is needed to avoid recurrence of seizure activity. Treatment with phenobarbital should be dose adjusted so that seizures can be controlled but the foal not overly sedated. Monitoring blood levels of the drug is advised and the **non-toxic therapeutic range** is approximately 5–30 μg/mL. The lowest dose that controls seizures should be used, as phenobarbital may sedate the foal and **discourage nursing**. The dose must be tapered down over 2 weeks before being discontinued, as abrupt discontinuation may precipitate seizures.

Table 17.1 Guidelines for selected anticonvulsant drugs used to treat seizures in adult horses and foals

Drug	450 kg adult horse dose	50 kg foal dose
Initial therapy		
Diazepam	50–200 mg IV slowly	5–20 mg IV slowly repeated 2–3 times
Phenobarbital	2–5 g IV	250–1000 mg IV
Pentobarbital	To effect	150–1000 mg IV
Xylazine	300–1000 mg IV	Not advised
Maintenance therapy		
Phenobarbital	1–5 g PO b.i.d. (monitor blood levels)	100–500 mg PO b.i.d.

Pediatric epilepsy generally subsides as the foal ages, as long as seizure-related brain damage has not occurred. If **blindness** persists in the postictal phase, vision usually returns within a few days after seizure activity is controlled. The incidence of recurrence after puberty is unknown.

CERVICAL VERTEBRAL MALFORMATION

Cervical vertebral malformation (CVM) describes a group of malformations and malarticulation abnormalities of the cervical vertebrae of horses. It is a common cause of **ataxia** (*q.v.*) in horses all over the world and affects any breed of horse, but particularly **Thoroughbreds**. The disease stems from bone and joint malformations and is seen as two broad categories. Younger horses and foals are predisposed to **deformation** of the vertebral bodies with malarticulation and subluxation on flexion, while the spinal cord compression in older horses is generally due to **osteoarthritis** of the caudal articular processes.

The disease in young horses may be a form of a developmental orthopedic disease, i.e. related to **rapid skeletal growth** in genetically predisposed horses. Cervical vertebrae in those animals have lesions of osteochondrosis and epiphysitis similar to those seen in the limbs. Familial predisposition, high dietary energy intake and trauma to the neck probably all play a role, as young, large, fast-growing animals (often males) are affected.

An accident or injury to the neck is sometimes in the history, and clinical signs may have an abrupt onset. Mild to moderately affected horses show **symmetrical ataxia** with circumduction of the **pelvic limbs**, especially when the animal is made to walk in small circles. Proprioceptive deficits, toe dragging, dysmetria and varying degrees of upper motor neuron weakness (assessed by pulling on the horse's tail at a walk) are also present. Thoracic limb deficits are usually less severe than pelvic limb deficits. The "**slap test**" for laryngeal adduction (*q.v.*) may be absent but there are no cranial nerve deficits. Neck pain or stiffness may be present, particularly in older horses.

The neurologic examination and plain radiographs of the vertebrae (C1–T2), while the horse is standing with the neck in a neutral position, are the most important diagnostic aids. In younger horses plain film radiographs reveal **stenosis of the vertebral canal**, often at C3–4 or C4–5. A corrected **minimum**

sagittal diameter (the ratio of the absolute minimum sagittal diameter of the vertebral canal to the sagittal width of the vertebral body) of <0.5 is highly suggestive of a compressive lesion at C3–4 or C4–5.

Enlarged caudal epiphyses, a caudal extension of the dorsal aspect of the vertebral arch across the ventral articulation site of adjacent vertebrae, vertebral malalignment and degenerative/osteochondrosis-like changes in the articular processes often coexist. Greatly **enlarged articular processes**, with osteophytes, associated with hypertrophy and fibrosis of synovial membranes and joint capsule, can cause acute onset compression in older horses. **Myelography**, a technique used to assess spinal cord compression by the injection of radiodense contrast medium into the subarachnoid space, may be useful in determining the extent of cord compression and should be performed on horses in which surgical decompression and/or vertebral fusion are being considered.

In a research setting, the radiographic and neurologic deficits may be reversed in young (≤1 yr of age) animals by confinement (to limit further injury to the cord) and a severely protein- and energy-restricted diet. On the whole, however, the prognosis for return to athletic function of horses with CVM is poor. Affected horses may become so ataxic that they become a danger to themselves and horse handlers. Humane destruction is then advised. **Surgical fusion** of the vertebrae has been used to treat, and may improve, affected horses, but residual deficits often persist.

OCCIPITOATLANTOAXIAL MALFORMATION

This rare syndrome is thought to be inherited in the **Arabian** and related **Haflinger** breeds. Some affected foals are born dead. Survivors may be neurologically normal at birth then develop degrees of ataxia and paresis. Other surviving affected foals have no neurologic abnormalities but exhibit **restricted head and neck movement**.

Palpable and audible crepitus may or may not be present with manipulation of the head or neck. **Scoliosis** is occasionally present as well. Radiographically, various malformations of the occiput, atlas and axis are apparent. Most often, the dens is hypoplastic and the occiput and atlas are fused. There is no treatment. Surgical attempts at stabilization have generally not been successful. Humane destruction is advised.

EQUINE DEGENERATIVE MYELOENCEPHALOPATHY

Equine degenerative myeloencephalopathy (EDM) is a disease of **young horses** of any breed, although a familial tendency has been observed in certain Appaloosa, Standardbred and possibly Morgan lines. The disease is thought to be related to **vitamin E deficiency** associated with lack of green forage, or the feeding of heat-processed pelleted rations. A history of vitamin E deficiency is, however, not evident in all cases. **Neuroaxonal dystrophy** in the brainstem and spinal cord results in gait abnormalities.

EDM is rarely seen in horses ≥4 yr of age. Symmetrical ataxia, hypometria and paresis usually appear in animals ≤6 mo of age. The disease is **progressive**, but the clinical signs have generally stabilized after the animal reaches 6–12 mo of age. Signs may be more severe in the pelvic than the thoracic

limbs. Clinically the disease can be difficult to distinguish from cervical vertebral malformation (*q.v.*).

The diagnosis is based on the characteristic clinical signs and lack of abnormal findings on plain cervical radiographs. Decreased serum vitamin E concentrations ⩽1.5 μg/mL are sometimes (but not always) present.

Dietary supplementation with 6000 IU of **vitamin E** can be effective when initiated early. Response to therapy in one study was seen within a few weeks and continued for over a year. **Low selenium supplements** should be chosen in order to avoid selenium toxicities (*q.v.*) when high levels of vitamin E are being supplemented. Large amounts of **fresh green forage** should be made available. The signs may improve or stabilize with therapy, but many animals do not completely recover.

There are no findings on gross pathology, but histologic examination of the brain and spinal cord reveals degenerative lesions such as swollen axons in white and gray matter of the caudal brainstem and spinal cord.

HYPOXIC-ISCHEMIC ENCEPHALOPATHY (NEONATAL MALADJUSTMENT SYNDROME)

Hypoxic-ischemic encephalopathy (HIE) is a manifestation of **perinatal asphyxia syndrome** and in humans is clinically defined as a syndrome of disturbed neurologic function in an infant at or near term during the first week after birth, manifested by difficulty with initiating and maintaining respirations, decreased reflexes, altered level of consciousness, and often seizures.

Foals should have a thorough **physical examination** in case other organs, such as the renal and digestive systems, are involved. Typically, affected foals are **normal at birth** but show signs of central nervous system (CNS) abnormalities within a few hours. However, some foals are obviously abnormal at birth and some will not show signs until 24–36 h of age. HIE is commonly associated with **adverse peri partum events**, including dystocia (*q.v.*) and premature placental separation (*q.v.*), but a fair number of foals have no known peri partum period of hypoxia, suggesting that HIE in these foals results from unrecognized acute or chronic **hypoxia in utero**.

A wide spectrum of clinical signs are associated with HIE and range from mild obtundation with loss of the suck reflex to generalized seizure activity. Rarely, spinal cord disease can be the only presenting sign.

Intensive supportive care (*q.v.*) is critical to the survival of a foal with HIE. Therapy for the various manifestations of hypoxia-ischemia involves control of seizures, general cerebral support, correction of metabolic abnormalities, maintenance of normal arterial blood gas values, maintenance of tissue perfusion, maintenance of renal function, treatment of gastrointestinal dysfunction, prevention/recognition/early treatment of secondary infections and general supportive care. It is important that seizures be controlled as **cerebral oxygen consumption** increases five-fold during a seizure (see Table 17.1). Parenteral antibiotics (2.2 mg/kg ceftiofur IV b.i.d.) are indicated if sepsis is suspected. Nutritional and respiratory support may be necessary. Correction of acid-base, electrolyte and glucose abnormalities is indicated. With intensive supportive care, 75–80% of HIE foals will survive. In survivors, the condition usually stabilizes by 2–3 days of age and improvement is noted by Day 4.

The neurologic signs often resolve in the reverse order in which they appeared. Complete recovery may take up to 3 mo. Failure of passive transfer of **colostral antibodies** concurrent with HIE is associated with a poor prognosis.

INFLAMMATORY AND TOXICO-INFECTIOUS DISEASES

BACTERIAL MENINGOENCEPHALITIS/BRAIN ABSCESS

Bacterial meningoencephalitis is a **suppurative inflammation** of the meninges. The condition is fairly uncommon in Equidae. In the adult horse, it may be associated with **brain abscesses** due to *Streptococcus equi* or *Strep. zooepidemicus*. Bacterial meningoencephalitis in neonatal foals is primarily caused by Gram-negative enteric bacteria (*Escherichia coli*, *Enterobacter* spp., *Salmonella* spp.), or *Streptococcus* spp., *Staphylococcus* spp., *Actinobacillus equuli*, *Klebsiella* spp., *Listeria monocytogenes*, and *Pasteurella* spp. Mixed infections may also occur.

Concurrent systemic illness is usually not evident in the adult horse (although on rare occasions previous infection with *Strep. equi* has been documented). The most common cause in neonates is **generalized septicemia** due to failure of passive transfer of colostral antibodies, and **hematogenous dissemination** of the bacteria to the CNS. In the latter case, a history of omphalophlebitis, polyarthritis, pneumonia, uveitis and other local infections is usually present.

The early signs of **meningitis** are non-specific but usually include fever, anorexia and obtundation. A stiff neck and hyperesthesia may also be present. Passive manipulation of the head and neck can elicit a **pain response**. As the disease progresses, **severe obtundation** or coma, hypertonia of limbs, paresis and tetraplegia are common clinical signs. Opisthotonus, intermittent prolapse of the third eyelid, and seizure activity may be observed.

Affected animals may or may not be **febrile**. It is important to exclude from the differential diagnosis tetanus, hepatoencephalopathy, equine protozoal myelitis, viral encephalitis (*q.v.*) and, in the foal, hypoxic–ischemic encephalopathy (*q.v.*) or metabolic disturbances (glucose or electrolyte and acid-base disturbances).

There are no changes in blood tests that are specific for bacterial infection in the CNS. The specific diagnosis depends on **CSF analysis**. An increased CSF white blood cell (WBC) count ($\geqslant$5 cells/μL), represented primarily by neutrophils, an increased total protein and decreased glucose levels (to $\leqslant$50% of the serum glucose value) are common findings. The CSF, which can be clear or turbid, should be **Gram stained** and cultured for microorganisms, though the results may be unrewarding. In foals with failure of passive transfer, blood or other body fluids should be cultured in an attempt to identify the organism.

Antimicrobial therapy should be based on culture and sensitivity along with the capacity of the drug to cross the **blood–brain barrier (BBB)**. The antibacterial agent should be highly lipid soluble, non-ionized and poorly protein bound to optimize penetration. In the early stages, or if microbial culture of CSF or other body fluids is negative, empiric treatment with bactericidal, IV delivered antibiotics is advised. Recommended antibiotics include **trimethoprim-potentiated**

sulfonamides (20–35 mg/kg IV b.i.d. or t.i.d.), or a third generation cephalosporin (**ceftiofur** 5–10 mg/kg t.i.d.), in combination with **benzylpenicillin** (20 000–50 000 IU/kg IV q.i.d.). Aminoglycosides such as **gentamicin** (6.6 mg/kg IV s.i.d.) could also be given in combination with penicillin, but as meningeal inflammation subsides, they may not penetrate the BBB as effectively. Only the cephalosporins and trimethoprim-potentiated sulfonamides have adequate penetration at all times. Therapy should be prescribed for a minimum of 6–8 wk. Tetracycline does not penetrate the BBB and should be avoided.

Additional treatment with anti-inflammatories such as 1.1 mg/kg flunixin PO or IV b.i.d. is also recommended. Anticonvulsant therapy (see Table 17.1) may be necessary.

Residual neurologic signs may persist or recur after treatment, especially if there is brain or vertebral abscessation. The long-term prognosis for such cases is grave.

WESTERN, EASTERN AND VENEZUELAN ENCEPHALOMYELITIS (WE, EE, VE)

These equine alphavirus encephalomyelitides are of **public health significance** because humans are susceptible hosts. Interepizootic maintenance of the virus depends on reservoir host–mosquito cycling. Reservoir hosts include birds, rodents and reptiles. The virus may persist in these reservoirs and periodically spreads from the focal host to the bird population and is then amplified via bird–mosquito–bird transmission. **Epizootic outbreaks** tend to occur in late summer in warm and humid conditions that favor the mosquito population. **Standing water** favors larval development. Epizootics decline with the onset of cool and dry weather.

The distribution of EE (also known as EEE) (*q.v.*) is primarily across the Atlantic and Gulf Coast regions in the USA. Serious outbreaks have occurred in eastern Canada, the Caribbean Islands, Central and South America. Over the last 30 years, the disease has become less prevalent due to the widespread use of vaccines and mosquito control programs. EE is transmitted to the horse mainly by *Culiseta melanura*, *Aedes sollicitans*, *A. vexans* and *A. canadensis*. EE is associated with a **high mortality rate** (up to 90%). Both humans and the horse are considered "dead-end hosts".

WE (*q.v.*) occurs primarily across the western and mid-western USA, west-central Canada, Mexico and South America. It is transmitted primarily by *Culex tarsalis*. The mortality rate in the horse is 10–50%.

VE (*q.v.*) occurs primarily across Central and South America, Texas and the southern USA. Mexico was declared free of VE in 1990. Several species of mosquitoes can transmit VE. The wild reservoirs are not identified. Infected horses develop viremia and can serve as an **amplifying host**, i.e. mosquitoes may become infected by feeding on the viremic horse. The mortality rate for VE is 30–90%.

Clinical signs of EE, WE and VE are generally similar and differ only in detail. These diseases frequently affect **younger horses** (1–2 yr of age), although horses of any age can be affected. A low grade infection may be present, characterized by low grade viremia, fever, lymphopenia and neutropenia. A generalized febrile illness may be observed and can be characterized by

anorexia, obtundation, tachycardia, diarrhea (VE), lymphopenia and neutropenia. A few horses may die in this stage of the disease. **Myeloencephalomyelitis** is classically characterized by clinical signs suggesting **diffuse cortical disease**. Affected animals may become obtunded, unresponsive or irritable. Head pressing, leaning on walls or fences, compulsive walking, circling, blindness, lack of menace response, cranial deficits, or an unsteady gait may be present. Clinical signs progress within 12–48 h. Death is usually preceded by recumbency, irregular breathing, cardiac arrhythmias, coma and convulsions. Survivors may recover over a period of weeks but may have residual deficits (**"dummies"**).

Based on clinical signs, the major differential diagnoses for alpha viral encephalitis include West Nile virus hepatoencephalopathy, rabies, equine protozoal myeloencephalitis, cerebrospinal nematodiasis, leukoencephalomalacia and bacterial meningoencephalitis (*q.v.*).

Serology, hemagglutination inhibition, or complement fixation tests are useful adjuncts to the ante mortem diagnosis, but most cases can be diagnosed based on neurologic and CSF examination, with the concurrent presence of a fever. The changes in **CSF analysis** consistent with EE, VE or WE include neutrophilic leukocytosis, increased total protein concentration and xanthochromia. Occasionally CSF eosinophilic pleocytosis may be seen with EE. **Paired serum titers** may also be helpful in supporting the diagnosis, though titers can **cross-react** between EE and WE. Paired serology is necessary for surviving horses in areas where WE prevails.

There is **no specific treatment** for any of these encephalitides. The prognosis for EE is grave, and it is poor for WE and VE.

At necropsy, diffuse meningoencephalitis, patchy congestion and hemorrhage of the brain are present grossly. Occasionally, occipital or cerebellar herniation has occurred due to brain swelling. Histology reveals a combination of neuronal and parenchymal necrosis, hemorrhage and meningitis. Neutrophilic infiltrate or eosinophils may be present.

For **prevention**, killed inactivated **vaccines** containing EEV and WEV are available (e.g. Encevac T, Intervet Inc., Equiloid, Fort Dodge Animal Health or Cephalovac, Boehringer Ingelheim Pharmaceuticals Inc.). Vaccination followed by a 3–4 wk booster is advised. Most manufacturers recommend yearly revaccination thereafter, however in enzootic areas, semi-annual vaccination is recommended. Brood mares should receive a booster 4–6 wk prior to parturition to maximize colostral antibody levels. Foals should be vaccinated at 2, 3 and 4 mo of age and then receive booster vaccinations at approximately 10 mo and every 6 mo thereafter. Breaks in vaccination protection have been documented. One survey reported that 17% of the cases of EE had been vaccinated within the preceding 7–12 mo, and 5% in the preceding 6 mo. **Mosquito control**, such as minimizing areas of standing water around stables, is also necessary.

WEST NILE VIRUS MYELOENCEPHALOMYELITIS

The West Nile virus (WNV) (*q.v.*) is a **mosquito-borne *flavivirus*** in the Japanese encephalitis complex, and is endemic in Africa and Asia. West Nile virus was first identified in the West Nile district of Uganda in 1937, and has

since been found in other parts of Africa, Eastern Europe, West Asia, the Middle East and the USA. It is maintained in cycles involving birds as vertebrate hosts and mosquitoes as vectors. The virus is transmitted by at least 10 genera of **mosquitoes** and has been identified in more than 100 species of **birds**, notably the American crow. Antibodies or disease have also been shown in humans and an impressive range of animals, from alligators to bears to horses. **Birds appear to be the only animal with sufficient viremia to infect mosquitoes**.

There are significant strain differences between isolates across the world and even between virus isolates within a given geographic region, which may be expressed by **differences in resulting clinical signs**. Genome data strongly suggest that the virus causing the 1999 New York epidemic/epizootic was introduced from the Middle East. Equine cases from the USA, Italy and France reported mainly spinal cord signs.

Clinical signs are referable to an **encephalomyelitis** but can be subtle. Increased rectal temperature, asymmetrical paresis or ataxia, and muscle fasciculations are reported to be the most common clinical signs in horses in the USA. Cases from Israel may show more signs of encephalopathy such as behavior changes.

The most commonly used WNV laboratory test is based on **IgM capture ELISA on serum or CSF**, further confirmed with plaque reduction neutralization. CSF cell counts and protein content can be normal in up to 75% of cases.

Treatment is supportive and includes the use of **anti-inflammatory medications**, e.g. 1.1 mg/kg flunixin PO s.i.d.–b.i.d.; fluids, e.g. maintenance of 30 liters of **lactated Ringer's** per day; **antimicrobials**, e.g. sodium benzylpenicillin 12 500–100 000 IU/kg IV b.i.d.; and **slinging of recumbent horses**. Unlike herpes myeloencephalopathy (*q.v.*), the use of corticosteroids is probably contraindicated.

An **equine vaccine** is available in the USA (West Nile Innovator, Fort Dodge Animal Health) but, rarely, fully vaccinated horses have developed clinical disease. Mortality rates in **horses** with **West Nile** encephalitis are reported to be 20–30% with some survivors having residual deficits. Neuropathologic lesions consist of mild to moderate, non-suppurative polioencephalomyelitis.

RABIES

There are six viruses in the genus *Lyssavirus*, family *Rhabdoviridae*, including rabies. Rabies virus (*q.v.*) is present in most continents except Australia and Antarctica and is restricted from some islands such as UK, Japan and New Zealand by quarantine of animals, although UK regulations for quarantine have been recently eased, and for many countries replaced with vaccination-based controls. There are approximately 700–1000 reported human cases per year worldwide.

In **endemic areas**, the frequency of rabies in livestock coincides with epizootics in the sylvatic reservoirs (skunks, raccoons, foxes and bats). The disease is usually transmitted to the horse via a bite wound from an infected wild animal. Less frequently, horses are infected by the bite of an infected domestic animal such as a dog or cat but the wounds are rarely identified.

After entry, the virus remains localized for periods that vary from days to many months, resulting in a large variability in the incubation period from

weeks to months. After virus multiplication in the connective tissue and muscle at the site of injury, virus is spread by replication in Schwann cells or by axoplasmic transport (it does not replicate in axoplasm). Early replication occurs in dorsal root ganglia and this correlates with the tingling sensation at the bite or scratch site seen in the prodrome of some human cases. After initial replication in the dorsal root ganglia, the virus disseminates rapidly and selectively in the CNS to infect neuronal cells of the brainstem, hippocampus, the subcortical nuclei, the Purkinje cells of cerebellum and limbic cortex. In the second phase, the virus spreads via the **nerves** (not blood) to diverse sites such as the eye, salivary gland, papillae of tongue, heart, hair follicles of skin, and some muscles. The clinical course of the disease is related to the dose and site of inoculation (i.e. proximity to the brain) and pathogenicity of the specific virus strain. In horses, **natural infection is invariably fatal**.

Classically, rabies in the horse (*q.v.*) has been described in two forms, depending on the neural structures predominantly targeted: **dumb** (medulla and the spinal cord), and **furious** (limbic system). In most cases the clinical signs of the specific forms tend to overlap or appear concurrently. The broad range of clinical signs often makes equine rabies difficult to diagnose. Although **aggressiveness** and **indiscriminate attack** are alerting clinical signs, rabies in the horse does not invariably manifest as the furious form. The initial clinical signs often include **progressive ascending ataxia** and paresis, lameness, colic, dysphagia, hyperesthesia or fever. A spectrum of other clinical signs have been described, but loss of tail and anal sphincter tone, and loss of sensory perception of the pelvic limbs often precede death. The disease **rapidly progresses** once clinical signs appear and may quickly render the animal recumbent. Horses usually die of **cardiac or respiratory arrest** 4 days or so after the onset of the clinical signs. Survival up to 10–15 days has been reported, but is uncommon.

Rabies is a **reportable disease** in most countries, and horses showing suspicious signs or with a known exposure to a suspected rabid animal should be isolated and observed.

There is no definitive ante mortem test that is fast enough or accurate enough to be clinically useful. CSF analysis may be helpful, but is not always abnormal in rabid horses. Serology and **positive fluorescent antibody testing (FAT)** on skin, cornea or salivary gland may aid in the ante mortem diagnosis, but false positives, false negatives and difficulties in interpretation hinder their usefulness. The characteristic eosinophilic **intracytoplasmic Negri bodies**, found in the hippocampus and Purkinje cells of the cerebellum at post mortem, are pathognomonic for rabies but are not present in all cases. They are more likely to be present in horses that survive >4 days. Thus, the definitive diagnosis can usually only be made at necropsy, and by FAT on the brain and/or spinal cord. The FAT, which can detect the disease in 98% of infected animals, remains the most accurate test.

The currently marketed inactivated rabies vaccines are thought to be safe and effective. **Annual vaccination** of horses against rabies is recommended in areas where the disease is endemic. Although the horse is moderately susceptible to rabies, transmission from a rabid equid to a human has not been documented. If an **unvaccinated horse** is bitten it should **not** be vaccinated immediately but isolated for 6 mo and vaccinated 1 mo before the end

of quarantine. If at any stage exposure to rabies is confirmed the horse should be euthanased immediately.

Regulations and quarantine protocols for rabies vary between countries and geographic regions within countries. For specific recommendations regarding human and animal post-exposure procedures, practitioners are advised to consult with federal or national authorities and physicians.

EQUINE HERPESVIRUS 1 (EHV-1) MYELOENCEPHALOPATHY

Myeloencephalopathy is caused by **equine herpesvirus 1 (EHV-1)** (*q.v.*), which is the same virus that causes abortions. There is no breed or gender predisposition, but foals are less likely to be affected with neurologic signs. It has been reported in almost all countries and may occur in outbreaks. It has also been seen after vaccination with a modified live virus vaccine. Respiratory disease may or may not precede onset of neurologic signs, and may be associated with abortion "storms" within a herd.

The onset of **EHV-1 myeloencephalopathy** is acute, and the signs are rapidly progressive (over 36–48 h). It can be characterized by **spinal cord signs** alone, or less commonly, in combination with **cranial nerve deficits**. The pathogenesis is suspected to be an immune-mediated mechanism in the endothelium of blood vessels of the CNS. The underlying lesion is a **vasculitis of CNS arterioles**. There is evidence to suggest that EHV-1 (*q.v.*) is neurotropic and as part of its normal life cycle establishes latency in sensory ganglia, specifically the trigeminal ganglion, from which virus can be reactivated.

Horses may be febrile at the onset (41°C). Signs may vary from a subtle abnormal gait to dog-sitting, progressing to recumbency. **Urinary incontinence** and **bladder distension** are common in the early stages. Decreased tail tone and perineal hypalgesia may be present, along with subsequent constipation. Head signs (cranial nerve deficits, obtundation or vestibular signs) are less frequent. Affected horses are **generally** alert and have a **good appetite**. The signs may stabilize quickly or progress over several days. Complications associated with recumbency (bronchopneumonia, decubiti) may occur.

CSF analysis may reveal **xanthochromia** with marked protein elevation (100–500 mg/dL). There are no changes in blood tests that are specific for EHV-1. Virus may be isolated from nasal swabs, transtracheal wash, CSF, endometrial tissues or buffy coat and is **good evidence** for the disease. Poor virus isolation from CNS may be due to virus bound to antibody. A 4-fold or greater rise in serum antibody titer between acute and convalescent samples collected 10–14 days apart is helpful.

The differential diagnosis includes equine protozoal myeloencephalitis, rabies, cervical vertebral malformation, polyneuritis equi, trauma, aberrant parasite migration, sorghum neuritis–cystitis, and perhaps equine degenerative myelopathy (*q.v.*).

There are no specific treatments for EHV-1. **Supportive care** is essential. Deep bedding, laxatives, enemas, manual rectal evacuation, urinary catheterization and antimicrobial therapy for secondary infections (bronchopneumonia, cystitis) may be necessary. The use of corticosteroids in the acute phase (dexamethasone, 0.1–0.25 mg/kg b.i.d. IM or IV for 1–3 days) is controversial but could be attempted if bacterial infection of the CNS has been ruled out.

Corticosteroids also have a depressant effect on lymphocytes, which may be undesirable in cell-associated viral infections such as EHV-1. Since the CNS lesions appear to be immune mediated, vaccination of horses showing neurologic signs could **worsen** the disease.

Recovery may support the validity of the diagnosis of EHV-1 infection. With EHV-1, complete recovery over several days or months is possible, although **residual neurologic deficits** may remain in some cases.

Histopathologic lesions include endothelial necrosis (characterized by accumulation of neutrophils), vasculitis and thrombosis in small arteries along the meninges. White and gray matter of brain and spinal cord may be affected. Multifocal lesions along the neuraxis may be present, in addition to evidence of vasculitis in nasal passages, lungs and endometrium.

The prophylactic value of **EHV-1 vaccines** (*q.v.*) has not been fully evaluated but vaccination in the face of infection cannot be advised. The EHV-1 vaccines probably provide some immunity to the **respiratory disease** but not to infection, thus the virus can still cause abortion or neurologic disease. It also appears that EHV-1 antibodies are involved in the **pathogenesis** of EHV-1 myeloencephalopathy. A regular vaccination program is still recommended (every 3–4 mo) to maintain antibody titers considered protective for the respiratory and abortive form. Stress (shipping, weaning, castration, foaling) and exogenous corticosteroid administration to pregnant mares can result in activation and shedding of EHV-1 in carriers.

PROTOZOAN MYELOENCEPHALITIS

Equine protozoal myeloencephalitis (EPM) (*q.v.*) is due to infection of the CNS with an as yet poorly characterized protozoan parasite. The putative agent has been named *Sarcocystis neurona* (*q.v.*) but the life cycle and natural history remain unclear. It is most commonly seen in horses that have been in North or South America but appears to be rare and has not been shown to cause disease in native, untraveled horses outside of the American continent. There has so far been no report of EPM in donkeys or mules.

Most cases occur during spring and summer and are seen in racing and **performance animals**. Clusters of cases have occasionally been seen, but affected horses appear to be dead end hosts not capable of transmitting the infection.

The disease definitive host is the **opossum**, and secondary hosts include the armadillo, the striped skunk, the **raccoon** and possibly cats. Horse owners should recognize that exposure to opossums poses the major threat to their horses. Exposure to armadillos, skunks, raccoons and especially cats is unlikely to pose a problem.

Most horses develop ataxia, paresis and muscle atrophy (all are often asymmetrical), and occasionally behavioral changes are seen. As the disease progresses, sensory deficits, obtundation, focal sweating, lameness, cranial nerve dysfunction (head tilt, pharyngeal or facial nerve paralysis), monoplegia and reflex loss may be observed. Neurologic signs are generally progressive and then stabilize. Marked **asymmetrical muscle atrophy** may persist.

There is no definitive ante mortem diagnostic test. Routine CSF analysis is often normal. Serology looking for antibodies is useful to rule out disease but has a low positive predictive value. CSF antibodies may be found in the absence

of CNS infection. The combination of clinical signs and a **positive response to therapy** has been used as a presumptive diagnostic tool. Electromyography can help localize lower motor neuron (gray matter) involvement.

At necropsy, a multifocal, non-suppurative myeloencephalomyelitis (with or without different stages of *Sarcocystis* organisms) may be present. There is an apparent topographic predilection for the spinal cord and brainstem. The lesions occur randomly in gray and white matter. Microscopically, widespread perivascular cuffing with inflammatory cells (macrophages and lymphocytes with occasional eosinophils) is present, along with edema, axonal spheroids and necrosis. The organisms may appear as basophilic meronts in rosettes or clusters but are difficult to find, especially if the affected animal has been treated.

Therapy is based on the use of **antifolate drugs**. The only currently licensed drug is **ponazuril** (Marquis), which is formulated as a paste containing 7 doses at 5 mg/kg dose PO s.i.d. The recommended treatment duration is 28 days (4 paste syringes). **Many horses relapse** after therapy is discontinued. The phenomenon may relate to the inability of the drugs to affect the encysted organism. The folic acid inhibiting effect should be monitored by observing the **complete blood count** for neutropenia and/or thrombocytopenia. Caution is advised when treating pregnant mares, as long-term use of these drugs may suppress the developing bone marrow of the fetus.

An **EPM vaccine** (Fort Dodge Animal Health) is licensed. Long-term efficacy studies have not yet been published.

Equine protozoal myeloencephalitis appears to be a treatable, but not necessarily curable disease. Horses with signs localized to the brainstem often respond best to therapy. Euthanasia may become necessary if there is extensive muscle atrophy, ataxia and loss of athletic capability.

TETANUS

Since the advent of routine vaccination of horses against tetanus (*q.v.*), this **highly fatal** disease has become less frequent although isolated cases still occur in most parts of the world. The cause of tetanus is *Clostridium tetani*, a ubiquitous spore-forming rod found in the soil and feces of many animals. The organism requires anaerobic, necrotic conditions, such as those found in contaminated, deep, puncture-type wounds, so that it can vegetate and produce its **potent exotoxin**. The toxin disseminates from the local wound and gains access to the CNS, hematogenously and through the lymphatics, where it localizes in the gray matter of the spinal cord and inhibits the release of inhibitor neurotransmitters, particularly **glycine** and **γ-aminobutyric acid (GABA)**. This "disinhibition" results in **uncontrolled tetanic extensor muscle spasms**.

Most horses showing signs of tetanus have a history of sustaining a laceration to the face, lower limbs or tail, or a puncture wound to a hoof. Enteric infection has been implicated in cases in which a wound could not be identified. The incubation period varies from hours to 2 wk but is usually 7–9 days. The initial clinical signs are characterized by gait stiffness, but generally progress to elevation of the tail head, erect ears, **trismus (lockjaw)**, flare of the nostrils and **prolapse of the third eyelid** (which can often be induced by flicking the muzzle). Difficulty in eating and drinking, muscle tremors and fever often develop. Recumbency rapidly ensues and death occurs due to uncontrolled

Box 17.1 Treatment aims in horses showing clinical signs of tetanus

1. Destroy the organism with cleansing of the local wound and parenteral administration of benzylpenicillin (20 000–50 000 IU/kg IV q.i.d.)
2. Neutralize the toxin with the antitoxin (1500–20 000 IU, SC or IV or IM s.i.d.)
3. Provide sedation and relief from muscle spasms with acepromazine (0.04–0.10 mg/kg IV, IM q 4–6 h), or diazepam (0.01–0.4 mg/kg IV, as needed) in combination with xylazine (0.5–1.0 mg/kg IV or IM)
4. Provide intensive supportive therapy, including IV fluids (e.g. lactated Ringer's solution at a minimum of 30 liters per day), feeding alfalfa cube slurry via nasogastric tubing, moving the animal to a darkened quiet environment, and placing the animal in a sling to prevent falling
5. Muscle relaxants (e.g. methocarbamol, Robaxin-V Fort Dodge, 10–20 mg/kg q.i.d. or diazepam 50–200 mg IV every 6–8 h) may be effective in controlling the muscle spasms and pain in some animals
6. Recumbent horses will require labor-intensive care
7. Anticonvulsant therapy (see Table 17.1) may be necessary
8. Intrathecal tetanus antitoxin is no longer recommended

muscle spasms and convulsions, respiratory paralysis and cardiac arrest. If the disease has not stabilized by Days 3–4, most animals will become recumbent and die by Days 4–5. The mortality is 50–80%.

There is no definitive ante mortem diagnostic test for tetanus. The CSF analysis is normal. Circulating levels of tetanus toxin are very low and difficult to detect. The diagnosis is based on clinical signs and wound history.

Unvaccinated horses that have sustained a wound require both **tetanus antitoxin** (for immediate passive protection) and a **toxoid** booster (for "acquired" longer term protection). A wounded but previously vaccinated horse requires only the tetanus antitoxin. Treatment aims in horses showing clinical signs of tetanus are listed in Box 17.1.

For horses showing signs of tetanus, the prognosis for survival is good:

1. If the initial wound was treated properly and the horse received parenteral antibiotics (metronidazole, 20 mg/kg b.i.d.) and the antitoxin early in the course of the disease
2. If the disease has stabilized and not progressed after 4–5 days
3. If the horse remains ambulatory and able to eat and drink
4. If the animal was vaccinated within 1 yr prior to sustaining the wound.

Tetanus is a **preventable disease**. Pregnant mares should be vaccinated (*q.v.*) with the toxoid 2–4 wk prior to parturition to ensure transfer of anti-tetanus antibodies to colostrum. Newborn foals suffering failure of passive transfer of colostral antibodies should receive one dose of the antitoxin. All horses should probably be vaccinated with the toxoid at 3–4, 6 and 12 mo of age to ensure protection, although there is some concern that this regimen may interfere with the foal's natural development of anti-tetanus antibodies. Tetanus toxoid and tetanus antitoxin can be given at separate sites at one time, to

ensure both immediate and long-term protection. Due to the susceptibility of horses to tetanus and the potential for highly contaminated wounds, yearly vaccination is advised.

TYZZER'S DISEASE (*BACILLUS PILIFORMIS*)

This sporadic disease, named after Ernest Tyzzer who initially described the syndrome in 1917, is caused by *Bacillus piliformis*, a Gram-negative, filamentous bacterium. Affected foals are usually between 1 wk and 1 mo of age. Infection is thought to occur through oral ingestion of the organism from soil, or from feces of another infected mare or foal. **Stress** and **rapid growth** are thought to be predisposing factors.

Affected foals die due to severe fulminant **acute hepatitis** and **hepatoencephalopathy**. Icterus may or may not be present. **Seizures**, often the presenting clinical sign, may not be responsive to anticonvulsant therapy. Foals quickly become comatose, succumbing 24–36 h after the onset of clinical signs. Ante mortem diagnosis of Tyzzer's disease (*q.v.*) is difficult to make because of its rapid progression. Although the organism should be sensitive to penicillin or oxytetracycline, the condition is usually so advanced when clinical signs become apparent that treatment may be ineffective.

At necropsy, the organism is detected by histologic identification of bacteria in the liver. The organism can only be cultured by mouse or chick embryo inoculation. There is little epidemiologic information on this infrequently reported disease, therefore methods for prevention are unknown.

METABOLIC DISORDERS

HEPATOENCEPHALOPATHY

Hepatoencephalopathy is the result of severe liver disease and is thought to cause cerebral signs through:

1. Ammonia acting as a **neurotoxin**
2. Endogenous **diazepines** produced by the small intestine and not metabolized by the liver
3. An imbalance of **GABA and glutamate** (disrupted glutamate transporter and receptor function)
4. **Perturbed monoamine neurotransmission** as a result of altered plasma amino acid metabolism
5. Altered **nitric oxide synthase (NOS)** expression.

In adult horses, hepatoencephalopathy has been reported in association with acute hepatic necrosis due to administration of the tetanus antitoxin (*q.v.*), or with liver disease due to ingestion of the **hepatotoxic pyrrolizidine alkaloid-containing plants** (*q.v.*) e.g. **ragwort** (*Senecio*) or **rattlebox** (*Crotalaria*). In foals, hepatoencephalopathy can be caused by infection of the liver with *Bacillus piliformis* (**Tyzzer's disease**) (*q.v.*), or less commonly with a congenital portosystemic shunt.

Physical signs of liver failure, such as weight loss, ascites or photosensitization, may or may not be present, depending on the acuteness and duration of

liver dysfunction. **Neurologic signs** consistent with hepatoencephalopathy include anorexia, obtundation or coma, dementia or violent uncontrollable frenzies, compulsive circling or walking, head-pressing, yawning, blindness and ataxia. Horses are often afebrile and have difficulty eating and drinking. Convulsions may develop and, uniquely in the horse, **bilateral laryngeal paralysis** and roaring may occur. The cause for the latter signs is unknown. In foals with congenital portosystemic shunts, intermittent obtundation and ill-thrift have been described.

Elevations in the **serum enzyme activities** of AST, GGT, SDH, ALP, LDH and concentrations of bilirubin and bile acids should be found. Hypoglycemia is common in acute failure, hypoproteinemia if chronic. A systemic inflammatory response may be evident in the presence of **septic cholangitis** or **liver abscessation** (*q.v.*). **Liver biopsy** (*q.v.*) may reveal necrosis, cirrhosis or hepatitis, but in the early stages of liver disease it may be normal.

Treatment for hepatoencephalopathy includes removal of access to hepatotoxic plants and protection from sunlight, **lactulose** (dose not established, but over 100 mL may have an effect) to decrease ammonia absorption, administration of **polyionic dextrose-supplemented IV fluids** (maintenance of 30 liters per day), and feeding a low protein and high carbohydrate diet. Sedation with conventional anticonvulsants (see Table 17.1) may be required. A protective **head helmet** may prevent further injury to the skull, particularly if the horse is head-pressing or is having seizures.

The prognosis is generally poor, particularly for animals with pyrrolizidine alkaloid toxicity. Most animals die within a week to a month or so after the onset of clinical signs. A few adult horses with mild signs of hepatoencephalopathy and cholangiohepatitis may survive if treated.

HYPOCALCEMIC AND HYPOMAGNESEMIC TETANY

Although these conditions are not as common in equids as they are in ruminants, they have been reported from time to time. In horses, tetany due to **low ionized calcium** has been described in heavily lactating, recently transported mares. It is characterized by muscle tremor, paresis, ileus, staggering high-stepping gait, seizures and "**thumps**" (synchronous diaphragmatic flutter) (*q.v.*). Tetany, seizures and death have been described in critically ill foals with profound **hypomagnesemia**.

These conditions can be corrected by IV administration of calcium or magnesium salt solutions, given slowly **to effect**, with continual monitoring of cardiac function during therapy. Some animals may require several days of calcium supplementation in order to replace total body calcium deficits.

TOXIC CONDITIONS

LEUKOENCEPHALOMALACIA (MOLDY CORN POISONING, MYCOTOXIC ENCEPHALOMALACIA)

Leukoencephalomalacia is a toxic disease that has been reported as a sporadic cause of equine mortality throughout the world. It is caused by the toxin of the **mold** *Fusarium moniliform*. This mold grows on cereals (particularly corn)

that have been contaminated prior to harvest. Kernels damaged by drought and insects and harvested under high moisture or humidity are often infested with *Fusarium*. This is a **seasonal disease** (late autumn/fall to early spring). There is no breed or gender predisposition, but usually it does not affect horses <1 yr of age. The clinical disease is characterized by an acute, severe neurologic disorder, hepatic syndrome or sudden death. Mortality ranges from 40% to 84%.

The course of the disease varies from 6 h to a few days. The mortality rate and severity of clinical signs are dose related: high doses subacutely will induce **hepatic syndrome** and small doses chronically will induce **encephalomalacia syndrome** (*q.v.*).

Clinical signs are variable but fall into one of several syndromes. The encephalomalacia or **neurologic syndrome** is characterized by cerebral signs such as anorexia, obtundation, cranial nerve deficits, central blindness (unilateral or bilateral) and mania. Hyperesthesia, ataxia and paresis may occur. Recumbency, seizures and coma ensue. Icterus may or may not be present. The **hepatic syndrome** is characterized by obtundation, icterus, recumbency and coma. Horses with leukoencephalomalacia are usually not febrile. **Sudden death**, in the absence of preceding clinical signs, may occur. The differential diagnosis includes viral (rabies) or bacterial encephalitis, hepatoencephalopathy or cerebrospinal nematodiasis (*q.v.*).

CSF analysis may be normal or may reveal increased total protein, xanthochromia, neutrophilic pleocytosis and negative microbial cultures. Liver enzymes and blood ammonia may be elevated. A peripheral neutrophilia may be present. Culture of the suspected contaminated feed is usually not rewarding, but isolation of *Fusarium* or its toxin from the feed may be supportive. Isolation of the organism or toxin requires specialized laboratories.

There is **no specific treatment** for horses with leukoencephalomalacia. Removal of contaminated food is advised and supportive care is important. Fluid therapy, control of seizures (see Table 17.1) and anti-inflammatory drugs are indicated. The prognosis is guarded for affected animals. Survivors may have residual neurologic defects.

Necropsy reveals macroscopic brain cavitations, hemorrhage, liquefactive necrosis, edema and unilaterally enlarged hemispheres. Microscopic examination of the brain reveals malacia and cavitation in centrum ovale and corona radiata of the brain along with thrombi, vasculitis, edema, cellular infiltration of eosinophils and plasma cells. There are no specific lesions in the liver but mild, diffuse vacuolization of the hepatocytes, diffuse centrolobular hepatic fibrosis and bile duct proliferation may be observed.

YELLOW STAR THISTLE (NIGROPALLIDAL LEUKOENCEPHALOMALACIA)

In horses, ingestion of **yellow star thistle** (*Centaurea solstitalis*) or **Russian knapweed** (*Centaurea repens*) causes necrosis of the substantia nigra and globus pallidus ("**nigropallidal encephalomalacia**"). These plants grow predominantly in Australia and the western USA.

Affected horses have usually been eating the plants for several weeks (especially the thistles) and may become **addicted**. Necrosis of the basal nuclei

causes muscle rigidity in Parkinson's disease, and the clinical signs in horses may have a similar pathophysiology, although **limited to the face**. The muscles of mastication become acutely rigid with excessive jaw tone. The animal cannot chew, open or close the mouth completely. Masseter muscle fasciculation may be present. Horses may attempt to lap up feed and water with the tongue. Aimless wandering, ataxia or compulsive circling can also be seen.

The diagnosis is based on the clinical signs, history and post mortem findings. The disease has been diagnosed by **magnetic resonance imaging**. Although horses can be temporarily maintained on IV fluids or feeding by nasogastric tube, there is no specific treatment. Starvation and dehydration usually ensue. Affected horses should be humanely destroyed.

RYE GRASS AND DALLIS GRASS TREMOROGENIC MYCOTOXICOSES (STAGGERS)

There are several tremorogenic or staggers syndromes of horses. The most common is probably **rye grass staggers**. Rye grass staggers has been reported in New Zealand, Australia, the UK and the USA. The causative mycotoxin, **lolitrem B**, is produced by fungal endophytes that parasitize rye grass plants and seeds. Dallis grass (*Paspalum dilitatum*) poisoning (**paspalum staggers**) has also been described in horses and has been reported in Australia, New Zealand, the USA and Europe. The toxin is contained in the **sclerotia** (ergots) of *Claviceps paspali*, the fungus that parasitizes dallis grass.

Ingestion of mycotoxins usually results in **generalized muscle tremors** or spasms, ataxia, swaying, or head-nodding in horses. Excitement or stress will exacerbate the signs. Initially there is diffuse intermittent, mild muscle tremor that progresses to varying degrees of ataxia with a wide-based stance. Affected horses may sweat, stumble, and become recumbent. Despite the spectacular signs, the condition is **not generally fatal**, providing the horse does not injure itself with a fall. The clinical signs usually resolve with time (over a few hours to several days). Affected horses should be removed from affected pasture and handled as little as possible. **Diazepam** (50–100 mg/450 kg IV) may be required for sedation. The clinical signs reflect vestibulocerebellar, diffuse spinal or peripheral nerve involvement, but definitive neuropathologic changes are not observed at necropsy.

SPACE-OCCUPYING LESIONS

NEMATODIASIS (ABERRANT PARASITE MIGRATION, VERMINOUS MYELITIS)

There is little information available on the incidence of natural (non-experimental) verminous infection of the CNS in horses and mules. However, aberrant migration of *Strongylus vulgaris*, *Halicephalobus deletrix*, *Angiostrongylus cantonensis*, *Setaria* spp., *Draschia megastoma* and *Hypoderma* spp. (*q.v.*) into the brain or spinal cord of horses or donkeys has been described.

These parasites generally cause signs of forebrain or spinal cord diseases, depending on their sites of entry and/or migration. Horses of any age can be

affected. The clinical signs vary from peracute onset of **asymmetric ataxia and paresis**, to forebrain signs with asymmetric cranial nerve deficits. Occasionally signs of diffuse cerebral disease can occur.

The clinical course may be marked by **stabilization** of the signs (for days or weeks) followed by **re-exacerbation**, which may be associated with reactivation, multiplication and migration of the particular parasite within the CNS. Physical examination is usually unrewarding, as the affected animal may not show outward signs of parasitism unless lesions from warble (*Hypoderma* spp.) larvae (*q.v.*) are evident along the back. **Verminous myelitis** can be difficult to diagnose based on the clinical signs alone, but the presence of **eosinophils** and/or **neutrophilic pleocytosis** in CSF is strong supportive evidence. Parasitic larvae or ova are rarely detected in the CSF.

Larvicidal doses of anthelmintics such as **moxidectin** (Quest, Fort Dodge, 0.4 mg/kg once) or **fenbendazole** (10 mg/kg for 5 days), **corticosteroids** (e.g. dexamethasone 0.1–0.2 mg/kg) or non-steroidal anti-inflammatories (e.g. flunixin 1.0 mg/kg s.i.d.–b.i.d.), are beneficial. The prognosis for complete recovery is guarded, as some degree of **residual neurologic deficit** may persist.

TUMORS AND CHOLESTEROL GRANULOMA

Neoplasms of the CNS in horses are extremely rare. The signs include **gait abnormalities** if the tumor involves the spinal cord, or brain dysfunction if the tumor is intracranial. The signs can appear suddenly and progress rapidly; however, in some cases the signs may also be slowly progressive. There is no treatment for any of these CNS tumors.

The most common equine brain tumor, **pituitary adenoma** (*q.v.*), occasionally induces blindness and obtundation. Carcinoma, melanoma and lymphosarcoma (*q.v.*) of the cranial cervical and cranial thoracic spinal cord have caused **Horner's syndrome** (*q.v.*) in horses. Lymphosarcoma, neurofibroma and melanosarcoma (*q.v.*) occasionally infiltrate the sacrococcygeal vertebral canal, entrap the cauda equina and cause cauda equina syndrome.

Up to 20% of older horses have **cholesterol granulomas** (*q.v.*) associated with the choroid plexuses of the lateral and/or fourth ventricles. Although there is potential for expression of ante mortem neurologic deficits associated with these lesions, most are found incidentally at necropsy. They may represent a chronic granulomatous reaction to cholesterol crystal deposition associated with chronic choroid plexus vascular leakage. Mature cholesterol granulomas are generally circumscribed, firm, granular and yellow-brown and can attain an impressive size. Clinical signs have included altered behavior, obtundation, somnolence and reluctance to move, generalized seizures, ataxia, paresis and unconsciousness resulting from direct pressure lesions and secondary hydrocephalus.

TRAUMA

Of all equine neurologic conditions, **trauma to the CNS** is probably most frequently encountered. Horses that have reared, fallen over backwards and landed on the poll may lie in recumbency, semiconscious, for varying lengths of

time. Upon closer inspection, nystagmus, pupillary constriction or dilatation, blindness or facial paralysis may be present. The ears, nostrils, mouth and ocular fundus should be examined for signs of hemorrhage. If the animal is successful on attempts to stand, it may show profound obtundation and a base-wide stance, along with head tilt, circling, leaning toward the affected side or ipsilateral facial paralysis. Occasionally, seizures occur after head trauma.

The **petrous temporal** or **basisphenoid** bones are not uncommonly fractured when horses fall over backwards, and can result in **profuse hemorrhage** from ears and nose and asymmetric vestibular signs. Atlanto-occipital fractures, dens avulsions and cervical vertebral fractures are common in **foals**, whereas adult horses tend to fracture lower cervical and thoracolumbar vertebrae. **Somersault falls** result in hyperextension and hyperflexion injury to the cervical vertebrae. Horses that run directly into a solid object usually injure the thoracic region. Horses that slip and land in a dog-sitting position most often injure the **thoracolumbar spine**.

Horses (or foals) with fractured vertebrae will demonstrate a range of very mild to severe neurologic signs. If spinal cord injury (compression, swelling and edema) has occurred, clinical signs are more likely to be present. Fractures of C1–T2 usually result in **tetraparesis** and **ataxia** in all four limbs. A recumbent horse with a lesion at C1–C3 may not be able to raise its head. A recumbent horse with a lesion at C3–T2 may be able to lift its head but cannot rise into sternal recumbency (but not all horses with cervical fractures follow these rules). Fractures of T3–L6 may cause paraparesis, ataxia and sometimes dog-sitting. Fractures of the sacrum and coccygeal vertebrae often produce fecal and urinary incontinence and gait abnormalities in the pelvic limbs. Depending on the nature and severity of the injury, some degree of asymmetry may be apparent in any of these fractures. Localization of **hyporeflexia** and **loss of sensation** along the neck and trunk may help to approximate the cranial extent of the lesion. **Whole body sweating** may also be present in horses with a broken back or neck. Very occasionally, the Schiff–Sherrington syndrome (**extensor hypertonia**) has been observed in horses and foals with severe thoracic spinal injury.

Plain radiography is helpful in determining the exact site of the fracture but does not directly evaluate the degree of spinal cord injury. Some spectacular looking fractures on plain radiographs may not cause significant spinal cord compression, while other less dramatic fractures do not reflect the severity of spinal cord injury. In addition, it is not always practical to obtain radiographs of the skull, neck or thoracolumbar spine. Therefore, localization of the lesion is often dependent upon the clinical signs. If the horse is not distressed it may be worth waiting for 2–24 h before euthanasing the animal.

CSF analysis can aid in the diagnosis of CNS trauma, but frequently the analysis is not abnormal. The presence of hemorrhage in the CSF is supportive. Collection of CSF from the lumbosacral site is advised if there is any suspicion of elevated CSF pressure associated with a concurrent head injury. In such cases, collection from the **atlanto-occipital** site exacerbates the risk of caudal herniation of the occipital lobes of the cerebrum and cerebellum. As with radiographs, it may not be practical to collect CSF in the field situation. After CNS trauma, the findings on serial neurologic examinations are often of greater diagnostic and prognostic significance.

Medical management of acute CNS trauma is controversial and complicated by the lack of proof of efficacy of many of the commonly recommended drugs. **Corticosteroids** may help reduce spinal cord and brain edema. The use of corticosteroids in CNS injury is controversial and dexamethasone has not been proven to alter outcome. In the peracute stage of injury, IV **dexamethasone** (0.1–0.2 mg/kg) up to 3 times daily for the first 2 days or so has been used. Injured horses, particularly recumbent patients, may thrash and struggle and should be kept sedated with low doses of tranquilizers, e.g. xylazine 0.5 mg/kg IV.

Anticonvulsant therapy (see Table 17.1) may be necessary. One to two standard doses of the diuretics **dimethyl sulfoxide (DMSO)** (1 g/kg as a 10% solution in 5% dextrose) or **mannitol** (slow IV 20% solution at 0.25 g/kg) may be helpful in minimizing acute brain or spinal cord edema. Caution is advised because these agents may exacerbate intracranial hemorrhage, however this undesirable side effect has not been proven in horses. **Mannitol** may be useful if there is a concern about intracerebral pressure.

Clinical trials suggest that **hypertonic saline** (4–6 mL/kg over 10 min, followed by conventional fluids within 1–2 h) can rapidly improve systemic blood pressure. Antibiotics, e.g. **benzylpenicillin** (20 000–50 000 IU/kg IV q.i.d.) may be required for treatment of pneumonia, cystitis (*q.v.*) and decubiti in chronically recumbent neurologic patients. Repair of skull fractures is usually impractical but **surgical decompression** of the spinal cord and stabilization of luxations and fractures could be attempted if the horse's condition continues to deteriorate after medical therapy.

The prognosis for horses with head trauma must be guarded, particularly if **stupor** or coma persists beyond 2–3 days or the **pupils** become fixed and dilated. A **head tilt** associated with a skull fracture may persist although many horses can accommodate quite well. The prognosis for spinal cord trauma associated with vertebral body fractures or luxation is also generally guarded. Patients that remain ambulatory and show only mild ataxia have the best chance of complete recovery, but **residual gait deficits** may persist. In general, if the horse is unsuccessful in its attempt to stand after 3–4 days of recumbency, the prognosis is grave. However, providing spinal cord compression from healing bone or surrounding soft tissue or re-injury does not occur, the spinal cord may heal and the neurologic signs improve with time.

POST-ANESTHETIC CENTRAL NERVOUS SYSTEM DISORDERS

POST-ANESTHETIC MYELOPATHY

This is a rare complication of **general anesthesia** (*q.v.*) and is most commonly reported in heavier (300–470 kg) but younger (6–24 mo) horses in placed dorsal recumbency for routine surgical procedures. Either gender can be affected. Although frequently not documented, the condition is thought to be related to **hypotension** and **vena caval and aortic compression**, which result in hemorrhage, ischemic injury and necrosis of the gray matter, usually in the thoracolumbar spinal cord.

Less frequently, the lesions have also been observed in the cervical spinal cord. Recently **equine cerebrocortical necrosis** secondary to general anesthesia has also been recognized.

The clinical signs appear either immediately upon recovery from general anesthesia (the horse may have an unusually difficult time standing up) or shortly thereafter, and consist of varying degrees of areflexia, hypotonia, paraplegia and analgesia involving the trunk, pelvic limbs, perineum, tail and anus.

Bilateral femoral nerve paralysis (*q.v.*) and **paraplegia** (due to hemorrhage along the femoral nerves) have also been seen after anesthesia and present with nearly identical clinical signs. Reports of CSF analysis with these conditions are rare, but elevation in total protein concentration, neutrophilic and red cell pleocytosis and xanthochromia might be expected.

Aggressive anti-inflammatory therapy (1.1 mg/kg flunixin) and IV **DMSO** (1 g/kg as a 10% solution in 5% dextrose) may be helpful and is advised. Residual, sometimes marked permanent neurologic deficits should be expected.

POST-ANESTHETIC MYONEUROPATHY

Like post-anesthetic myelopathy (*q.v.*), this condition occurs in horses after general anesthesia (*q.v.*) and is thought to be due to **compartmental pressure elevation** affecting specific muscle groups and nerves, systemic hypotension, and resulting ischemic injury. There are degrees of muscle pain and swelling and paresis, usually on the dependent side. Evidence of **neuropraxia** (particularly radial or peroneal nerve paralysis) due to involvement of major nerves at the anatomically affected site may complicate the clinical picture. Elevation of serum muscle enzymes can be dramatic. **Myoglobinuria** (*q.v.*) is often present.

Treatment requires **intensive supportive care** aimed at maintaining hydration and correcting electrolyte and metabolic derangements. Recumbent animals should be placed in a sling or kept in a sternal position. Tranquilization (if necessary using 0.5–1.0 mg/kg xylazine) and analgesics, including NSAIDs such as 1.1 mg/kg flunixin b.i.d., are advised. Furosemide or corticosteroids should be avoided. Topical and/or systemic **DMSO** may be helpful. Massage, hydrotherapy and manipulation of the affected limb may encourage blood flow.

The prognosis is best for animals that remain standing. Some loss of muscle mass may occur with recovery. Adequate padding, elevation of the upper limbs, minimizing general anesthesia time, and maintenance of the mean arterial blood pressure above 65 mmHg will minimize the risk.

CONDITIONS OF THE LOWER MOTOR NEURON UNIT

BOTULISM

Botulism (*q.v.*) is caused by *Clostridium botulinum*, a Gram-positive, anaerobic, spore-forming rod that produces a toxin that acts as a powerful presynaptic blocker of acetylcholine release at the neuromuscular junction and preganglionic autonomic synapses. Progressive muscle weakness results. Horses are **extremely sensitive** to the toxin. All ages can be affected.

C. botulinum produces several types of toxins (*q.v.*) that are each antigenically distinct from one another but have similar effects. Horses are particularly susceptible to types B and C. Type B has been found in the soil along the mid-Atlantic seaboard and in Kentucky, whereas type C is found in Florida and Europe.

There are three major routes of infection: **forage poisoning**, which usually occurs in adults, and results from the ingestion of preformed toxin in grain or silage; **wound botulism**, which occurs rarely in horses and results from infection of a wound (similar to tetanus); and **toxico-infectious botulism**, which is most common in foals. In the latter, the spores vegetate in the gastrointestinal tract, liver abscesses, gastric ulcers, or in wounds and produce the toxin. This toxico-infectious form of botulism in foals has been referred to as the **shaker foal syndrome** (*q.v.*). Increased incidence of infection in foals has been loosely associated with stress and increased fat and steroid content in the mare's milk. Typically, affected foals are **strong and fast growing**. They are usually <8 mo old and often <8 wk old (foals as young as 1 wk have been diagnosed). Cases can occur sporadically or present as outbreaks in a particular geographic area. The incubation period ranges from 24 h to 7 days.

Progression of clinical signs can be rapid, over several hours, or take several days. Onset is marked by **flaccid tetraparesis**, dysphagia and muscle tremor, in both horses and foals. Foals may have milk dribbling from their mouths and nostrils as suckling ability may be impaired by poor tongue tone. Some strains appear to produce more brainstem signs than others. **Dysphagia** with pharyngeal paralysis can be the presenting sign. A weak tongue is common. **Muscle fasciculations** and profound **generalized muscle weakness** may develop. Pupils may be intermittently dilated and slowly responsive to light due to sphincter muscle paresis. Recumbency and hyporeflexia occur in the late stages of the disease. **Aspiration pneumonia** from failure to swallow, urine retention, ileus and constipation are common complications. Intercostal muscle paralysis may lead to death from respiratory failure. Inflammatory lesions in the bowel, such as gastric ulcers, are often seen and could be potential sites of bacterial colonization and toxin production.

In adults, differential diagnoses include pharyngeal or esophageal obstruction, severe dental disease, grass sickness in endemic areas, and other CNS diseases causing dysphagia such as rabies (*q.v.*). Additionally, in foals, hypoglycemia, septicemia and rarely rhabdomyositis/steatitis (*q.v.*) should be considered.

Diagnosis of botulism is presumptive and is based on clinical signs. *C. botulinum* can be cultured from feces or spores and can be found in the intestine, but the organism has also been isolated from normal animals. Detection of the toxin in serum or intestinal content is very difficult because levels are often too low for conventional laboratory methods. **Electromyelography** may aid in diagnosis.

Aggressive treatment and intensive supportive care is imperative for survival and can often affordably be given only to foals. A **polyvalent equine type B antitoxin** is available in the USA (Veterinary Dynamics, Templeton, Ca). Best results are achieved when the antitoxin is given early in the disease process. The antitoxin is very expensive but considerably improves the prognosis. Nasogastric tube feeding and assisted respiration may be required to

minimize secondary complications. Wounds should be thoroughly cleansed. **Crystalline penicillin** (**benzylpenicillin** 20 000–50 000 IU/kg IV q.i.d.) is recommended to further reduce colonization and toxin production in the gut. Procaine benzylpenicillin, tetracyclines and aminoglycosides should be avoided because they may potentiate the paralyzing effects of the toxin.

Forage poisoning is usually fatal in adult horses unless they remain standing. Without supportive care (including mechanical ventilation and antitoxin treatment), mortality approaches 90% for foals ⩽12–48 h old. Older foals will die within 72 h. Prognosis is guarded if there is rapid onset of clinical signs (⩽12–36 h) and slightly better if the onset progresses over 2–4 days. If the foal recovers, weakness may last up to 3 wk.

Vaccination of pregnant mares with a **botulism type B toxoid** is practiced in some areas where **shaker foal syndrome** is common.

EQUINE MOTOR NEURON DISEASE

Equine motor neuron disease (EMND) was initially documented in the northeastern USA but is now being recognized all over the world. EMND is equivalent to a type of human motor neuron disease and is characterized by the **degeneration** and loss of **motor neurons in the spinal cord and brainstem** and neurogenic atrophy of skeletal muscle. The etiology is unknown but may be due to oxidative stress. Cases in North America consistently have a history of very limited access to grass and **low vitamin E** levels (*q.v.*), however this is not necessarily the case in European cases.

Clinical signs in classic cases are marked by **symmetrical muscle wasting** and weight loss, muscle trembling, sweating, and extended periods of recumbency. Animals adopt a "tucked up" stance similar to cases of **grass sickness** (*q.v.*), have a low head carriage, and shift weight when forced to stand. Affected horses "walk better than they stand", probably because of the preferential denervation atrophy of type I fibers. Type I fibers are found in greater proportion in antigravity postural muscles. Denervation and contracture of sacrocaudalis dorsalis medialis, a muscle that has a high proportion of type I muscle fibers, leads to **elevation of the tail**. Excessive lipopigment deposition in the retina can be detected by funduscopic examination in many affected horses.

The most consistent laboratory findings in EMND have been mild to moderate increases in muscle enzyme activity in the serum and **extremely low values of plasma α-tocopherol** (active form of vitamin E). Intestinal glucose absorption is decreased while results of xylose absorption tests are more normal.

Ante mortem diagnosis is based on the history, clinical signs, laboratory findings (elevated muscle enzyme activity and low plasma α-tocopherol concentration) and the demonstration of neurogenic atrophy in a muscle biopsy of sacrocaudalis dorsalis medialis. Some cases stabilize and regain normal weight with nursing care and administration of vitamin E; however, some of those relapse 3–4 years later.

HYPERKALEMIC PERIODIC PARALYSIS

Hyperkalemic periodic paralysis is characterized by intermittent episodes of muscular paresis and fasciculations, often resulting in recumbency. Exercise,

a period of rest after exercise, stress such as transport or athletic competition, or ingestion of alfalfa hay may precipitate episodes. Episodes are accompanied by a transient increase in **serum potassium** concentration (5.5–9.4 mEq/L) without major acid-base imbalances or high serum activity of muscle-derived enzymes. The disease occurs in young, heavily muscled, stock-type horses such as American Quarter Horses, Appaloosas and Paints and is similar to a well-described human syndrome. It is an inherited disease in the **Quarter Horse**: affected animals in this breed can all be traced to a common sire, and have a **gene defect** affecting sodium channels.

Between episodes, horses appear normal. The onset of a mild attack may begin with **repeated yawning** and intermittent flicking of the third eyelid or facial muscle spasms followed by **fasciculation and tremor** involving muscles of the flank, shoulders and neck. During an episode the horse is alert, appears distracted and reluctant to move, and may stumble and buckle at the knees. A severe episode, perhaps following forced exercise, results in severe tremor and tetany of many muscles with recumbency and sweating. This is followed by a state of flaccidity, possibly with depressed spinal reflexes. Episodes can be initially confused with colic, seizures or exertional rhabdomyolysis (*q.v.*). Attempts to move result in further tremor and tetany, although the horse remains alert. If the horse does not become recumbent, **profound paresis** manifested as gait deficits (swaying or staggering) or paresis of the hindquarters (dog-sitting) may be observed. **Respiratory stridor** is occasionally observed during episodes and has recently been reported in several neonatal foals thought to be affected with the condition. Episodes may last from 30 min to 1 h.

Hyperkalemic periodic paralysis is typically diagnosed by a combination of clinical signs and concurrent **serum hyperkalemia**. Electromyographic (EMG) examination during an episode reveals fibrillation potentials and myotonic discharges in most muscles. **Genetic testing** of tail hairs (Veterinary Genetics Laboratory, Davis) can detect the disease with a high degree of accuracy.

Attacks of tremor and tetany appear to be short lived, although treatment of horses during attacks with **IV fluids** containing calcium, sodium bicarbonate and glucose may shorten an attack. The diuretics **acetazolamide** (0.5–2.2 mg/kg PO b.i.d.) or **hydrochlorothiazide** (0.5 mg/kg PO b.i.d.) may also be effective but the true mechanism of action is unknown. They may stabilize the Na^+/K^+ pump at the level of the muscle membrane. When administered prophylactically, they appear to lessen the frequency and severity of attacks in horses known to be affected with hyperkalemic periodic paralysis. Limiting dietary potassium may also be helpful; low potassium commercial diets are available in some countries.

The severity and frequency of episodes reportedly lessen as the horse ages. The disease may be fatal in some severely affected animals. If an episode is triggered by an **anesthetic agent**, potentially life-threatening complications may be encountered.

MYOTONIA

Myotonia is the clinical sign of a skeletal muscle abnormality that results in a **prolonged contraction** of the muscle cell. Voluntary, mechanical or electrical stimulation of skeletal muscle produces episodes of prolonged contraction.

It has been reported in Morgan horses, Thoroughbreds, Standardbreds, Swedish half-breds, Appaloosas and Quarter Horse foals and in a Welsh pony. Heritability has not been proven in horses but **familial predisposition** is suspected. In other species a chloride channel defect has been demonstrated.

The disease is characterized by **generalized muscle stiffness** that improves with exercise and worsens with cold or anxiety. Hypertrophy of skeletal muscles may be present and production of a "**dimple**" on percussion is characteristic. Muscles of the hindquarters are most severely affected and usually are prominent. The exact cause is not known but the defect is thought to be at the level of the skeletal muscle cell membrane or transverse tubular system.

The clinical diagnosis can be made by seeing and feeling prominent and prolonged muscle contraction with "knotting" or "dimpling" following mechanical percussion. The clinical diagnosis is confirmed by **electromyographic examination**, which reveals bizarre spontaneous electrical discharges from affected muscle membranes.

Affected animals do not appear to be debilitated by the disorder, although limb deformity with contracture may occur. Phenytoin has not been effective in treating horses with myotonia.

SHIVERING, POLYSACCHARIDE STORAGE MYOPATHY AND STIFF HORSE SYNDROME

Three distinct syndromes characterized by hypertonia and hyperreflexia are recognized in horses.

Shivering is a neuromuscular disorder characterized by **abrupt onset excessive flexion** of muscles of the pelvic limbs and tail. Draft horses and Warmbloods are most often affected, ponies very rarely.

A defect in the myotactic reflex arcs or in the upper motor neuron pathways has been postulated. Walking the horse out of its stable in the morning often initiates signs. **Backing affected horses** will usually greatly exacerbate signs. Pelvic limbs are held in a fully flexed and slightly abducted position. Spasmodic contraction of the gluteal and flexor muscles of the limb produces the "shivering" of the muscle bellies which gives the disease its name. The leg may be held in this manner for several minutes. The tail head may be elevated and tremulous. Animals are usually completely normal between episodes.

Affected animals may still be able to work on the flat, but their jumping ability will eventually be impaired. The frequency and intensity of "shivering" episodes may gradually increase and affected muscle groups may waste. The long-term prognosis for athletic function is grave.

Equine polysaccharide storage myopathy (EPSM) is a myopathy recognized most often in draft horses and Quarter Horses. The disease is characterized by the accumulation of excessive glycogen or complex polysaccharides in principally type II muscle fibers.

Horses can present with signs of stiffness and exaggerated pelvic limb action similar to shiverers, or show muscle atrophy, paresis and recumbency. Exertional rhabdomyolysis is one of the most common signs of EPSM in Quarter Horses and has also been found in the other light breeds. The manifestations of EPSM may be subtle, with mild loss of muscle, energy, gait, and/or performance, or they may be catastrophic, leading to spontaneous or

post-surgical recumbency and death. Pathologic findings do not correlate with clinical severity.

The definitive diagnosis of EPSM at this time relies entirely on pathologic findings in muscle biopsies. Following PAS staining for glycogen the diagnosis may be obvious, with numerous fibers containing amylase resistant complex polysaccharide, or it may be subtle, with primary findings being overall atrophy and increased glycogen staining. Testing of pre- and 4 h post-exercise blood samples often reveals a mild to moderate increase in serum CK and/or AST. A specific metabolic defect has not yet been identified in EPSM horses. Clinical signs may improve dramatically with increased dietary fat. Diets low in carbohydrates, such as alfalfa pellets or commercially available diets, should be supplemented with 500 mL of vegetable oil per day.

Stiff horse syndrome may be the equine equivalent of "stiff man syndrome" in humans. It is characterized by muscle rigidity and episodic and often violent muscle cramps. This rare condition is associated with antibodies produced against the enzyme **glutamic acid decarboxylase (GAD)**, responsible for converting the inhibitory neurotransmitter GABA into its active form.

Clinical signs appear to wax and wane and range from mild muscle stiffness to sudden and often violent muscle contractions. Generally there is an insidious onset, and exercise intolerance associated with mild to moderate muscle stiffness may be the only initial clinical sign. This may easily be attributed to a primary myopathy, with pain on muscle palpation, although serum muscle enzyme concentrations remain in the normal range. If untreated, the degree of stiffness seems to progress and episodes of muscle spasms may become apparent. Between episodes the horse may appear normal. Clinical examination is generally unremarkable. Unlike EPSM, biopsies of semitendinosus are unremarkable. The most useful diagnostic test is detection of antibodies against GAD in serum and CSF, run in some human laboratories. Human patients are treated with benzodiazepines and glucocorticosteroid administration but use of these drugs has not been critically evaluated in equine patients.

Attempts should be made to stabilize the disease as good response to therapy with **prednisolone** 1–2 mg/kg has been recorded, although the prognosis is generally poor due to the apparent progression of this condition. There is a **welfare implication** as some of the spasms are likely to be very painful and there is the strong likelihood of disease progression.

STRINGHALT

Stringhalt is a motor disorder that can affect any breed and is of unknown etiology. The disease is characterized by **delayed protraction and excessive flexion of the hock** during progression and may affect one or both pelvic limbs. Possible associations include trauma and degeneration of the sciatic and/or peroneal nerves, generalized distal axonopathy, spinal cord lesions (e.g. EPM) (*q.v.*) and articular lesions within the hock and stifle joints. It occurs in both sporadic and epidemic forms. The **epidemic form** reported to occur in New Zealand and Australia has been associated with ingestion of certain plants, particularly **dandelion** (*Taraxacum officinal*) and **false dandelion** (*Hypochaeris radicata*), suggesting a toxic etiology, but a specific toxin has not been isolated.

Affected horses appear normal at rest but have a **characteristic involuntary hyperflexion and delayed protraction of the hock** when moving. The disorder may be unilateral or bilateral and can vary in severity from a slight exaggeration of normal movement to a motion wherein the rear foot strikes the belly. The limb may remain flexed for several minutes. When both pelvic limbs are severely involved, forward movement is only possible by a bizarre "bunny hopping" action.

With **chronic stringhalt**, there may be atrophy of distal limb muscles. Some horses with the epidemic form of stringhalt also have **thoracic limb involvement** evident as spasticity, toe scuffing and stumbling. In nearly all cases, the signs are exaggerated when the horse is **turning or backing**. The condition is most noticeable after the horse has rested, and cold weather may exacerbate it. **Inspiratory stridor** due to left laryngeal hemiparesis may also occur due to the involvement of the recurrent laryngeal nerves.

No consistent pathologic lesions have been documented in classical stringhalt but the endemic form is characterized by severe distal axonopathy of large myelinated fibers resulting in neurogenic atrophy of abaxial and laryngeal musculature. Why these cases present with hyperflexion and not paresis is not known, but involvement of the feedback system of muscle spindles to spinal cord is thought to be involved.

Stringhalt is diagnosed by the characteristic pelvic limb hyperflexion. The condition must be differentiated from fibrotic myopathy (*q.v.*) in which the foot is jerked suddenly downward and backward before being put to the ground. It must also be differentiated from intermittent upward fixation of the patella (*q.v.*) and the condition known as "shivering" (*q.v.*), which occurs primarily in draft and heavily muscled breeds.

The treatment for sporadic stringhalt consists of the **surgical removal** of the proximal portion (containing the Golgi tendon organs) of the lateral digital extensor tendon as it passes over the lateral surface of the hock. Some cases show an almost immediate improvement, with complete recovery within 2–3 wk. Other cases may take several months for significant improvement to occur and may never show complete recovery. Some cases of sporadic stringhalt may improve with rest. The majority of horses suffering from the epidemic form of stringhalt recover spontaneously without treatment once they are removed from pasture, however this can often be protracted from several weeks to months.

VESTIBULAR SYNDROME (HEAD TILT)

The **vestibular system** consists of receptors within the semicircular canals in the petrous temporal bone, the vestibular nerve that passes through the internal acoustic meatus, and nuclei in the rostral medulla and caudal cerebellar peduncles. The vestibular nerve does not leave the skull **Acute asymmetric vestibular disease** is often due to head trauma (e.g. fracture of the petrous temporal or basisphenoid bones) or **osteoarthrosis** of temporohyoid bones and subsequent hemorrhage into the inner and middle ear canals. Other causes of head tilt in the horse include equine protozoal myelitis, aberrant parasite migration, viral infection, tumors, neuritis of the cauda equina, otitis media interna or lightning strike (*q.v.*). Mycotic lesions of the tympanic bullae

may also extend into the middle or inner ear, involve cranial nerves VII or VIII, and result in facial paralysis and/or head tilt, respectively. An acute idiopathic vestibular syndrome has also been described in horses.

Neurologic signs are due to a loss of ipsilateral extensor tone and an increase in contralateral extensor tone. When unilateral this results in a **head tilt**, leaning and circling toward the affected side, and an ipsilateral ventral strabismus (accentuated by lifting the head). Nystagmus is rare. If present in unilateral peripheral vestibular disease, nystagmus is horizontal and the fast phase is directed away from the side of the lesion. In central disease, the nystagmus can be horizontal, rotary or vertical. Blindfolding the horse will exacerbate the clinical signs and should be done with care. The specific cause can sometimes be determined by radiography of the skull or CSF analysis.

Treatment of vestibular disease should be aimed at the suspected inciting cause. A head tilt attributed to acute trauma or equine protozoal myelitis will probably respond to treatment better than one attributed to otitis media interna or proliferative bony lesions of the hyoid or temporal bones. Many horses will not completely recover, but will accommodate for the visual and proprioceptive deficits, allowing them to function normally. Acute idiopathic vestibular syndrome in horses usually completely resolves.

HORNER'S SYNDROME

Horner's syndrome was first described by Swiss ophthalmologist Johann Horner in 1869. It is an eponym applied to the collection of clinical signs associated with pathology of the **sympathetic nerve supply to the head**. Symptoms can be caused by lesions anywhere in this sympathetic pathway. The horse is **susceptible** to Horner's syndrome because sympathetic postganglionic fibers from the cranial cervical ganglion are superficial as they pass over the caudodorsal aspect of the guttural pouch and course down the neck along the jugular groove, and hence are vulnerable to trauma or infectious conditions.

Common causes of Horner's syndrome in the horse include cervical trauma, guttural pouch infection (*q.v.*), neoplasia (*q.v.*), focal infections, foreign bodies ("choke"), periorbital disease (*q.v.*), perivascular injections and carotid artery ligation. Grass sickness (equine dysautonomia) (*q.v.*) results in **bilateral** Horner's syndrome.

Interruption or loss of sympathetic innervation results in **ptosis**, **droopy eyelashes**, and **enophthalmos** with protrusion of the third eyelid (the latter sign may be quite subtle). Myosis is not consistent in this species. **Sweating**, which may be seen on the side of the face, neck or shoulder, is a very early sign, the pathogenesis of which is not completely understood. If the lesion includes postganglionic sympathetic neurons, i.e. including or rostral to the cranial cervical ganglion, then sweating is restricted to the face.

Diagnosis of Horner's syndrome is made primarily on the basis of clinical signs. Physical examination or radiographs of the head or neck may help to identify the specific site of the denervation. A simple diagnostic test is the administration of **0.5% phenylephrine** (N.B. most commercial eye drops are a 10% solution). Twenty minutes after administration the ptosis and angle of the eyelashes (assess by standing in front of the horse) are significantly reduced.

The **treatment** of Horner's syndrome depends on the underlying cause of the denervation. The appropriate medical or surgical therapy for the inciting cause should be instituted. For example, palpable swellings over the site of perivascular injections should be cold or hot packed. Reversibility of the disorder is related to the seriousness of the neurologic injury. Neuron avulsion, severance, and invasion or destruction by neoplastic or infectious processes would usually be irreversible.

Stretching, contusive and inflammatory injuries (secondary to perivascular injection) may result in transient clinical signs (≤48 h) of Horner's syndrome. In general, the prognosis for these cases is good, but complete recovery may require several weeks to months. Horner's syndrome has been known to persist, in rare cases, up to 1 yr.

FACIAL NERVE PARALYSIS

Facial paralysis is fairly common in horses. The facial nerve and its branches (auricular, palpebral, buccal) innervate the ear, eyelids, lips and external nares respectively. Dysfunction of the facial nerve results in **drooping of the ear and lips** on the side of the lesion. The muzzle will lack tone and is therefore pulled to the opposite side. Areflexia of the **muscles of facial expression** is often observed and the animal may be unable to close its eyelid. As a result, **exposure keratitis** and corneal **ulceration** (*q.v.*) may be present. Occasionally, bilateral facial paralysis occurs and the horse will present with severe dysphagia. With chronic paralysis, facial muscle atrophy and hemi-spasm (grimacing) may be seen.

A common cause of facial paralysis is associated with **lateral recumbency** and pressure on the side of the face due to a halter and its metal buckles and rings. Facial paralysis due to recumbency usually only involves the nose and lips, but the ear and eyelid may droop due to direct pressure on the auricular and palpebral nerves. Other conditions, such as a **direct blow**, various **skull fractures** (e.g. mandibular, temporomandibular, petrous temporal, zygomatic arch or stylohyoid bones, or obtundation fractures of the face), or **lacerations** can also directly or indirectly involve the facial nerve. Pathology to the facial nuclei in the medulla oblongata results in facial nerve paralysis. **Equine protozoal myeloencephalitis** (*q.v.*) often causes such a lesion and can produce marked facial paralysis. Central lesions above the brainstem have also been rarely noted to cause ipsilateral facial paresis, due to interruption of corticobulbar tracts.

The **treatment** of facial paralysis is primarily symptomatic. Application of **ophthalmologic ointment** to the affected eye will help prevent keratitis sicca and ophthalmitis. **Anti-inflammatories** (1.1 mg/kg flunixin PO or IV b.i.d.) are useful in the management of facial paralysis due to lacerations and head trauma. **Antifolate antibiotics**, e.g. ponazuril (Marquis, Bayer), are indicated for EPM (*q.v.*).

Facial paralysis due to pressure associated with lateral recumbency will usually resolve in 2–3 days. The prognosis for facial paralysis due to laceration or skull fracture depends on the severity of the injury. In the absence of severe skin laceration, the prognosis is fair, although recovery may be partial or incomplete after weeks or months.

SUPRASCAPULAR NERVE PARALYSIS (SWEENY)

Damage to the suprascapular nerve is commonly due to an accident that involves **direct collision** of the horse's **shoulder** with another object. Typically, the owner may report that the horse ran directly into a tree, fence post or another horse several weeks prior to the onset of the shoulder muscle atrophy. As the suprascapular nerve winds around the front of the scapula, it is especially prone to shoulder impacts.

Damage of the nerve at the cranial border of the scapula results in **atrophy** of the supraspinatus and infraspinatus muscles (**sweeny**). The force of the impact can also involve the brachial plexus (the origin of most of the nerves that supply the shoulder and thoracic limb). If this occurs, in addition to supraspinatus and infraspinatus, other supporting structures, prominently those innervated by the radial nerve, will be denervated. Gait deficits will result due to **laxity of the shoulder joint**. The shoulder may subluxate or "pop" as it slips laterally and the thoracic limb is circumducted during forward motion.

Horses with suprascapular nerve injury treated with stall rest alone have a **good prognosis** for recovery of normal gait and return to performance; however, the recovery period may be prolonged. Shoulder joint instability has been reported to resolve in most horses within 3–12 mo after the original injury, allowing animals to return to pre-injury activities.

Exercise should be **restricted** while the joint is unstable. Surgery probably will result in a faster return to athletic function but should be delayed for several months. Surgery consists of removal of a 1.5 cm section of bone from the front of the scapula to relieve compression on the suprascapular nerve.

RADIAL NERVE PARALYSIS

The radial nerve derives its origin chiefly from the eighth cervical and first thoracic roots of the brachial plexus and innervates the extensor muscles of the elbow, carpus and digits and the lateral flexor of the carpus (ulnaris lateralis).

A common cause of radial nerve paralysis is **direct trauma** to the nerve as it crosses the musculospiral groove of the humerus. Such trauma often accompanies **fractures of the humerus**, kicks or falls on the lateral surface of the humerus or prolonged **lateral recumbency**. Radial nerve paralysis may also be a result of overstretching the nerve by **hyperextension of the thoracic limb**, fractures of the first rib or compression of the nerve by enlargement of axillary lymph nodes, tumors or abscesses in the cranial thorax or tumors of the brachial plexus.

The signs of radial nerve paralysis vary depending upon the degree and location of the injury. Unlike other species, the radial nerve in the horse does not have an autonomous zone.

Lesions at or near the elbow joint result in a "high radial nerve paralysis", which is characterized by a **dropped elbow, scuffing of the toe and inability to extend the distal limb joints**. Affected horses have great difficulty getting up and down and stand with the shoulder extended. The foot is knuckled over at rest and the animal collapses on the limb when forced to bear weight. In severe paralysis, dragging of the limb may damage the dorsal surface of the fetlock.

Lesions of the distal radial nerve result in **knuckling** of the carpus, fetlock and pastern joints. The animal can support weight on the affected limb if the metacarpus and distal limb are held in extension. If the injury occurs at the point of the shoulder secondary to humeral trauma, the suprascapular nerve may be paralyzed causing atrophy of supraspinatus and infraspinatus (sweeny) (*q.v.*). Occasionally, radial nerve paralysis will be accompanied by paralysis of the entire brachial plexus. In this case, the limb shows paralysis of the flexor and extensor muscles and is unable to bear weight.

Mild cases of radial nerve paralysis may present with subtle gait abnormalities. The horse may **stumble** when walking and may show a **sliding motion** of the foot when the limb is extended. Detectable sensory deficits resulting from radial nerve paralysis tend to be vague and vary among patients. Atrophy of triceps brachialis, extensor carpi radialis, ulnaris lateralis and digital extensors is present when radial nerve paralysis has existed for several weeks.

The diagnosis is made on the basis of clinical signs. If traumatic paralysis has occurred more than 2 wk prior to evaluation, needle EMG in the extensor muscles of the carpus and digits may be helpful in defining the extent of denervation.

Treatment is **palliative** and involves stall rest and bandaging with support bandages of the distal limb to prevent trauma to the dorsal surface of the fetlock. If a myopathy accompanies the radial nerve paralysis, anti-inflammatories, hydrotherapy and IV fluid administration may be indicated.

Most cases of **post-anesthetic radial nerve paralysis** resolve spontaneously within 24–48 h. For other types of radial nerve paralysis, the prognosis is guarded to poor and depends largely on the location and extent of the injury. If significant nerve regrowth is required for recovery, the prognosis is grave. Most cases of humeral fracture with associated radial nerve damage are euthanased due to the poor prognosis.

SCIATIC NERVE PARALYSIS

In horses, sciatic nerve paralysis is most frequently associated with misplaced **hypodermic injections** and/or **local abscessation** at the site of the injection. This condition is often seen in foals receiving IM injections. The sciatic nerve supplies both the tibial and peroneal nerves, and so paralysis is characterized by an **inability to flex and advance the limb**, such that it remains hanging behind the animal with the stifle dropped and extended. The dorsum of the foot rests on the ground, with the hock in flexion. The horse can bear some weight on the limbs since the femoral nerve innervates extensors of the stifle. Cutaneous hypalgesia may be present below the stifle.

Systemic administration of **NSAIDs** (e.g. flunixin 1.0 mg/kg s.i.d.–b.i.d.) and topical treatment of the area with hot or cold packs may be helpful. Lavage and drainage is appropriate if there is an abscess. Bandaging the lower limb may prevent further injury to the dorsum of the foot and coronary band. Several weeks of therapy and **nursing care** may be required. The prognosis for complete recovery depends on the persistence of clinical signs and the nature and severity of the injury to the nerve.

FEMORAL NERVE PARALYSIS

Femoral nerve paralysis has been reported in mares after **parturition** (*q.v.*), in horses after **general anesthesia** (*q.v.*), and rarely, after a penetrating wound to the caudal flank. The condition is characterized by **inability to support weight on the limb or extend the stifle** (the femoral nerve innervates the quadriceps muscle). The horse rests the limb with all joints in flexion. With bilateral involvement, the horse assumes a crouched position and has difficulty rising from recumbency. **Quadriceps atrophy** will occur within several weeks. Anti-inflammatories and analgesics are appropriate and some horses may benefit from a sling for support.

The prognosis for this condition must be guarded. Light-framed horses may eventually be pasture sound, but heavy-framed horses often break down in the contralateral limb. The prognosis for bilateral involvement is grave.

POLYNEURITIS EQUI (CAUDA EQUINA NEURITIS)

Polyneuritis equi is a distinct pathologic syndrome characterized by **chronic granulomatous inflammation** of various **nerve roots**, particularly the extradural spinal nerve roots of the cauda equina and cranial nerves. The etiology is unknown. The lesions produced by the disease bear some histopathologic resemblance to experimental allergic neuritis of rats, Coon hound paralysis of dogs and Guillain–Barré syndrome of humans, all of which are suspected to have an **autoimmune basis**. Anti-P_2 myelin protein serum antibodies have been detected in horses with confirmed polyneuritis equi.

Other etiologies that have been proposed include a hypersensitivity reaction following aberrant migration of helminth larvae, equine adenovirus, EHV-1 or equine viral arteritis infections (*q.v.*). There is no breed or gender predilection. The disease usually occurs in mature or aged horses, although it has been described in a yearling filly.

The onset of clinical signs is usually insidious and slowly progressive. In the initial stages of the disease, horses may show signs of **hyperesthesia around the tail head and gluteal region** and may rub and chew at this area. Later, hypalgesia or analgesia of the tail, perineum and penis or vulva and gluteal area will be observed. Tail tone is absent and the urinary bladder, urethral sphincter, rectum, anal sphincter and penis or vulva are paralyzed. This leads to fecal retention and urinary incontinence. The **bladder is atonic**, distended and easily expressed. Dribbling of urine causes scalding of the perineum and inner thighs. In males, the **penis** may be relaxed and protruding, with decreased sensation of the perineal skin. The preputial skin usually retains normal sensory function.

As the disease progresses, **pelvic limb weakness** may occur due to inflammation of the sacral and lumbar nerve roots and extension of the perineuritis to the lumbosacral plexus supplying the gluteal, sciatic and, rarely, the femoral nerves. Gait abnormalities are often subtle and asymmetric. Atrophy of the gluteal, biceps femoris and other muscles can occur. Cranial nerve signs may also be present: V, VII, and VIII are most commonly involved, resulting in atrophy of the temporal and masseter muscles, drooling, dysphagia and sensitivity around the head.

Involvement of the **facial nerve** results in unilateral or bilateral facial paralysis, which may lead to keratitis or corneal ulceration. A head tilt and other signs of cranial nerve dysfunction may also be present. Clinical signs resembling this disease may be seen in cases of instability of the caudal spine due to luxations or fractures, equine herpesvirus myelitis and sorghum intoxication (*q.v.*).

The diagnosis is based on clinical signs and post mortem findings. **CSF analysis** may reveal a mononuclear or neutrophilic pleocytosis and an elevated protein level. EMG abnormalities occur as a result of denervation of affected muscles. Circulating antibodies to bovine P_2 myelin protein have been demonstrated in a limited number of cases.

There is **no effective treatment**. Various routines of antibiotics as well as systemic, epidural and subarachnoid administration of corticosteroids have been attempted unsuccessfully.

Neuritis of the cauda equina is progressive and invariably fatal. Affected horses may be maintained for long periods of time with supportive care including manual evacuation of the rectum and catheterization of the bladder. Due to the severity of clinical signs, the progressive nature of the disease and the poor prognosis for recovery, euthanasia is usually the eventual outcome.

LEAD TOXICITY

Lead toxicity is relatively uncommon in horses, but is still occasionally seen in animals grazing on pastures near smelting industries where aerial fallout contaminates grass and hay. Lead-based herbicides and paint have also been associated with lead toxicosis in horses (see also page 292).

Dysphagia and roaring due to **laryngeal paralysis** (*q.v.*) are classical signs of lead toxicosis in horses and are probably the result of a peripheral neuropathy. Rarely, horses present with profound obtundation, ataxia and recumbency. Lead interferes with normal heme synthesis, thus erythrocytes have a decreased oxygen-carrying capacity. Peripheral and central nervous tissue is affected by the resulting anoxic-ischemic injury.

The diagnosis of lead toxicity based on blood levels of lead is not accurate because blood levels do not reflect total body lead content. Free RBC porphyrin estimations are not strongly correlated with lead levels. Urine lead and δ-aminolevulinic acid (≥200 mg/dL) levels are also variable, but **urinary excretion of lead (≥1 ppm) after chelation treatment** (*q.v.*) is strongly supportive of the diagnosis.

Horses may or may not be anemic. Basophilic stippling of the RBCs is occasionally present. Tissue analysis for lead, especially bones, liver and kidney, is helpful.

Treatment of horses for lead toxicity (*q.v.*) consists of removal of access to the source, and **chelation therapy** with **calcium sodium EDTA**. A suggested dose for chelation therapy is 50–100 mg/kg calcium sodium EDTA, slowly IV, s.i.d. or b.i.d. for 2 days then repeated as necessary at 3–4-day intervals.

The prognosis is poor for chronically exposed animals or if ataxia, recumbency or profound cerebral signs are present. In the acute stage, mildly affected horses may slowly respond to treatment.

GUTTURAL POUCH DISEASE (CRANIAL NERVES VII, IX, X, XI, XII)

Trauma, surgery or disease (mycosis, empyema, stylohyoid bone fracture) of the **guttural pouch** (*q.v.*) frequently results in neurologic signs because the facial (VII), glossopharyngeal (IX), vagus (X), spinal accessory (XI) and hypoglossal (XII) nerves, cranial cervical sympathetic trunk and ganglion lie in the lining of the guttural pouch.

The neurologic consequences of guttural pouch disorders include **dysphagia** (IX, X), **soft palate paresis and displacement** (IX, X), **laryngeal paresis** (X), **Horner's syndrome** (sympathetic trunk and cranial cervical ganglion) and **tongue paralysis** (XII). Occasionally, fungal plaques in the guttural pouch may spread to involve the facial nerve (VII) and mandibular nerve (a branch of cranial nerve V), which lie in the medial wall of the pouch, resulting in **facial paralysis** and **masseter muscle atrophy**.

The treatment of guttural pouch disease is discussed elsewhere (*q.v.*). In general, the neurologic signs associated with cranial nerve damage due to guttural pouch mycosis are unlikely to improve.

NEUROLOGIC ASPECTS OF "VICES"

INTRODUCTION

Behavioral disorders in the horse are often referred to as "vices" or stereotypical behavior. They are thought to be related to removing the horse from its natural environment (the free range), confining it, and thus interrupting free access to continual grazing and social contact with other horses. They are frequently annoying to owners, and occasionally dangerous for the horse. Treatment broadly consists of attempts to modify the environment, i.e. to improve it to a more natural state. Offering the animal distractions, including companions and toys, may help if major alterations in the environment are not practical. A more detailed consideration of behavioral problems is given in **Chapter 18** (*q.v.*).

CRIBBING

Cribbing (aerophagia, wind sucking) (*q.v.*) is a behavior in which the horse grasps an object (usually a fence or feed bunk) with the incisors and swallows air. **Aerophagia** may be associated with colic (*q.v.*), and cribbers will show **excessive wear on the incisors**. Some horses may accomplish "wind sucking" without grasping onto an object, by simply flexing the neck and "gulping" air.

A behavioral approach to therapy is given in Chapter 18 (*q.v.*). Alternatives that have been tried include cribbing straps, which inflict discomfort when the horse flexes the neck to swallow air and have been said to deter some horses. Surgical treatments include neurectomy of the spinal accessory (cranial nerve XI) nerve or surgical resection of sternocephalicus, omohyoideus and sternothyrohyoideus, all of which are neck muscles that function in the act in cribbing. Long-term follow-up studies regarding the efficacy of these techniques have not been published and some practitioners have observed that horses relearn cribbing, even after the surgery has been performed. These procedures may also leave cosmetic defects at the site of the surgery.

WOOD CHEWING

Wood chewing (*q.v.*) is associated with feeding low-fiber, high concentrate "complete ration" pelleted feeds, and **boredom**. It is often observed in stabled horses, but pastured horses (with access to grass) may also chew trees, fences or shrubs. Cold, wet weather appears to increase wood chewing. **Increasing the roughage** in the horse's diet is the obvious treatment, but eliminating wood edges or providing toys or companions for stalled horses may also help.

COPROPHAGIA

Coprophagia (eating feces) is normal in foals, but adult horses will avoid eating manure unless they are starving or are very bored. It is esthetically unappealing but, more importantly, may increase the risk of transmission of parasites or bacterial or viral pathogens. Evaluation of the diet for adequate protein and fiber content is advised.

STALL WALKING AND WEAVING

Stall walking and weaving (*q.v.*) appear to be **exacerbated by stress**. The incessant activity causes the horse to spend less time eating, thus weavers and stall walkers often lose body condition. These behaviors are best treated by turning the horse out into a field or pasture. Numerous mood-altering, antipsychotic and sedative drugs have been tried, however improvements are usually temporary. The horse will often revert to weaving or stall walking after the medications are discontinued.

STALL KICKING/PAWING

Stall kicking and/or stall pawing in a horse without signs of colic usually reflect **frustration**. Horses may resent being confined and tend to exhibit these vices especially at feeding time. Stall kicking can cause injury to the horse. The only generally successful management is to turn the horse out to pasture.

SELF-MUTILATION

Self-mutilation usually affects **young stallions** but has occasionally been seen in geldings and mares. The behavior appears to be triggered by a stressful event, such as a major change in the breeding or exercise program, or relocation into a new herd.

Self-mutilating horses **obsessively bite** specific areas of their body (usually the thoracic limbs, flanks, pectoral area, stifle or thighs) and can inflict serious lacerations. Frequently, the horse will stare at the area, squeal, grunt, bite at the air, or spin in circles before biting at its body. Skin biopsies and other diagnostic tests are unrewarding. **Focal neuritis** (*q.v.*), seizures or abdominal pain should be considered as the differential diagnoses.

Treatment for this stereotypical behavior is to alter the environment, feeding, breeding or exercise patterns. A companion such as a goat, pony or barren mare may help. Castration has been suggested but may not be successful.

Antipsychotic or sedative drugs have also been tried, but must be used with caution since they may exacerbate the signs or produce undesirable side effects. Several progesterone hormone preparations have been used in controlling aggressive or hypersexual horses and may be temporarily helpful in managing self-mutilating horses. Sometimes, if a major change in a horse's environment is not possible, animals have been fitted with muzzles or neck cradles, or cross-tied to prevent serious self-injury.

HEAD SHAKING

Head shaking is most often noted in middle-aged horses during spring or summer. The syndrome appears to be progressive in many cases with increases in severity and loss of the characteristic seasonality.

The etiology is unclear but several causes have been suggested including middle ear disorders, ear mites, cranial nerve disorders, guttural pouch mycosis, dental periapical osteitis, allergic rhinitis and vasomotor rhinitis (*q.v.*). However, only very rarely can it be shown that correction of the abnormality leads to elimination of the head shaking.

Clinicians in California have determined that the condition appeared to be **light stimulated** in approximately 60% of affected horses. The close association of the optic and trigeminal nerves in the midbrain may allow optic stimulation to cause referred itching, tingling or electric-like sensations in areas innervated by branches of cranial nerve V, a condition similar to "photic sneezing" in man.

The majority of horses with idiopathic head shaking in one study in the USA showed improvement of signs after oral administration of **cyproheptadine** (0.3 mg/kg b.i.d. q 12 h then after 7 days 0.4–0.5 mg/kg q 12 h), a drug with antihistaminic and antiserotonergic properties. This contrasts with studies performed in the UK where cyproheptadine alone was ineffective but a **combination therapy** of **cyproheptadine** and the sodium channel blocker **carbamazepine** (20–30 mg/kg q 6 h) resulted in very significant improvement in the majority of cases.

Trigeminal neuritis or **neuralgia** may be the basis of the underlying etiopathology of idiopathic equine head shaking, but no histopathologic lesions have been found. The etiology, as in the human equivalent, is not known. Head shaking is a frustrating syndrome, and although a particular case may respond to single or multiple management or therapeutic measures, the prognosis for cases of idiopathic head shaking is poor.

NARCOLEPSY/CATALEPSY

Narcolepsy is a REM-sleep disorder characterized by excessive daytime sleepiness and **striking transitions from wakefulness into rapid eye movement (REM) sleep** without passing through slow wave sleep. A syndrome that has the clinical appearance of narcolepsy has been noted in older horses (usually when undisturbed, e.g. in the back of a paddock) and has also been seen in newborn light-horse foals. It appears to be familial in some miniature horses.

The clinical signs can range from **buckling at the knees**, usually when the horse is quiet, to **total collapse and areflexia** with maintenance of some eye and facial responses and normal cardiovascular function. The syndrome resolves in some foals.

Demonstrating the existence of narcolepsy in horses by classical electroencephalographic techniques may prove to be very difficult as ongoing work indicates that horses, being prey animals, may normally be able to go into REM sleep directly from a period of arousal (i.e. after having one last look around to make sure there are no predators around).

Canine and human narcolepsy is associated with dysfunction of a group of neurotransmitters involved in sleep regulation and satiety, the **hypocretin** system. In narcoleptic foals, narcoleptic episodes are often associated with nursing, and it is intriguing that the hypocretin system is involved in the regulation of sleep as well as appetite.

The tricyclic antidepressant **imipramine** (1–2 mg/kg b.i.d. or t.i.d. PO) can resolve clinical signs, but is rarely indicated for long-term management.

INTRACAROTID INJECTION

Intracarotid injection is a common **iatrogenic** side effect of attempted jugular vein injection in the horse. Affected animals tend to have a violent and immediate reaction. The risk is relatively high because of the close anatomic arrangement of the carotid artery and the jugular vein in the neck. Attempted venepuncture in the lower half of the neck carries a greater risk. Reported histories of struggling to restrain the horse during venepuncture, difficulty entering the vein, obtaining a pulsatile jet of bright red blood on entering the blood vessel, and sometimes the presence of a hematoma at the injection site, suggest the possibility of accidental intracarotid injection.

The typical description is that the horse "drops off the needle". The reaction begins while the needle is still in the neck. The horse will rear up on its pelvic limbs and fall on to its back or side. Some horses react by **collapsing suddenly**, dropping to the floor. After the initial reaction the horse may begin to seizure. Some animals may become comatose while others remain conscious but stuporous. The duration of the effects varies. Some animals will remain recumbent for a few minutes before standing and appearing dazed but otherwise normal. Severely affected horses may not regain consciousness. Following the initial violent reaction, other neurologic deficits (such as blindness or seizures) may be seen.

Histologically, lesions are most severe in the rostral brainstem and cerebrum on the ipsilateral side. Cytotoxic effects of the drug lead to endothelial injury, hemorrhagic foci, necrosis with attraction of macrophages and ultimately cavitation.

Treatment is empirical. Therapy should aim to minimize any further injury as a result of the reaction, and to support the animal until fully recovered. The seizuring horse may require sedation with **diazepam** or **phenobarbital** (see Table 17.1). Treatment with corticosteroids and diuretics (**mannitol**, slow IV 20% solution at 0.25 g/kg) in the acute phase may help to minimize cerebral edema.

The prognosis is better if the injected substance is water soluble (such as many tranquilizers and analgesics). Intracarotid injection of a lipid-soluble substance (such as certain antibiotic preparations) produces a more serious and longer lasting effect. Animals showing signs of recovery early in the post-injection period have a better prognosis, and those that remain recumbent for prolonged periods have a poorer prognosis. **Residual effects**, such as blindness or varying degrees of incoordination, may be permanent. Neurologic problems secondary to head trauma suffered during the episode can occur.

GRASS SICKNESS (EQUINE DYSAUTONOMIA)

Grass sickness (*q.v.*) is a disease of horses at pasture. Affected animals have lesions of neuronal chromatolysis and loss principally in postganglionic sympathetic and parasympathetic neurons. The disease is prevalent in the UK, in restricted northern areas of continental Europe and in Patagonia, Argentina.

Younger horses (aged 3–8 years) are more commonly affected. Grass sickness is most often seen in horses **permanently at pasture**. Horses kept stabled have been affected, but this is rare. The cause of grass sickness remains elusive despite considerable research effort. Recent studies following the death of the exceptional Group I racehorse, DUBAI MILLENIUM in 2001, have, however, produced some interesting new leads. Fungal toxins have long been suspected but new evidence suggests that a *Clostridium botulinum* toxin (*q.v.*) may be involved in the etiology of grass sickness.

Horses **recently moved** to a farm are more likely to be affected than horses that have been grazing that same pasture for a prolonged period of time. The disease may occur with greater incidence after periods of cool, dry weather together with irregular ground frosts. The majority of cases occur in spring and early summer, with a smaller peak of incidence in the autumn; however, cases may be seen throughout the year. The disease is generally sporadic, but outbreaks have occurred.

Classical clinical signs include dysphagia, anorexia, cachexia, gut stasis, tachycardia, inappropriate sweating, trembling of axial and appendicular muscles, rhinitis sicca and ptosis. Animals that have severe signs have what is called **acute grass sickness**. Clinical signs are related to stasis of the entire gastrointestinal system, which in turn causes distension of the gut lumen with fluid. Abdominal pain is usually mild to moderate.

Gastric and small intestinal distension is frequently seen, and passage of a nasogastric tube may result in **copious reflux** of pungent, green gastric fluid. **Dysphagia** is invariably present at some time. Prehension and mastication of food is normal; however, swallowing of food and water is difficult. Gastrointestinal sounds are decreased. Tachycardia is usually present even in horses that do not appear overtly painful. Horses with acute grass sickness do not recover.

Chronic grass sickness is generally insidious in onset. Dysphagia occurs to a varying degree and, as in the acute disease, swallowing appears to be difficult. **Intestinal stasis** results in a decrease in intestinal sounds and a decrease in fecal production. **Impactions of the large colon** may occur. Tachycardia, patchy sweating and muscle tremors are seen, along with signs of mild to moderate

abdominal pain. Horses may be anorexic, however the cachexia is often more rapid and severe than can be accounted for by lack of caloric intake alone.

The ante mortem diagnosis is based on the clinical examination and ruling out other causes of colic or dysphagia. The administration of **0.5% phenylephrine eye drops** to one eye results, in 20 min, in a significant increase in the size of the palpebral fissure, assessed by measuring the angle of the eyelashes to the head from a frontal view (i.e. the **eyelashes "stand up"**).

There is no treatment for acute grass sickness. Some animals will recover with **very intensive supportive nursing care**, which specifically involves offering a wide variety of palatable foodstuffs. Animals should be encouraged to eat as much as possible. Affected horses will invariably lose significant amounts of weight.

Histologically, the disease is characterized by **chromatolysis** of enteric neurons, pre- and post-ganglionic sympathetic and parasympathetic neurons in the CNS and ganglia, and specific somatic lower motor neurons in the brainstem.

The disease is known as a **dysautonomia** but clinical signs of grass sickness do not fit clearly into an uncomplicated picture of autonomic disease. Cases usually do not have alterations in pupillary diameter, enophthalmos or corneal ulceration due to decreased tear production, or overt orthostatic hypotension. Primary dysautonomias with markedly similar enteric and sympathetic ganglionic lesions exist in cats, dogs, hares and rabbits.

Chapter 18

Behavior

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Chapter contents

INTRODUCTION

If we examine statues of humans or horses sculpted in ancient Greece or Rome, it is immediately apparent that their creators were masters of anatomy. Similarly, men with scientific minds have studied physiology for centuries. Thus, anatomy and physiology, basic medical sciences, have a long history. Yet the third basic aspect of living organisms in the animal world, behavior, is a relatively new science. Not until the late nineteenth century did medical scientists like Jung, Freud and Adler begin an analytical study of behavior.

Every living creature has adapted anatomically and physiologically to the habitat in which it has evolved. Its behavior too must adapt to the **environment** in which it exists. All three adaptations—anatomy, physiology, and behavior—are essential for survival and propagation of any species. All three are **genetically predetermined**. Thus if an animal enters the world, say a newborn calf, we can accurately predict its anatomic appearance: what it will look like, its approximate size, what its digestive system will be, etc. We can also make accurate predictions regarding its physiology: its normal body temperature, heart rate, gestation period, and so on. Because it is a bovine we can also know how it will behave: its defensive actions, social interactions with other bovines, its courting behavior, its body language of aggression, dominance or submission.

All three characteristics—anatomy, physiology and behavior—are however subject to a certain degree of modification. For example, **malnutrition** may alter the potential anatomy of an animal. Exercise or living at high altitude may cause physiologic changes. Learning after birth will shape its behavior. The behavior of horses, therefore, is to a great extent **programmed prenatally**, but from the moment a foal enters this world learning begins.

THE SCIENCE OF BEHAVIOR

The science of behavior is so new that only in recent decades have we begun to understand its complexities. Until the middle of the twentieth century it was widely accepted that animals behaved according to **instinct**, but human behavior was all learned. Now we know that every newborn animal is endowed with behaviors that are **genetically predetermined**, and will also **acquire behaviors** as a result of learned experiences.

The horse, in the wild, is a **prey animal**, providing a source of food for the large carnivores. The horse evolved in North America, preyed upon by a variety of large felines such as the saber toothed tiger and the cave lion, and a variety of large canines such as the dire wolf. Its primary defense was flight.

Many herbivorous species are equipped with formidable anatomic weapons of defense such as, for example, the horn of the rhinoceros, the tusks of the hippopotamus or wild boar, the horns of a Cape buffalo or musk ox, or bighorn sheep. When threatened, these species lower their heads, charge, and can use their weapons very effectively. The horse, however, is not so equipped. Its defense is to **sprint** away from perceived danger, and its anatomy and physiology are well equipped for flight. The equine cardiovascular system, musculoskeletal system, respiratory system and senses are those of a flight creature. Because it is dependent upon flight to survive in the world, the horse is **uniquely endowed** with behavioral characteristics that must be appreciated and respected if we are to get along with this animal.

BEHAVIORAL CHARACTERISTICS

Horses are the **most perceptive** of all domestic mammals, equipped with hearing, a sense of smell and a tactile sense far exceeding those of humans. Its vision, while inferior to that of humans in color recognition and depth perception (due to the lateral placement of the eyes), is much superior in detecting movement, in night vision, in peripheral vision and in speed of accommodation, which is accomplished by swiftly altering the position of the head.

The **reaction time** of the horse is the fastest of all domestic mammals. As the horse evolved, those that reacted slowly did not survive to reproduce. The **memory** of the horse is the best of all domestic animals. Moreover, horses learn faster than any other domestic animal. The slow-learning ancestors of the horse did not survive.

Interestingly, this timid, flighty creature—this ultimate prey—can be more **swiftly desensitized** to frightening stimuli than other animals. Why? Because

flighty species must quickly desensitize to frightening sensory stimuli once they are determined to be harmless, or else they would be running all the time. There would be no time to eat, drink, rest or reproduce. The fact that horses can be quickly and lastingly desensitized to frightening stimuli is one of the main reasons they are so suitable for **domestication**. In warfare, for hunting, as a draft animal, the horse had to accept endless normally terrifying stimuli.

The horse, one of only a dozen mammalian species which mankind has successfully domesticated, became the most important factor in the spread of cultures and civilizations.

DOMINANCE AND HIERARCHY

Like most domestic animals, with the exception of the cat, the horse is an animal that lives in groups led by a leader, a **dominant mare** as a rule. Horses, then, readily accept humans as surrogate herd members and as herd leaders. This is why, for thousands of years, horses were so useful to mankind. They worked for humans.

Now, a remarkable change has occurred in the industrialized world—the horse is increasingly becoming a companion animal. Indeed, in many cases, the horse has become a surrogate human: a friend, even a child. An animal that throughout history primarily played the role of a slave, now sometimes becomes the master.

Animals that live in groups have what is called a **dominance hierarchy**. This hierarchy is established in varying ways, depending upon the species. In horses the dominance hierarchy is established by **control of movement**. This is a flight species. Horses establish leadership—dominance—by controlling the movement of their peers. This control can be expressed in either of two ways. Movement can be **caused** by the dominant individual: observe how the lead mare **threatens her subordinates**, causing them to yield space. Conversely, movement can be **inhibited** by the dominant individual: observe how a herd sire will drive his harem, then bunch them up and, head swinging from side to side, forbid them to move. **Controlling movement** of the horse is part of every horsemanship training technique. Properly done it causes the horse to view the human handler as a surrogate leader.

Each species has a **body language** unique to that species and instinctively understood by members of that species. That language can be learned by other species, just as humans learn to understand the snarl of a dog, the lowered head and pawing of the bovine, or presented hindquarter and elevated hindleg of a horse. A creature that lives in groups may **signal surrender** by assuming a position of **vulnerability** for the specific species. The dog, therefore, lies down exposing throat and abdomen to signal, "You are in charge. I won't question your leadership". Human beings in every culture bow in submission, exposing the back of the head to mankind's primary defense, the club. Cattle elevate the nose, and horses, which are most vulnerable when grazing or drinking, lower their heads and make mouth movements to signal submission. Head elevated and lips tightly closed, the horse says "I want to flee". Head lowered and lips loose or licking and chewing means "I accept you as my leader".

HUMANS, HORSES AND HORSEMANSHIP

Humans domesticated the horse six or seven thousand years ago. The methods we have used to control this animal have been largely **coercive**. Humans are, biologically speaking, a predatory primate: an intelligent, reasoning, tool-using species. Primitive man established his leadership with the use of intimidation and the use of force, a characteristic of the larger primates. It is natural for us to want to control the horse with such methods, especially if we are young, and even more so if we are male. Our species survived prehistorically because the younger males were willing and able and even eager to confront wild beasts.

However, throughout the course of human history, certain men, endowed with special sensitivity, perception and communication skills, were able to control horses in a remarkably superior way. Rather than coercion, they used **persuasion**, implemented by **communicating** with horses in a way that they instinctively understood. A majority of such individuals have been lost to history. A minority recorded their methods in writing, and many of these records still exist. Unfortunately, the horsemanship espoused by these rare and talented people never became popular with the masses that utilized horses regularly.

Then, late in the twentieth century as the horse became increasingly obsolete in the industrialized world as a source of power and transportation, and increasingly a recreational creature, a remarkable thing occurred. It may be considered a **revolution in horsemanship**. Methods once known primarily to the masters became popularized within the horse industry as a whole. This revolution began in an improbable place, within the cowboy culture of the Pacific Northwestern United States. The pastoral agriculture of frontier cultures such as Argentina, Australia and western North America developed horsemanship that was expedient, inexpensive and often crude. Men and horses were cheap and the methods that evolved were often abrupt and sometimes brutal. It is a tribute to the remarkable **adaptability** of the horse that so many dependable and useful horses were produced this way. They are forgiving creatures.

In Spanish colonial California, a form of horsemanship was developed that, although still crude in some respects, was more refined than any other form of native horsemanship. Early in the twentieth century a man named Tom Dorrance, a cowboy and rancher, was influenced by the horsemanship of the "Californios". He mastered and embellished the techniques, developing a great ability to communicate with horses and influence their behavior. A skilled protégé of Dorrance, Ray Hunt, took these methods and went on the road with them, profitably teaching them to the horse-owning public.

Soon other exceptional horsemen, all cowboys or former cowboys but possessing skills not typical of the working cowboy culture, joined what was to become a revolution which would spread all over the world. Men like Pat Parelli, Richard Shrake, Monty Roberts, Buck Brannaman and Dennis Reis, all cowboys from the western USA, would evangelically spread the gospel of gentler and more humane horsemanship. By the mid 1980s the unorthodox methods espoused by these men had spread worldwide, and by the turn of the century they were being accepted by the racing industry and all horsemanship disciplines.

Why did this happen so late? Why didn't it happen a century earlier when the horse was at the pinnacle of its importance to mankind? There are several reasons:

1. The science of behavior—psychology—had finally become accepted and respected by society as a whole.
2. Horses were now owned by educated people. This was the exception a century earlier when, in fact, many horse handlers were actually illiterate, a situation common in developing countries today.
3. The information explosion of the late twentieth century—the Internet, videotapes, books and horse magazines, and clinicians flying by jet all over the world—rapidly dispersed the technological information involved.
4. Finally, and probably most significant, an industry historically dominated by men is for the first time increasingly dominated by women. The solicitous, compassionate, less intimidating and nurturing attitude so many women have greatly facilitates communication with the horse.

This revolution in horsemanship, known by a variety of names originated by the trainers involved in it, is probably best known internationally as "natural horsemanship". Its methods are by no means natural to the human species, but they are natural to the horse, and utilizing them has enabled us to communicate with the equine as never before.

Feral horses, captured in the wild and never before handled by human beings, are being gentled and accepting a rider in just a few hours time using natural horsemanship. "Outlaw" horses, some of them exceedingly dangerous to handle, are being reformed and turned into safe and useful steeds with these methods.

VETERINARIANS AND NATURAL HORSEMANSHIP

By the year 2005, scores of trainers in all disciplines were using the methods of natural horsemanship and many of them had become teachers and advocates. Veterinarians in equine practice must become familiar with this revolution. Its teachers have produced a few good books and many fine videotapes teaching the methods.

It is incumbent upon the practitioner to become familiar with the great social changes that are occurring. These include recognition of the **human–animal bond**, the increasing role of the horse as a companion animal, the influence of the animal rights movement, and increasing social awareness of the concept of humaneness, a rejection of violence (even as it increases in the popular media) as a means to an end, and a recognition of the intelligence and emotions possessed by our domestic animals.

It is not the veterinarian's role to train horses. But we must be cognizant of what is happening in the industry and encourage our clientele to familiarize themselves with natural horsemanship and to minimize some of the more coercive techniques of restraint that have become traditional in the horse industry. It is our responsibility at least **not to create behavior problems** in

our patients, to attempt to establish rapport with them, and to use the variety of tranquilizing and behavior modifying drugs available to us as needed.

Horses are a **precocial species**, born with all of their senses fully functional and neurologically mature. Their socialization periods and critical learning times occur immediately post partum, and are not delayed as they are in altricial species such as the dog, the cat and the human infant. If horses are not trained during the minutes, hours and days after they are foaled, the most powerful learning times of their lives are being wasted. Teaching breeders this fact and encouraging them to work patiently and formally with newborn foals will ensure gentler future patients for our profession, lessen the likelihood of injury to either horse or human, and help to create a more equitable and profitable relationship between them.

STEREOTYPICAL BEHAVIORS

Stereotypical behaviors, or **stereotypies**, defined as stylized, repetitive, and apparently motor responses or sequences*, or as an intentional, repetitive, non-functional behavior often performed in a rhythmic manner†. They are commonly seen in animals subjected to stressful situations such as isolation or confinement. Examples include feather pulling in caged birds, paw chewing or habitual scratching of the body in bored or confined dogs, repetitive ritualized pacing in caged zoo animals, and tail sucking in cats. In children, nail-biting and pulling out eyebrow or eyelid hairs are examples of stereotypies.

The horse is **particularly susceptible** to such anomalous behaviors because, in domestication, its environment is often drastically different from that which would be natural for the species; namely open, unlimited grasslands, in the company of other horses. Certainly stereotypies are rarely, if ever, seen in wild horses.

Traditionally, the stereotypies of horse have been called "vices", or, more commonly, "stall vices" simply because they are seen most often in closely confined individuals. In any species, stereotypy is expressed as an **oral activity**, a **locomotor activity** or a **combined activity**. In horses, oral examples include cribbing (crib biting), windsucking, wood chewing, protrusions of the tongue and biting of the flanks (*q.v.*). Locomotor stereotypies are weaving, circling, pawing and stall kicking (*q.v.*). **Cribbing** and **weaving** are probably most commonly seen.

CRIBBING AND OTHER STEREOTYPIES

Cribbing and windsucking

Cribbing (*q.v.*), wherein the horse grasps a horizontal surface with its incisor teeth, flexes its head and neck, pulls back drawn in air and grunts, is very

*Houpt, K.A. (1995) New perspectives on equine stereotypic behaviour, *Equine Veterinary Journal* 27: 82–83.

†McClure, S.R., Chiffin, M.K., Beaver, B.V. (1992) Nonpharmacologic management of stereotypic self-mutilative behavior in a stallion. *Journal of the American Veterinary Medical Association* 200: 1975–1977.

much disliked by horse people. The upper incisor teeth wear excessively and abnormally, and in some cases this dental damage can be extreme. However, cribbing, as a rule, is not nearly as damaging as is popularly believed, and the vehement dislike of the habit by so many horsemen is **disproportionate** to the ill effects produced.

Admittedly certain rare cribbers are so addicted to their vice that they do not eat enough, suffer **malnutrition**, and develop **anatomic changes** in the neck as well as the teeth. However, for generations the damaging effects of cribbing have been greatly exaggerated. The **folklore** associated with it often results in a depreciation of the fiscal value of an otherwise sound and useful horse. For example, it is popularly believed that the cribber, swallowing air, is predisposed to colic. Recent studies reveal that, in fact, **the cribber does not swallow air**. Fluoroscopic studies have revealed that air is expelled when horses crib. The incidence of colic in cribbers is not significantly higher than in the general population. Indeed, chronic gastrointestinal problems may **cause** a horse to crib.

Another long accepted bit of lore is that cribbing can be learned by foals observing the behavior of confined cribbers. Research studies fail to confirm this and it may be that the conditions that predispose to stereotypical behaviors **on a given premise or property** are likely to produce more cribbers. Additionally, there may be a **genetic predisposition** to such behaviors, so if the horses are related, and live in a similar environment, then a high incidence can be expected. It is well recognized that cribbing is more common in certain bloodlines. Therefore the idea of an allelomimetic (imitative) cause for cribbing is invalid at the present time.

Windsucking (*q.v.*) is often considered to be synonymous with cribbing, or a more advanced form of the vice. Cribbing and windsucking can be minimized but rarely controlled completely with muzzles or a variety of "cribbing collars". One, called a "miracle collar", is particularly helpful but, again, these measures usually lessen rather than eliminate the problem.

When these vices are so severe as to harm the physical condition of the horse, myotomy of the sternomandibularis, sternothyrohyoideus and omohyoideus muscles (Forssell's procedure) or a modification of Forssell's procedure by partial removal of the sternothyrohyoideus and omohyoideus muscles and neurectomy of the ventral branches of the spinal accessory nerves can be used. The modified version of Forssell's procedure provides a more cosmetic approach.

Wood chewing

When horses are confined and/or deprived of company, wood chewing (*q.v.*) is a common result. Bored, and deprived of the opportunity to graze at will, many horses begin to chew wood, often causing marked damage to fences and stables. Ideally, this vice should be prevented by providing horses with environmental stimulation including the company of other animals, adequate living space, and either constant grazing opportunity or, at least, available grass hay.

Once the wood chewing habit is established, exposed wood surfaces may be protected by sheathing them in metal, by electric wire fencing, or painting them with unpalatable substances. Creosote, which was particularly effective, is no longer used because it is considered to be environmentally unsafe.

However, several commercial products designed to discourage wood chewing are on the market.

Weaving, circling and stall kicking

These stall vices are almost entirely the result of box stall confinement and isolation from other horses. Only a change in environment can prevent or solve weaving, circling and stall kicking. The moment such a tendency is observed, an immediate change may abort the vice before it becomes a fixed stereotype. Young racehorses are especially susceptible to these highly motile vices. Raised in open pastures, energetic and athletic, racehorses are usually confined to box stalls once training commences, and it is understandable how stressful this change in environment can be.

Biting of the flanks

This vice is seen most often in stallions. Biting is particularly offensive because afflicted horses often severely traumatize their flank region. The use of neck cradles, keeping the horse in a tie stall, muzzling, or a protective blanket may physically prevent the habit. Better, a drastic change in environment may be provided, including as large an enclosure as possible, nearby company of other animals, toys, and visual stimulation such as that provided by a constant view of other animals, people or automobile traffic.

Protrusions of the tongue

Although protrusion of the tongue is often a typical stall vice, originating like the others as the result of boredom, confinement and isolation, it is more often a form of **displacement behavior**. Many colts when started in the snaffle are uncomfortable, especially if the rider or driver is rough-handed, and develop the harmless but very unsightly vice of "tongue dragging" or "tongue lolling" or "tongue rolling" or "tongue play". As soon as it is detected, an immediate change of methodology including removal of the bit and substitution with a hackamore, sidepull or halter may abort the habit. At the very least, a completely different bit should be tried, such as a Mullen Mouth or a Doctor Bristol or other multijointed bit. Consider, too, the hands of the rider.

Horses with confirmed tongue vices are often subjected to such extreme controlling measures as tying the tongue down, tightly tying the mouth closed, and pricking of the tongue. For show horses, spoon bits and nets have been used. Amputation of the tongue is a drastic and inhumane solution that can never be condoned.

DEALING WITH STEREOTYPIES

It is only in recent decades that controlled scientific studies have been done to better understand stereotypies. What has been established thus far is that there is a physiological chemical mechanism involved. It involves the mediation of **endogenous opioids** (endorphins) elaborated as a response to chronic stress, and it is believed that **the addiction displayed by cribbers is to these**

opioids, rather than to the act itself. This has been demonstrated by the administration of opioid antagonists such as **naloxone** and related compounds, which tends to suppress the cribbing behavior, probably due to opioid interference. However, the use of these drugs, at this point, is not clinically applicable.

Confinement has long been considered the most common cause of cribbing, but **isolation** is probably a more significant factor. Horses confined to tie stalls are more confined than those in boxes, but if they have other horses adjacent to them they seem to be less inclined to begin cribbing than those in box stalls. Even in box stalls, horses that can look out and see other horses are less likely to crib. Thus, the more viewpoints available to the stalled horse, the less inclined it is to crib or exhibit other stereotypies. The **more social interaction** that occurs between stabled horses, the better.

Recently, **diet** has been shown to be a factor in stereotypical behaviors. The more **roughage** fed, the busier it keeps the horse, distracting it from misbehavior. Feeding a mixture of **chaff and hay** seems to be even more effective. Also, horses on **straw bedding** crib less. **High concentrate diets contribute to stereotypies** in two ways. First, they reduce the amount of roughage that must be fed and therefore give the horse more idle time. Second, high concentrate/low roughage diets result in periods of food deprivation, and this results in **gastric hyperacidity**, which can cause ulcers (*q.v.*). High levels of dietary concentrate, which is, after all, an unnatural diet for this grassland grazing species, can also alter cecal fermentation, lowering the pH of the cecal contents. It is possible that cribbing increases the production of saliva, which is alkaline. Horses, unlike carnivores that may salivate at the odor or smell of food, only salivate when chewing. Perhaps cribbing, by increasing saliva flow, normalizes the pH of the ingesta in horses fed excessive concentrates. In one study, **foals** began to crib only after concentrates were introduced. Even after weaning, the incidence of cribbing was four times higher in concentrate fed foals.

Social interaction will also reduce the incidence of weaving in horses confined to box stalls. The presence of large mirrors on the walls of box stalls is believed by some caretakers to inhibit the occurrence of stereotypies. If complete confinement is necessary, then as much "outside" time as possible should be provided, and the opportunity to graze and/or to eat hay should be allowed as often as possible.

Chapter 19

Ophthalmology

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Chapter contents

INTRODUCTION

Equine ophthalmology has always been, and continues to be, an interesting and challenging aspect of equine practice. For both esthetic and functional reasons, disorders of the eye are of great concern to the horse owner. The horse, perhaps more so than other domestic species, can have devastating complications from ocular trauma or inflammations.

Management of ophthalmic disorders in the horse requires knowledge of the anatomy of the structures involved, an understanding of the pathophysiology of the disease process, and an appreciation of the therapeutic options available. This section is designed to aid the practitioner through the diagnosis and management of the common, and not so common, ocular disorders encountered in practice.

Over the 10 years since the first edition of this volume significant advances have been made in equine ophthalmology, as documented in this chapter. And yet, as will be shown below, there are all too many areas where our understanding of the pathobiology of the equine eye is not sufficient to allow rapid and successful diagnosis and treatment of equine ophthalmic disorders from herpetic keratitis at the very front of the eye to retrobulbar neoplasia behind it.

THE ORBIT

ANATOMY

The orbit is the bony fossa that surrounds and supports the eye. It is composed of the frontal, lacrimal, zygomatic, sphenoid, temporal and palatine bones. The supraorbital process of the frontal bone forms the dorsal rim of the orbit, and provides a complete orbital rim. The ventral floor of the orbit is composed of soft tissue, which, along with a large amount of orbital fat, serves to support the globe.

The orbit is in close proximity to the paranasal sinuses. The frontal sinus is located medial to the orbit and extends dorsally and ventrally along the orbit.

The maxillary sinus is ventral and medial to the orbit. The medial canthus of the eye serves as **a reference point for trephination of the maxillary sinus**. A third smaller sinus, the sphenopalatine, which communicates with the maxillary sinus, is also located ventral and medial to the orbit.

Orbital foramina allow for nerve and blood vessel entry into the orbit. These include, with their associated vessels and nerves, the rostral alar foramen (the maxillary artery and nerve), the orbital fissure (the abducens, ophthalmic, trochlear and oculomotor nerves), the optic foramen (the optic nerve and internal ophthalmic artery), the ethmoidal foramen (ethmoidal nerve and vessels), and the supraorbital foramen (the supraorbital nerve and vessels). The first four of these foramina are clustered on the ventromedial wall of the orbit near its apex, and are important when performing **retrobulbar injections for anesthesia**. The supraorbital foramen is located medially in the supraorbital process of the frontal bone, and serves as a landmark for injection for regional anesthesia of the upper eyelid. It can be easily found by grasping the supraorbital process, at the point where it begins to widen, between the thumb and middle finger, and palpating with the first finger.

The orbit also contains the extraocular muscles. The dorsal and ventral rectus muscles rotate the eye around a horizontal axis, while the lateral and medial rectus muscles rotate the eye on a vertical axis. The dorsal and ventral oblique muscles rotate the eye on an anteroposterior axis. The retractor bulbi muscle lies within the cone formed by the rectus muscles and extends posteriorly around the optic nerve. The main diagnostic importance of the extraocular muscles is in **neurologic examination**, as the position of the globe may indicate lesions of certain cranial nerves.

A sheet of connective tissue, the periorbita, lines the orbit. It is reflected to sheathe the extraocular muscles, and extends onto the globe as Tenon's capsule.

ORBITAL DISEASES

Congenital anomalies

Microphthalmia/anophthalmia

Microphthalmia is an abnormally small eye. **True anophthalmos** (the absence of any ocular tissue) is rare, with most cases having some remnants of eye present. Microphthalmia, which results from degeneration or abnormal growth of the optic vesicle, may be pure (nanophthalmia), with a normal but small eye, colobomatous, or complicated with other ocular anomalies. There can also be **associated systemic anomalies**. The absence of a normal-sized eye may result in the failure of the orbit to develop, with subsequent cranial asymmetry.

Clinical signs

Affected animals are generally presented shortly after birth, with the complaint of small or absent eyes. Affected eyes are **frequently blind**. The palpebral fissure is often correspondingly reduced. A common clinical problem can be ocular surface infection since the conjunctival sac is necessarily enlarged given the small globe size.

Treatment

Therapy is seldom indicated. Enucleation may be performed if irritation or excessive ocular discharge is present. Bilaterally affected foals are most frequently euthanased.

Prognosis

Foals affected unilaterally may perform adequately if allowances are made for the vision loss.

Orbital cellulitis

Unlike the dog, the horse rarely develops orbital cellulitis. When it occurs, it is frequently an extension of inflammation from sinusitis, guttural pouch infection, blunt trauma or penetrating orbital wound, dental disease, or an extension of panophthalmitis (*q.v.*).

Clinical signs

Edema of the eyelids and supraorbital fossa is usually severe, and the region is painful on palpation. Ocular discharge is frequently heavy and ranges from serous to mucopurulent. Prolapse of the third eyelid is common, especially if exophthalmos is present. Fever may or may not be present.

Skull radiographs and **guttural pouch examination** (*q.v.*) may aid in identifying a primary cause. Orbital ultrasonography may be useful in locating pockets of exudate or fluid accumulation.

Treatment

Specific therapy for the primary cause, if identified, is indicated. Broad-spectrum systemic antibiotics are necessary. Non-steroidal anti-inflammatory drugs (NSAIDs), such as **phenylbutazone** or **flunixin**, may be useful in relieving pain and reducing the inflammation. A topical lubricant may be required to prevent corneal exposure; antibiotic ointments may be necessary to control secondary infection. Aspiration or drainage of exudate is useful if possible. Warm compresses may also give some relief.

Prognosis

The prognosis will vary according to the initiating cause, but is frequently guarded to poor due to the severity of the inflammation. Optic nerve degeneration may be a secondary complication.

Exophthalmos

Protrusion of the globe may occur with orbital cellulitis or may be seen as the only clinical sign in cases of neoplasia, orbital cysts, or chronic sinusitis with bony proliferation of the orbital wall. Orbital cysts may be caused by larval forms of *Echinococcus* within the orbit, or occur as extensions of cystic sinus proliferations.

Clinical signs

Exophthalmos may be best seen when viewing the eyes from the front. Subtle changes in eye position may be appreciated by comparing the angle of the eyelashes. The globe will resist retropulsion. Skull radiographs, orbital ultrasonography and guttural pouch examination will aid in diagnosis.

Treatment

Treatment varies with the primary cause, as does prognosis.

Enophthalmos

The eye may appear **sunken** in horses that are dehydrated or debilitated, due to shrinkage of the orbital fat pads. The eye will be actively retracted in cases of ocular pain. Loss of sympathetic tone (**Horner's syndrome**) will create an enophthalmos. Orbital fractures may also present with a sunken globe, due to displacement of bone fragments or orbital fat.

Clinical signs

The eye is recessed. Viewing the eye from the front, the angle of the eyelash will aid in detecting subtle changes in eyelid position. Pain will be associated with orbital trauma or lesions of the globe. Miosis (constriction of the pupil) and sweating on the ipsilateral side of the face and neck are seen in Horner's syndrome.

Treatment

Treatment is aimed at the underlying cause.

Prognosis

In most cases the prognosis is favorable, depending on the primary cause.

THE EYELIDS

INTRODUCTION

The eyelids and third eyelid are necessary for protection of the eye, maintenance of normal corneal and conjunctival health, production, distribution and outflow of tears, and the removal of foreign bodies and debris. **Neoplasia** is possibly the most common disease process involving the eyelid (squamous cell carcinoma and sarcoid) and nictitating membrane (squamous cell carcinoma) (*q.v.*).

ANATOMY AND FUNCTION

The eyelids serve to protect the globe and have important roles in the production, distribution and removal of tears. The outer, oily layer of the tears is produced by the Meibomian glands. This oily film decreases tear evaporation and coats the eyelid margins thus preventing epiphora (watering of the eye)

(*q.v.*). Eyelid closure moves the precorneal tear film toward the nasolacrimal puncta, the first components of the tear drainage pathway.

The **vibrissae** are long, tactile hairs of the dorsal and ventral orbit. **Eyelashes**, or cilia, are always present on the upper eyelids but may not be present on the lower eyelids. Both vibrissae and cilia serve a protective role supplying sensory input for the blink response.

The **Meibomian (tarsal) glands** are positioned perpendicular to the eyelid margins. These glands excrete their sebaceous product onto the globe through openings that lie in a furrow at the mucocutaneous junction of both the superior and inferior eyelids.

The superior and inferior lacrimal puncta and respective canaliculi are located within the nasal aspect of the upper and the lower eyelids and serve as the normal route for tear removal.

The eyelids have a **profuse vascular network**. The primary muscles of the eyelid include the orbicularis oculi, levator palpebrae superioris and Müller's muscles. The orbicularis oculi muscle completely encircles the palpebral fissure and is responsible for eyelid closure. The upper eyelid is more mobile than the lower eyelid and thus is responsible for most of the blink response. The levator palpebrae superioris muscle elevates the upper eyelid. The upper and lower eyelids also contain smooth muscle tissue, Müller's muscle, which serves to open the palpebral fissure.

The sensory innervation of the eyelids is derived from branches of the trigeminal (fifth cranial) nerve. The upper eyelid is innervated by the lacrimal, supraorbital and infratrochlear nerves, which are branches of the ophthalmic nerve. The lower eyelid is innervated by the zygomatic and infratrochlear nerves, which are branches of the maxillary and ophthalmic nerves, respectively. The orbicularis oculi muscle is innervated by dorsal and ventral palpebral nerves, which are distant branches of the facial (seventh cranial) nerve. The oculomotor (third cranial) nerve innervates levator palpebrae superioris, and the sympathetic component of the autonomic nervous system innervates the smooth muscle of Müller via the trigeminal nerve. A **normal palpebral reflex** demonstrates intact trigeminal (sensory) and facial (motor) nerve pathways.

CONGENITAL ANOMALIES

The eyelids of foals are normally open at birth. **Ankyloblepharon** is a persistent fusion of the eyelid margins. The eyelids can usually be separated manually, however insertion of scissors between the eyelids and globe may be necessary to "unzip" the adhesions, without closing the scissor blades. Scarring can occur with adhesion of the lid margin to conjunctiva, resulting in **symblepharon**. Frequent massage and hot compresses should thus be used over the days following separation of lids in a case of ankyloblepharon.

Many other congenital eyelid defects may occur but are very rare. **Eyelid agenesis** may be characterized by epiphora, conjunctivitis and possibly keratitis (*q.v.*). Surgical correction, **blepharoplasty**, may be required.

An imperforate nasolacrimal punctum is uncommon in Equidae, but may cause chronic epiphora. If the canaliculus is present but a membrane obstructs the punctum, the membrane can be surgically removed thus opening the tear outflow pathway.

ABNORMAL EYELID POSITION AND CLOSURE

Entropion is inversion of the eyelid margin toward the eye and usually involves the lower eyelid. Entropion is rare in adult horses but not uncommon in foals. Entropion does not appear to be a familial disease process, but **Thoroughbreds** may have an increased prevalence. The cause is unknown, but affected newborn foals may be slightly enophthalmic (*q.v.*) at birth thus predisposing to the condition. The abnormal eyelid position may resolve as the foal gains body weight and retrobulbar fat.

The eyelid margin may rub against the conjunctiva and cornea causing a painful keratoconjunctivitis characterized by epiphora, blepharospasm (involuntary closure of the eyelids), conjunctival hyperemia and possibly corneal ulceration (*q.v.*). **Treatment** of entropion is by eversion of the eyelid margin. An everting suture pattern (e.g. interrupted Lembert pattern using 4-0 or 5-0 non-absorbable monofilament suture material) placed in the eyelid skin is a temporary measure but may be sufficient for permanent correction. Surgical removal of a wedge of skin is reserved for severe cases with recurrent entropion following the skin eversion technique or in adults with acquired entropion. A skin incision is made approximately 3–4 mm from and parallel to the eyelid margin. The second incision is spaced as needed to correct the defect. The wedge of skin is removed and the cut edges are opposed with a small diameter, non-absorbable suture material in a simple interrupted pattern.

Ectropion is an eversion of the eyelid margin that is usually secondary to a wound that heals improperly. Surgical intervention is required if the defect causes chronic epiphora, conjunctivitis or exposure keratitis (*q.v.*).

Symblepharon is an abnormal adhesion of the inner conjunctival surface of the eyelid (palpebral conjunctiva) to the conjunctiva overlying the sclera (bulbar conjunctiva). This is a rare condition that may restrict eyelid movement and necessitate surgical intervention.

Ptosis is a drooping of the upper eyelid due to loss of oculomotor innervation to levator palpebrae superioris or loss of sympathetic innervation to Müller's muscle (Horner's syndrome) (*q.v.*). Absence of oculomotor nerve function is also associated with lateral strabismus. Horner's syndrome is not commonly diagnosed in horses because the clinical signs may be subtle. In addition to ptosis, loss of sympathetic tone can produce ipsilateral miosis, slight enophthalmia and passive elevation of the nictitating membrane, conjunctival and nasal mucosal hyperemia, and an increase in skin temperature with sweat production on the face and neck. If a specific cause is identified, appropriate treatment should be initiated.

Lagophthalmos is an inability to close the eyelids completely. Lagophthalmos may be caused by marked buphthalmos, exophthalmos or facial nerve paralysis. Secondary exposure keratitis is common.

EYELASH DISORDERS

Distichiasis

Distichia are extra cilia that emerge from Meibomian gland openings; they are rare in horses. If present and causing **secondary corneal and/or conjunctival irritation**, the aberrant cilia should be surgically removed with electro- or

cryo-epilation in an effort to prevent regrowth. **Resection of the Meibomian gland** that forms the follicle of the aberrant lash may be found to be a more permanent solution and may cause less postoperative scarring, than procedures that involve manipulating the eyelid margin itself.

Trichiasis

The condition in which facial hair or eyelashes grow toward and irritate the eye is known as trichiasis. Trichiasis is rare in horses but may be caused by previous trauma and secondary cicatrization altering normal adnexal conformation. Clinically significant trichiasis may require blepharoplastic procedures (eyelid surgery).

Ectopic cilia

An eyelash that arises from a Meibomian gland, penetrates the palpebral conjunctiva, and is directed toward the cornea, often causing a persistent corneal ulceration, is called an ectopic cilia. This condition is very rare but has been reported in the horse. **En bloc resection of the cilia and its follicle** with adjunctive cryotherapy of the surgical bed is the treatment of choice.

BLEPHARITIS

Inflammation of the eyelid, blepharitis, may be caused by blunt trauma, an allergic reaction (e.g. insect bites), exposure to intense solar radiation, and infectious agents (e.g. fungal organisms, mites and parasitic larvae).

Solar-induced blepharitis is an inflammatory condition that generally affects horses with minimal periocular pigmentation and may be a **precursor to squamous cell carcinoma**. Solar-induced blepharitis can be reduced and its recurrence prevented by decreasing exposure to high levels of UV radiation. An affected horse can be housed indoors during peak hours of sunlight or, if prevention is not feasible, the susceptible tissues can be tattooed.

Dermatophytosis

Ringworm (*q.v.*) occasionally affects the periocular region. *Trichophyton equinum* is the most common fungal agent that causes clinical disease in horses; however, *T. mentagrophytes, Microsporum canis* and *M. gypseum* may also infect Equidae. Lesions are characterized by alopecia, erythema, scaling and crusts. Fungal culture is required for definitive diagnosis. Treatment should include clipping hair and application of topical antifungal agents, e.g. miconazole or clotrimazole cream. In addition, the horse should be isolated and the environment and tack decontaminated using chlorine bleach (1:20) diluted with water.

Demodectic mange

Demodex equi and *D. caballi* (*q.v.*) seldom present clinically significant disease in horses. The mites live within hair follicles and occasionally cause periocular papules, crusts, alopecia and granulomas. Skin scrapings and cytology may reveal the causative agent. A localized manifestation can be treated with **topical**

rotenone ointment. If the lesions become generalized, application of a miticidal dip is indicated.

Cutaneous habronemiasis

Habronema are parasitic gastric nematodes of horses (*q.v.*). Aberrant larval migration of *Habronema muscae, H. microstoma* and *Draschia megastoma* causes rapidly developing, raised, **non-healing ulcerative granulomas** containing caseated and calcified particles. Lesions may be pruritic and painful. The medial canthus and/or nictitating membrane are usually affected since the infective larvae are carried by flies (*Musca domestica* or *Stomoxys calcitrans*), which are attracted to moisture at the medial canthus. Definitive diagnosis is by histopathology, which usually reveals granulation tissue, eosinophils, mast cells, neutrophils and intact or fragmented larvae. **Ivermectin** is the treatment of choice and may be administered in conjunction with a topical antibiotic–corticosteroid ointment.

TRAUMA

Trauma caused by sharp objects such as barbed wire and nails is common in horses. A complete ophthalmic examination, including palpation of the facial bones, should be performed in order to ensure that additional ocular or periocular structures are not damaged. The therapeutic goal is the **re-establishment of a functional and cosmetic eyelid**. Attaining the desired outcome usually requires surgical intervention, which may include debridement and primary closure.

Tetanus prophylaxis should be administered prior to corrective surgical procedures. In addition, systemic antibiotics and NSAIDs are indicated pre- and postoperatively. If corneal ulceration or secondary uveitis is present, treatment with topical antibiotic and atropine ophthalmic ointments should be initiated.

If the presenting wound is >12 h old, contaminated or severely edematous, surgical closure should be delayed. The open wound should be managed medically for 12–24 h with application of a dressed bandage which will cleanse the laceration, soften the traumatized tissue and decrease swelling. **Nitrofurazone ointment** can be used for this purpose as it is well tolerated by the eye and inexpensive.

Following induction of general anesthesia (*q.v.*), the surgical site is prepared in a routine manner and the wound thoroughly cleansed. Excessive suture and tissue tension is avoided by conservative debridement and a two-layer closure. The deep, connective tissue layer should be apposed with absorbable suture (e.g. 5-0 or 6-0 chromic gut or polyglactin). Non-absorbable suture should be used in the skin (e.g. 4-0 or 5-0 monofilament nylon, polypropylene or silk) beginning at and restoring the eyelid margin. Small suture material in a simple interrupted pattern will yield the best results. A bandage and stockinette or protective hood with eye cup may be beneficial for 3–5 days postoperatively, especially during the fly season.

Severe tissue loss may necessitate reconstructive grafting procedures, e.g. **sliding H-blepharoplasty**, to re-establish an eyelid margin. Because of the absence of readily moveable facial skin in horses, extensive reconstructive procedures are difficult to perform. Blepharoplastic procedures are more successful when performed on the lower than the upper eyelid since the lower

eyelid normally has limited motility. In addition, the surgeon should restrict dissection of tissue immediately beneath the orbicularis oculi muscle of the upper eyelid since levator palpebrae superioris function is necessary to prevent secondary postoperative ptosis (*q.v.*). A split-thickness **eyelid tarsorrhaphy** (*q.v.*) (in which the outer parts of the upper and lower lids are joined) may promote uncomplicated healing by relieving postoperative tension.

THE NICTITATING MEMBRANE

ANATOMY AND FUNCTION

The nictitating membrane, or third eyelid, serves to protect the globe, distribute tears, and produce immunoglobulins and part of the precorneal tear film. The caruncle is a small, finely haired prominence within the nasal canthus that may or may not be pigmented. The nictitating membrane has an exposed, palpebral conjunctival surface and a bulbar conjunctival surface that is in contact with the underlying globe. Superficial lymphoid follicles are located on the bulbar conjunctival surface and presumptively produce IgA, which becomes a component of the tear film. The nictitating membrane has an internalized **T-shaped section of cartilage** that serves as structural support. The gland of the nictitating membrane, located at its base, produces a portion of the aqueous part of the tear film and possibly immunoglobulins. The gland's excretory ductules empty their products onto the bulbar conjunctival surface. Movement of the nictitating membrane is passive. As the globe is pulled deeper into the orbit by the retractor bulbi muscles, the nictitating membrane moves across the corneal surface. Sensory innervation of the nasal canthus, caruncle and nictitating membrane is supplied by the infratrochlear nerve, a distant branch of the trigeminal nerve.

TRAUMA

Because of its important functions, the nictitating membrane **should always be salvaged** unless it is irreparably damaged. Absorbable suture material (6-0 chromic gut or polyglactin) should be used to repair conjunctival defects. The surgeon should ensure sutures are placed such that they do not have the potential to cause **secondary corneal ulceration**.

SOLAR-INDUCED INFLAMMATION

The most common tumor of the nictitating membrane is squamous cell carcinoma. Solar-induced inflammation of a non-pigmented nictitating membrane may be a precursor of neoplasia. If avoidance of excessive UV radiation is not practical, the nictitating membrane can be **tattooed**, which may reduce its susceptibility.

FOLLICULAR CONJUNCTIVITIS

Follicular conjunctivitis is uncommon in horses. However, the **nematode *Thelazia lacrimalis*** (*q.v.*) commonly infests the conjunctival sac and nasolacrimal

system. Depending upon the parasitic load, their active serpentine movement may cause **secondary conjunctivitis** or **dacryocystitis** (inflammation of the lacrymal sac) (*q.v.*). Treatment with topically administered, long-acting organophosphorus anticholinesterase compounds is reportedly effective (0.03–0.25% echothiophate [ecothiopate] iodide q 12 h, or 0.1% isoflurophate [dyflos] q 12 h for 7–10 days). The anthelmintic treatment should be administered in conjunction with an antibiotic–corticosteroid ophthalmic ointment. Since the intermediate host is believed to be the face fly, *Musca autumnalis*, **fly control** may prevent recurrence.

PROTRUSION (ELEVATION) OF THE NICTITATING MEMBRANE

One or both nictitating membranes may protrude more than normal. The specific etiology should be sought and appropriate treatment initiated. Concomitant clinical signs, diagnostic work-up, treatment and prognosis vary considerably depending upon the actual cause. Protrusion may be associated with enophthalmia (*q.v.*), due to passive elevation over a retracted eye, or with exophthalmia (*q.v.*), due to displacement of the nictitating membrane by a space-occupying lesion. Some causes of unilateral protrusion of a nictitating membrane include pain, Horner's syndrome, phthisis bulbi (shrinking of the eyeball), microphthalmia, orbital fractures and a retrobulbar mass (e.g. neoplasia, abscess, cyst, cellulitis or foreign body granuloma) (*q.v.*). Bilateral protrusion of the nictitating membranes can be caused by dehydration, cachexia (loss of retrobulbar fat), tetanus (*Clostridium tetani*) and hyperkalemic periodic paralysis.

THE CONJUNCTIVA

ANATOMY

The conjunctiva is the mucous membrane that lines the eyelids (palpebral conjunctiva) and is reflected onto the surface of the globe (bulbar conjunctiva). The junction between the palpebral and bulbar conjunctiva is called the **fornix**. Ventrally, a fold in the conjunctiva covers the nictitating membrane. Palpebral conjunctiva is adherent to the underlying tissue, but the bulbar and fornix conjunctiva is mobile, to permit free movement of the globe.

The conjunctiva is composed of a non-keratinizing stratified columnar epithelium and an underlying layer of loose connective tissue, the substantia propria. The fornices and palpebral conjunctival epithelium are rich in goblet cells, which produce mucin. This allows for adhesion of the tear film to the ocular surface. The epithelium also contains melanin pigment. This is frequently most pronounced in the limbal and temporal bulbar conjunctiva and on the nictitating membrane. The bulbar conjunctival epithelium is continuous with the corneal epithelium and changes at the limbus, the corneoscleral junction.

The substantia propria contains **many small superficial and deep blood vessels**, allowing for the red appearance of the inflamed conjunctiva. The superficial portion of this layer contains lymphoid tissue that becomes active with **antigen stimulation**. This is particularly prominent on the bulbar surface of the nictitating membrane, adjacent to the limbus and in the ventral fornix. Lymphatic drainage is through the parotid lymph node.

DERMOIDS

Dermoids are choristomas, areas of normal skin tissue growing in abnormal sites, such as the conjunctiva, cornea or eyelids. **Lesions are congenital**, but not known to be inherited in the horse.

Diagnosis is based on the typical appearance of skin, frequently haired, growing on the conjunctiva. Treatment is by excision of the affected tissue. General anesthesia may be indicated, depending on the size and location of the dermoid. Conjunctival closure should be done to prevent herniation of orbital fat. Prognosis is excellent, assuming total excision of dermoid tissue.

CONJUNCTIVITIS

Inflammation of the conjunctiva may be caused by bacterial, viral, fungal or parasitic infections, or due to dacryocystitis or environmental factors, such as trauma, or irritants such as foreign bodies or solar irradiation (*q.v.*). Conjunctivitis must be distinguished from the ciliary flush, or deep hyperemia associated with uveitis or glaucoma (*q.v.*). The normal equine conjunctival flora consists of many bacteria, particularly staphylococci, as well as a variety of fungi.

Bacterial conjunctivitis

Frequently secondary to trauma, local irritants or systemic disease, compromised resistance may allow overgrowth of normal flora or opportunistic pathogens. *Moraxella* spp. may be associated with a primary conjunctivitis.

Diagnosis is based on conjunctival hyperemia and purulent ocular discharge. Culture is indicated in persistent cases or in outbreaks.

Treatment consists of removing the primary cause, if identified. Topical broad-spectrum antibiotics, such as **gentamicin** or triple antibiotic, 3–4 times daily, are usually sufficient to control the infection. Corticosteroids may also speed the resolution of the clinical signs, but should be used with caution if a specific cause of the conjunctivitis has not been identified, and are contraindicated in the presence of corneal ulcers. With uncomplicated bacterial conjunctivitis, prognosis is good with appropriate therapy.

Viral conjunctivitis

Generally seen in association with upper respiratory infections, viral conjunctivitis may be caused by rhinopneumonitis, influenza, adenovirus or viral arteritis infections (*q.v.*). The conjunctivitis is usually not a serious component of the disease, although an **ocular examination** should be carried out to rule out concurrent uveitis (*q.v.*). A **severe hyperemic conjunctivitis** can be the presenting sign in equine viral arteritis (*q.v.*), and this differential diagnosis of conjunctivitis is thus particularly important in countries free of the disease where early diagnosis of an infected animal is critical.

Diagnosis is usually best accomplished with serology. Treatment is nonspecific. Topical broad-spectrum antibiotics may be used if secondary bacterial infection occurs. Prognosis for the eyes is good, as the conjunctivitis is usually self-limiting.

Fungal conjunctivitis

Fungal conjunctivitis rarely occurs in the absence of keratomycosis (*q.v.*).

Parasitic conjunctivitis

Habronemiasis

The eye is a common site for habronemiasis (*q.v.*), as the moisture of the medial canthus attracts the flies that act as vectors. Larvae of *Habronema muscae, H. microstoma* or *Draschia megastoma* deposited by the flies migrate into the conjunctiva, skin and nasolacrimal system, where they incite an **intense granulomatous reaction**.

Granulomatous conjunctivitis/blepharitis, often at the medial canthus, is typically seen. Nodules are frequently ulcerated, with caseous, often mineralized "sulfur granules" being characteristic. Secondary corneal abrasions are common. Diagnosis may be confirmed by demonstrating larvae in the exudate or in a biopsy of the granuloma. The presence of a marked eosinophilic and mast cell infiltrate is supportive of the diagnosis.

Systemic ivermectin (0.02 mg/kg PO, single dose) is the treatment of choice. Echothiophate 0.03% solution applied topically twice daily is larvicidal. Antibiotics and corticosteroids are helpful in controlling secondary infection and inflammation. The latter is important since an immune reaction against dead larvae can cause severe reactive signs. **Fly control** will reduce re-infestation. **Surgical excision** of granulomas may be required.

Chronic granuloma formation and re-infestation are possible. However, resolution of conjunctival lesions is generally good.

Onchocerciasis

The adult *Onchocerca cervicalis* nematode (*q.v.*) lives in the ligamentum nuchae and produces microfilaria that migrate to subcutaneous tissues. Microfilaria are spread from horse to horse by biting midges (*Culicoides* spp.). Migrating microfilaria frequently reach the eye and adnexal structures. The disease, which includes conjunctivitis, keratitis, uveitis and chorioretinitis (*q.v.*), results from the inflammatory response to dying microfilaria.

Although demonstration of microfilaria in bulbar conjunctival biopsy may support the diagnosis, microfilaria may be found in many **normal horses**. Therefore, diagnosis should also be based on the finding of characteristic lesions. These include **depigmentation** of the lateral limbal conjunctiva, perilimbal keratitis and follicular perilimbal conjunctivitis.

As the dead microfilaria are more pathogenic than the living microfilaria, treatment with microfilaricidal drugs may **exacerbate** the condition. Therefore active inflammation should be controlled prior to antiparasitic treatment, using topical or subconjunctival corticosteroids. Specific therapy includes **ivermectin** (0.02 mg/kg PO, single dose), diethylcarbamazine (4.4–6.6 mg/kg PO daily for 21 days), or echothiophate (0.25% q.i.d. in both eyes for 21–28 days). Ivermectin may be the preferred drug as it is associated with less local inflammatory response.

Prognosis is good for conjunctival lesions. Corneal lesions and uveitis (*q.v.*) may be more chronic and are potentially recurrent problems.

Thelaziasis

Thelazia is a nematode found in the conjunctival fornix. Infections in horses have been attributed to *T. lacrimalis*, *T. skrjabani*, *T. gulosa* and *T. californiensis*. Infection may be common in some areas, but is frequently subclinical. Larger numbers of worms are found in younger horses. The **face fly**, *Musca autumnalis*, serves as the intermediate host.

Most infections show no clinical signs. However, epiphora, photophobia and keratitis (*q.v.*) may be seen along with the conjunctivitis. A seromucoid discharge and follicular conjunctivitis is seen in chronic cases. Nasolacrimal duct obstruction and keratoconjunctivitis sicca (*q.v.*) may also be seen. The worms are large (10–25 mm long) and are readily seen when they are moving. Topical anesthesia will immobilize them, making diagnosis more difficult.

Many anthelmintics may be ineffective for treatment. Topical anesthetics immobilize the worms and may allow for mechanical removal of some of the worm burden. **Echothiophate** may also be effective, given as 0.03% t.i.d. in both eyes. Fly control will reduce re-infestation and spread.

Prognosis is good, as most cases are asymptomatic.

CONJUNCTIVAL NEOPLASMS

Neoplasms include squamous cell carcinoma, hemangioma, angiosarcoma, mastocytoma and melanocytoma.

SYMBLEPHARON

Symblepharon is an **adhesion between the conjunctiva and cornea**, or between two areas of conjunctiva or nictitating membrane. It may be a congenital malformation or be acquired following conjunctivitis, a conjunctival injury or a corneal ulcer.

Diagnosis is based on conjunctival overgrowth of the cornea, or on the presence of adhesions. Treatment depends on the condition of the eye. If vision is possible, **surgical intervention** can be undertaken to excise adhesions. Prognosis is fair to poor, as recurrence is common after surgery.

THE LACRIMAL/NASOLACRIMAL SYSTEM

ANATOMY

The precorneal tear film consists of three layers: the inner mucin layer, produced by conjunctival goblet cells; the middle aqueous tear layer; and the outer oily layer, produced by the Meibomian glands at the eyelid margin. The mucin serves to bond the aqueous film to the hydrophobic epithelial surface, improving wetting ability. The outer oily layer reduces evaporation and prolongs the surface tension of the tear film, stabilizing its distribution. The aqueous portion, which makes up the bulk of tear film, is produced from the orbital lacrimal gland and the gland of the nictitating membrane. The orbital gland is located in the dorsolateral orbit and empties into the dorsal conjunctival fornix through multiple small ducts.

The action of the eyelids during blinking moves the tear film toward the medial canthus, and actively moves tears into the nasolacrimal puncta. There are two puncta, one on each eyelid. The dorsal and ventral puncta are approximately 8 and 5 mm from the medial canthus, respectively.

The puncta open into the canaliculi, which run medially and ventrally under the palpebral conjunctiva. The canaliculi drain into the lacrimal sac, located in the lacrimal fossa. The sac is drained by the nasolacrimal duct, which runs rostrally to the distal nasal meatus. The proximal one third of the duct runs through the lacrimal and maxillary bones. Distally, the duct runs through the lacrimal groove, a sulcus in the nasal wall of the maxilla, then turns ventrally to open on the floor of the nasal vestibule at the mucocutaneous junction. Multiple openings may be present in some animals and all may or may not connect with the nasolacrimal duct.

CONGENITAL ATRESIA

Atresia may occur at any point of the nasolacrimal duct, but is most frequent at the distal meatus.

Diagnosis

Epiphora is an early clinical sign, and may progress to a mucopurulent discharge. The nasolacrimal meatus is often absent. The location of the atresia may be determined by cannulation of the nasolacrimal duct through either punctum or, preferably, by dacryocystorhinography (i.e. flushing of the tear duct with a contrast agent visible on X-ray).

Treatment

Atresia requires **surgical correction** under general anesthesia. Distal atresia can be corrected by approach through the nostril, or through a paramedian incision through the dorsal nostril wall. The duct is identified by **catheterization** through the dorsal punctum, or by distending the duct with fluid. The nasal mucosa is incised through into the duct and the catheter is advanced through the incision. The catheter is sutured in place and left for 3–4 wk to maintain patency. A topical ophthalmic antibiotic–corticosteroid solution will also reduce stenosis during healing.

More proximal atresia may necessitate a conjunctivorhinostomy by which a silicone tube is passed from the ventral conjunctival recess into the nasal passage after production of a stoma using a Steinman pin. After several weeks the new canaliculus becomes endothelialized and the tube can be removed. Postoperative management is as described for distal atresia repair.

Prognosis is fair to good, with distal atresia having a better prognosis for long-term cure after surgery than cases requiring **conjunctivorhinostomy**.

ACQUIRED DISEASES

Nasolacrimal duct obstruction

Acquired nasolacrimal obstructions may be the result of dacryocystitis, facial trauma, or bone remodeling associated with sinusitis, osteomyelitis, dental disease or neoplasia (*q.v.*).

Clinical signs include epiphora, although most cases progress to a mucopurulent ocular discharge. Skull radiographs and contrast studies are indicated. Cases related to dacryocystitis (*q.v.*) are the most easily treated, as discussed below. In other cases, the nasolacrimal obstruction may be of secondary importance until the primary cause is dealt with.

Dacryocystitis

Inflammation, or infection, of the nasolacrimal duct may be unilateral or bilateral and can result from a variety of causes. Foreign bodies such as plant matter or sand, parasites such as *Habronema* spp. or *Thelazia* spp., adnexal neoplasia (most frequently squamous cell carcinoma) and infections of the upper respiratory tract or sinuses are all possible differential diagnoses (*q.v.*). A wide variety of **secondary bacteria** may be involved and cultures of exudate are indicated.

Clinical signs

Clinical signs include conjunctivitis, which may be chronic and/or recurrent in nature, and mucopurulent discharge from the eyes and possibly from the distal meatus as well. Hemorrhagic exudate may also be seen. Differential diagnosis of such a mucopurulent discharge includes an imperforate distal nasolacrimal orifice in a young horse and squamous cell carcinoma in an older animal (*q.v.*).

Treatment

After collection of exudate from the duct for cultures and cytology, the duct should be **flushed thoroughly** to remove the maximum amount of debris and exudate, and to restore patency if possible. It may help to pass a size 5 French catheter to provide optimal flushing. If the catheter can be passed in its entirety, it should be sutured in place for several weeks to maintain patency. If patency cannot be restored, plain radiographs and **dacryocystorhinography** (*q.v.*) should be performed to identify the obstruction and to find any bony changes. Treatment with an appropriate ophthalmic antibiotic–corticosteroid solution will frequently lead to resolution after patency is restored. Systemic antibiotics may also be indicated. If an obstruction resists flushing, treatment with an antibiotic–corticosteroid may reduce the swelling sufficiently to allow flushing of the duct after a few days of treatment.

Prognosis is generally good, depending on the primary cause, although recurrence is possible. Stenosis is possible in chronic cases and may necessitate surgical intervention.

Lacerations

Eyelid lacerations involving the medial canthal area may be associated with severing of the canaliculi or nasolacrimal duct. During the reconstruction of the eyelid, it is essential to **re-appose the duct** to prevent epiphora. This is achieved by catheterizing the duct prior to closure of the wound. This may be done from the nasal meatus if necessary to identify the distal portion of the

duct. The catheter is left in place during closure to maintain apposition, and is sutured in place for several weeks to prevent stenosis during healing. Antibiotics should be given parenterally and topically postoperatively.

Keratoconjunctivitis sicca

Inadequate tear production resulting in **corneal or conjunctival inflammation** is termed keratoconjunctivitis sicca (KCS). KCS is rare in the horse. It may be idiopathic or result from **head trauma** causing skull fractures, facial paralysis or parasitic infection of the lacrimal gland, or occur transiently during general anesthesia. Certain toxins, such as locoweed (*Astragalus mollissimus*), may also cause KCS. It should be noted that tear film deficiencies can be related either to reduced production of the aqueous phase of the tear film or to increased evaporation secondary to a reduction in the lipid layer that exists to reduce evaporation. **Meibomitis** (inflammation of the Meibomian glands, *q.v.*) may result in this evaporative form of dry eye. While differentiation of aqueous deficiency versus evaporative dry eye has been discussed in the literature, it is difficult to achieve in practice, and tear replacement is the treatment of choice in both.

Clinical signs

KCS usually presents as a chronic keratitis, or conjunctivitis, with a dry dull-appearing eye. A mucoid to mucopurulent exudate is frequently present. The low tear production can be documented by **Schirmer tear test**. In this test, commercially available paper strips are placed in the conjunctival fornix and left for 1 min. The amount of wetting of the strip is measured upon removal of the paper. Normal values are 20–30 mm of wetting/min. Use of **topical Rose Bengal** can be valuable in assessing health of the ocular surface since a healthy cornea does not show adherence of the vital dye whereas areas of mucus deficiency demonstrate a punctate staining pattern.

Treatment

Treatment consists of **tear replacement** and control of secondary infection. Tear replacement may be achieved by use of an **artificial tear solution** with a methylcellulose or polyvinyl base several times daily, or a lubricant ointment twice daily. More recently, replacement using carbomer-based lubricants has been successful with a greater residence time on the ocular surface and thus a reduced frequency of application. Acetylcysteine 5% is useful in some cases as a mucolytic agent. Pilocarpine 0.25–0.5% may stimulate tear production. Topical antibiotic therapy for secondary infection should be based on culture results. **Topical corticosteroids** will provide relief from irritation, but should be used with caution because of the risk of corneal ulceration.

Chronic cases, especially those associated with facial paralysis, may benefit from temporary or permanent **tarsorrhaphy** (where the upper and lower eyelids are surgically joined). Parotid duct transposition has been described but is not routinely done.

In acute, idiopathic cases the prognosis is good as the KCS may be transient. KCS associated with trauma or facial paralysis has a more guarded prognosis, as does any case that becomes chronic.

THE CORNEA

ANATOMY

The large, prominent cornea of the horse is horizontally elliptical. It measures 28–32 mm in width, 23–26 mm in height, is 1.0–1.5 mm thick in the center, and 0.8 mm thick at the periphery. The equine cornea is a three-layered structure composed of an anterior epithelium–precorneal tear film complex, a thick collagenous stroma, and a single-layered posterior epithelium (endothelium) with its thick basement membrane. The non-keratinized anterior epithelium consists of basal, wing and stratified squamous cells, and a basement membrane. The major thickness (90%) of the cornea comes from the stroma. The stroma consists of bundles of small diameter collagen fibrils arranged in parallel layers. The posterior endothelium is a single layer of metabolically active cells and a basement membrane, known as **Descemet's membrane**. Attachments of the pectinate ligaments from the iris base to Descemet's membrane can be seen as a gray line at the limbus. The cornea is densely innervated with sensory nerves of the trigeminal nerve.

CONGENITAL ANOMALIES

Dermoids are congenital tumors (choristomas), composed of hair and many other tissue types, that can affect the temporal limbus and conjunctiva in foals. The hairs cause conjunctivitis, keratitis and blepharospasm (*q.v.*). Surgical keratectomy is the therapy of choice.

Persistent pupillary membranes (PPM) can cause varying degrees of corneal opacification and cataract formation due to damage to the endothelium and lens. These membranes normally atrophy by 9–12 mo.

CORNEAL ULCERS

Corneal ulcers are defects in the corneal epithelium that may also involve the stroma, Descemet's membrane and the endothelium. **Every ulcer in a horse is potentially serious** and sight threatening as the equine cornea appears prone to develop infection and heals slowly with extensive scarring. Most ulcers in the horse are associated with trauma. Entropion, ectopic cilia, fly sprays, facial nerve paralysis or anesthesia can also result in corneal ulceration. The risk of bacterial, fungal or mixed infections is quite high in the horse following damage to the corneal epithelium.

Clinical signs

Corneal ulcerations will generally be **painful** and the horse will exhibit photophobia, blepharospasm and increased tearing. The eyelashes will point downwards, rather than being perpendicular to the corneal surface. The corneal surface of superficial ulcers will appear dull, cloudy and roughened. Vascularization may be present in chronic cases. The corneal stroma may appear to be melting in rapidly progressive, infected ulcers. Infiltration of neutrophils into the stroma can cause **abscess formation**. Ulcers that expose Descemet's membrane will appear clear at the deepest portion of the lesion.

The **diagnosis** of a corneal ulcer is made by the application and retention of **fluorescein dye** on the cornea. Corneal scrapings should be examined, as **cytology** will enable the initiation of appropriate medical therapy for bacteria and fungi. Gram-negative bacteria known to be associated with equine corneal ulcers include *Pseudomonas* spp. and assorted coliform bacteria. *Staphylococcus* and *Streptococcus* spp. are Gram-positive bacteria found in infectious equine keratitis. *Aspergillus* and *Fusarium* spp. are common causes of fungal ulceration in the horse. Culture and antimicrobial sensitivity for bacteria and fungi are recommended, particularly in non-responding cases.

Treatment

Once a corneal ulcer is evaluated presumptively by cytology, or conclusively by culture, the objectives of medical therapy must be carefully considered to ensure comprehensive treatment. First, **bacterial and fungal growth must be halted** and the microbes rendered non-viable. Secondary anterior uveitis (*q.v.*) must then be controlled to prevent blinding sequelae. **Corneal perforation** caused by direct microbial extension or endogenous stromal proteolysis must be averted.

Medical therapy almost always comprises the major thrust in ulcer control, although the judicious use of adjunctive surgical procedures may be required in refractory cases. This intensive pharmacologic attack should satisfy the therapeutic objectives and be modified according to its efficacy. Treatment frequently needs to be sustained for weeks or, occasionally, months.

Horses with ocular disease are often in **pain** and topical treatment is usually difficult. Subconjunctival injections and the use of subpalpebral lavage systems are particularly useful in treating severe eye disease in the horse. **Subconjunctival injections** provide a depot of medication (Table 19.1) that leaks slowly from the injection site and, in effect, provides continuous corneal

Table 19.1 Dosages for subconjunctival injections

Antibiotics	
Amikacin	25 mg
Ampicillin	250 mg
Cefaloridine or cefazolin	100 mg
Chloramphenicol succinate	200 mg
Erythromycin	100 mg
Gentamicin	50 mg
Kanamycin	20 mg
Lincomycin	150 mg
Benzylpenicillin	500 000 IU
Tobramycin	5 mg
Antifungal drugs	
Amphotericin	125 μg
Miconazole	20 mg
Nystatin	5000mg
Autonomic drugs	
Atropine (15 mg/mL)	5 mg
Phenylephrine (10 mg/mL)	5 mg

lavage. A **subpalpebral lavage** system can be produced by placing a fenestrated length of silastic tubing (1.65 mm [0.065 inch] outside diameter) in the superior palpebral fornix using a 12-gauge needle or trocar. Sedation, eyelid akinesia, sensory eyelid blocks, and topical anesthesia are generally sufficient for placement. Recently, lavage systems using a placement system into the medial lower eyelid have been advocated as more simple to position than an upper eyelid system, and with the cornea protected by the third eyelid from potential damage from the footplate.

Soft contact lenses are available to fit the horse cornea. In the UK, Veterinary Speciality Products is the main provider (http://www.sjhales.co.uk), while in the USA, Ocularvision (http://www.ocularvision.com) is one of a number of retailers. Bandage contact lenses are used to enhance epithelial adhesion in corneal ulcers, and may have a use as drug delivery systems. Tinted lenses are used to cover corneal scarring and have been advocated to reduce light intensity in uveitis (*q.v.*) where photophobia is a problem. Contact lenses should not be used where there is any suggestion of an infectious ulcerative keratitis (*q.v.*).

Antimicrobials

Several antibiotics (see Table 19.1) may also be used topically to treat bacterial ulcers. On the basis of susceptibility testing, most bacterial isolates from equine corneal ulcers are sensitive to **gentamicin**, although more recently gentamicin resistant organisms have led to increased use of fortified preparations or **fluoroquinolone** antibiotics. Antibiotic administration may need to be frequent (q 1 h) in rapidly progressing ulcers. IV **miconazole** (10 mg/mL) has been used successfully topically to treat **fungal ulcers** in horses. It may need to be administered q 1–2 h for several weeks in severely affected eyes. This high frequency of application renders a lavage system almost mandatory in such cases: an indwelling nasolacrimal cannula or a transpalpebral lavage system is most commonly used. Whereas in the past the upper eyelid was most commonly used for these systems, recent reports have suggested use of an indwelling catheter in the lower eyelid, placed medially so that the third eyelid protects the cornea from possible traumatic ulceration caused by the footplate of the lavage system.

Uveitis control

In horses, as in other species, **iridocyclitis** (inflammation of the iris and ciliary body), or arterior uveitis is a usual and expected sequel to ulcerative keratitis. Uveal inflammation is incited through an axon reflex mediated by the ophthalmic branch of the trigeminal nerve that is sensory for the cornea, conjunctiva and uvea. Anterior uveitis in horses with corneal ulcers should be treated by both topical and systemic routes. Phenylbutazone (2 mg/kg b.i.d.), aspirin (50 mg/kg b.i.d.) and flunixin meglumine (0.5 mg/kg b.i.d.) used orally or parenterally are effective in reducing uveal exudation and relieving ocular discomfort. Topical NSAIDs such as **ketorolac** or **flurbiprofen** have been shown to reduce uveitic signs secondary to ulcerative keratitis.

Topically applied anticholinergics, such as 1–2% atropine, may be effective in stabilizing the blood–aqueous barrier through their pupillary dilatation effects. Relaxation of the ciliary muscles also eliminates **ciliary spasm**, a major factor in ocular discomfort. Pupillary dilatation protects the visual axis from

occlusion and may minimize the development of **synechiae** (adhesions). Horses on topical atropine should be watched closely for symptoms of colic. Measurement of girth circumference can be a useful tool to detect gaseous distension of the intestine as a subclinical early sign of **impending gut statis** as a consequence of topical atropine use.

Collagenolysis prevention

Severe corneal inflammation secondary to bacterial (especially *Pseudomonas* spp.) or fungal infection may result in sudden, rapid corneal liquefaction and perforation. Activation and/or production of proteolytic enzymes (matrix metalloproteinases) by corneal epithelial cells, leukocytes and organisms are responsible for stromal collagenolysis. Acetylcysteine (up to 10%) or sodium EDTA should be instilled hourly, in addition to the other indicated drugs, until stromal liquefaction ceases. Fresh autogenous plasma or serum used topically is also beneficial in reducing the collagenolysis since a number of anti-collagenolytic factors such as α_2-macroglobulin are to be found in serum. Different matrix metalloproteinases require different factors to inhibit them: some are calcium dependent requiring EDTA, others have zinc as a cofactor necessitating use of acetylcysteine which chelates zinc in the same manner that EDTA chelates calcium. The rich diversity of tissue inhibitors of matrix metalloproteinases (TIMPS) to be found in serum renders this a particularly useful addition to the therapeutic armamentarium of anti-collagenolytic agents.

Inappropriate therapy

Corticosteroid therapy by all routes is contraindicated in the management of equine corneal infections. Even topical corticosteroid instillation, to reduce the size of post-mycotic corneal scarring or vascularization, may be disastrous if fungi remain indolent in the corneal stroma.

Surgical therapy

Keratectomy (or surgical removal of corneal tissue) may prove useful both in the early stage of ulcerative keratomycosis, while infection is confined to the corneal epithelium and anterior third or half of the corneal stroma, and also in later stages of stromal mycosis when the epithelium has healed. Some clinicians suggest **epithelial debridement** with 7% tincture of iodine applied with a cotton-tipped swab to the corneal surface as routine management. Where fungal infection occurs, therapeutic full thickness corneal transplantation has been advocated but clearly this requires referral to a **specialist center** accustomed to performing such surgery.

To augment lost corneal thickness and strength as well as providing ocular surface protection, deep corneal ulcers threatening perforation may require conjunctival or nictitans flap placement. The former requires mobilization of a **conjunctival flap**, which is sutured to the corneal surface at the edge of the ulcer and acts to adhere to and close the corneal deficit. The latter involves suturing the nictitating membrane to the perilimbal sclera or upper eyelid and merely provides physical protection and support. If, as in these latter cases, the apposed conjunctiva adheres to the denuded stroma, drug penetration may be slightly impeded, but ocular perforation will be averted. The use of a conjunctival pedicle flap also has the advantage of continuous serum supply to

the denuded area of cornea with provision of serum matrix metalloproteinases on a continual basis.

Panophthalmitis (inflammation of all tunics of the eye) following perforation through a stromal ulcer has a grave prognosis, and carries a high risk for loss of vision. Medical therapy includes injection of antimicrobial drugs into the anterior chamber, and systemic antibiotics. Whether or not treatment is applied, **phthisis bulbi** (*q.v.*) is likely to result after a chronically painful course. To spare the unfortunate horse this chronic discomfort, enucleation is the humane alternative.

PERSISTENT EROSIONS

Non-healing ulcers characterized by circumferential lips of non-attached epithelium are found in neonatal foals. Causes to be ruled out include entropion, ectopic cilia, keratoconjunctivitis sicca, nictitans foreign bodies, and bacterial, fungal or viral infection (*q.v.*). Treatment consists of removal of the epithelial lip with a soft cotton swab, cautery of the edges of the ulcer with 7% tincture of iodine, and administration of topical autogenous serum, hyperosmotic solutions, and ophthalmic antibiotic/cycloplegic solutions.

Non-healing ulcers have also been reported in the adult. Treatment of these ulcers includes debridement of the redundant epithelium, the use of soft contact lenses, and performing **multiple punctate keratotomies** (MPK). MPK can be performed with topical anesthesia and sedation. A 22–25 gauge needle is pressed into the anterior stroma just enough to indent it. These micropunctures are made every 0.5–1 mm over the entire ulcer and extended a few mm into the adjacent epithelium. These allow the exposure of the underlying stroma and enhance the production of a more adherent basement membrane.

STROMAL ABSCESSES

In cases with a small but deep corneal ulcer, the epithelium may heal over the ulcer bed, **trapping microorganisms** beneath the epithelium. This may permit the growth of the bacteria and result in the formation of a suppurative infiltrate. The resulting keratitis, and secondary uveitis, may be intense.

Clinical diagnosis is based on the finding of a **non-ulcerative keratitis** with a yellow-to-white stromal infiltrate. Cultures and cytology should be based on deep corneal scrapings.

Treatment is as for ulcerative keratitis (*q.v.*), and should include systemic NSAIDs as well as atropine for **cycloplegia** (paralysis of the ciliary body). It may be desirable to repeat corneal scraping (as often as necessary) to prevent re-epithelialization. This will allow increased antibiotic penetration. Antibiotic therapy should be aggressive topically, and the horse may also benefit from systemic antibiotics.

Prognosis is guarded, as the inflammatory response is difficult to control and may run a prolonged course.

NON-ULCERATIVE KERATOUVEITIS

Non-ulcerative keratouveitis is a painful, progressive keratitis characterized by a flesh-colored stromal infiltrate at the limbus. This condition appears to be

immune mediated. It must be differentiated from stromal abscessation. Treatment consists of topically and systemically administered corticosteroids and NSAIDs. The prognosis for recovery is poor.

PUNCTATE KERATITIS

Multiple, superficial, punctate opacities are characteristic of viral keratitis in the horse. Fluorescein dye retention is variable, but Rose Bengal solution is helpful in identifying devitalized cells. Equine herpesvirus 2 has been isolated from affected horses. Treatment with trifluridine or idoxuridine 6 times per day is recommended.

CORNEAL LACERATIONS

Corneal lacerations are common ocular injuries in the horse. They may or may not be associated with **iridal prolapse**. The sclera should be carefully examined for any hidden defects if the laceration involves the limbus. Prompt surgical correction is required to prevent infection and maintain vision. The prognosis for retention of vision is guarded in most cases due to the risk of endophthalmitis (*q.v.*).

THE ANTERIOR UVEAL TRACT

ANATOMY

The uveal tract consists of the iris and ciliary body (**the anterior uvea**) and the choroid (**the posterior uvea**). The iris serves to regulate the amount of light that enters the posterior segment through the central aperture, the pupil. Pupil size is a function of the sphincter muscle, which runs primarily horizontally in the horse, and the dilator muscle which runs radially deep in the iris. The pupil margin is lined by granula iridica at the center of its upper and lower border. These pigmented bodies are extensions of the posterior pigmented iris epithelium, and are frequently vacuolated.

The iris stroma contains melanocytes and fibroblasts as the predominant cell type. The blood supply is derived from the long posterior ciliary arteries, which form an incomplete major arterial circle at the base of the iris, and numerous small radial arteries.

The ciliary body is divided into two portions, the anterior pars plicata and the pars plana posteriorly. The pars plicata is composed of numerous processes that project into the posterior chamber. A double epithelial layer covers the processes, and is responsible for aqueous humor production. The ciliary muscles are responsible for lenticular accommodation, albeit limited, through the zonular fibers. The pars plana is a flat transition zone from the ciliary processes to the peripheral retina. The uveal tract continues posteriorly as the choroid.

CONGENITAL ANOMALIES

Aniridia

Failure of iris development is rare, but has been reported in the Belgian Draft Horse and sporadically in other breeds. The defect is inherited as an autosomal

dominant in the Belgian horse. Although visual acuity appears to be lower in affected horses, the predominant problem is **photophobia** (*q.v.*): without an iris to constrict the pupil in bright light, higher than normal levels of solar irradiation can impinge upon the retina. In these cases the use of **tinted contact lenses** can be helpful.

Persistent pupillary membranes

In normal development, the mesenchymal tissue covering the pupil regresses, leaving the pupillary aperture. Remnants of this tissue may be seen arising from the iris collarette, and are termed **persistent pupillary membranes** (PPM). PPM may attach to the cornea, creating a focal area of edema, to the lens where focal cataracts may result, or bridge the pupil from iris to iris. These may be an incidental finding or be associated with other ocular anomalies. Treatment is usually not indicated. No genetic predisposition is known.

Heterochromia

Pigment variations of the iris may occur and may involve all or part of one eye, or both. Eyes with blue-colored irides are often referred to as **wall-eyes** or **china eyes**. They are most frequently seen in horses such as Paints or Appaloosas that have **excessive white markings of the face**. Pigment variations of the posterior segment of the eye are commonly seen concurrently. **No functional deficit** is associated with heterochromia. One problem that can occur in these eyes with deficient pigmentation is the appearance of what resembles an **iris cyst**, but is in fact stromal hypoplasia of the iris allowing aqueous produced by the ciliary body behind the iris to "balloon" forward the iris tissues, giving the appearance of a cyst.

ACQUIRED UVEAL DISEASE

Uveitis

Intraocular inflammation is a leading cause of blindness in the horse. Uveitis may be acute or, frequently, recurrent. Many etiologies have been implicated in acute cases, including trauma, bacteria (*Leptospira* spp., *Brucella* spp., *Streptococcus equi*), viruses (parainfluenza 3, equine influenza, equine viral arteritis), fungi (*Chlamydia, Mycoplasma*), parasites (*Onchocerca cervicalis, Microfilaria, Strongylus, Toxoplasma gondii*), hypersensitivity reactions, phacoanaphylaxis, endotoxemia and neoplasia (*q.v.*). In cases of ocular trauma or endotoxemia/septicemia, the uveitis may be due to a breakdown of the blood–eye barriers without a specific ocular immune response occurring. Uveitis may also be caused by corneal ulcers (*q.v.*). Stimulation of corneal nerve endings initiates an axonal reflex, creating miosis and protein leakage into the aqueous humor.

In infectious or immune-mediated causes of uveitis, antigens encountered by the eye must be processed at distant sites, as there is normally no lymphatic drainage from the eye. In the normal eye the lymphocytes migrate through blood vessels to the spleen where they present antigen to splenic antigen-presenting cells. This so-called "camerosplenic" access allows antigen presentation to occur

in a specific splenic immunologic environment. Here the immunologic conversation between lymphocytes and antigen-presenting cells results in development of a population of Th2 helper T lymphocytes. These lead to an immunologic response which results in the proliferation of antibody-producing B cells and not the cytotoxic and Th1 helper cells that yield the delayed type hypersensitivity reaction. Theoretically, this down-regulates damaging tissue reactions that would lead to profound intraocular inflammation and subsequent blindness. Whether this occurs in practice is unclear—in the inflamed eye sensitized immune cells and a "soup" of inflammatory cytokines are sequestered in the vitreous. The presence of these cells and cytokines may create a recurrent nature to the uveitis, which may be reactivated by these cells if they are challenged by appropriate antigens at a later date.

With regard to **leptospirosis** (*q.v.*), tests have shown that intraocular responses against leptospira occur in a large number of cases of equine **recurrent uveitis**. Recent work on **therapeutic vitrectomy** in equine recurrent uveitis has shown the presence of intravitreal leptospiral nucleic acid by polymerase chain reaction (PCR), confirming that **intraocular leptospira** are associated with a number of cases of equine recurrent uveitis. It may be that vitreally sequestered leptospiral organisms are responsible for the recurrent nature of much equine uveitis. In such a case "**bystander injury**" may be responsible for the ocular findings in uveitis as the immune system responds to these organisms and the intraocular structures are damaged as a result. Another possibility is highlighted by findings of molecular mimicry between leptospiral surface antigens and uveal and posterior corneal antigens. This suggests that immunologic responses to certain leptospiral antigens may also result in responses directed against these cross-reacting intraocular antigens. Another possibility is that in horses subject to recurrent uveitis the uveal response may be exaggerated, or may be lacking in suppressor T cells. In such cases, local derangement in immunoregulation may be the determining factor in the development of equine recurrent uveitis.

Not all cases of acute uveitis result in recurrent episodes. Uveitis after trauma may not recur but it seems that, all too often, a previously inflamed eye can easily become the focus for further inflammation at a later date.

Clinical signs

Active uveitis may show signs of ocular pain, such as blepharospasm, photophobia, epiphora and depression. Decreased vision may or may not be evident. Ocular pain may necessitate sedation and/or palpebral nerve blocks to facilitate ophthalmic examination.

Ophthalmic findings cover a spectrum of clinical signs that vary with the severity of the inflammation. **Low grade uveitis** may show only **ocular hypotony** (decreased intraocular pressure) and **aqueous flare** (turbidity due to increased protein in the aqueous humor). Most cases of uveitis will show some degree of **conjunctival hyperemia**. Deeper ciliary vessels are often injected. **Miosis** (*q.v.*) is a fairly consistent clinical sign. In mild inflammation, where the **anisocoria** (unequal size of the pupils) may not be dramatic, the affected eye will usually show a resistance to dilatation by mydriatics. The iris may appear thickened and edematous. Inflammatory cell infiltrates may contribute to the aqueous flare and may lead to **hypopyon** formation (i.e. pus in the anterior chamber).

The cells may organize with fibrin to form keratic precipitates (adherent deposits on the corneal endothelial surface). **Hyphema** (blood in the anterior chamber) may also be present. Corneal edema (*q.v.*) is commonly present, and usually indicates decreased endothelial cell function due to inflammation. The edema may be generalized, or may begin peripherally and follow ingrowth of corneal neovascularization. Corneal vessels usually indicate chronicity, and may be a branching superficial pattern, or a deep ciliary "paintbrush" type.

Posterior uveitis may be manifested as **chorioretinitis**, often seen as cellular infiltration or edema adjacent to the optic nerve. The vitreous may appear cloudy due to inflammatory cells and proteins. Clumps of these cells may form vitreous "floaters". With chronicity, the vitreous may liquefy, and the movement of these floaters will become exaggerated. This liquefaction, combined with the organization of vitreal exudates into fibrous traction bands, may lead to **retinal detachment** (*q.v.*).

Other signs consistent with chronicity, or suggestive of recurrent episodes, include increased iris pigmentation, nodule formation within the iris, and synechia formation. **Posterior synechiae**, adhesions of the iris to the lens capsule, are most common, and may be seen as a distorted or immobile pupil, or as pigment deposits on the lens capsule. **Anterior synechiae** (adhesions of the iris to the cornea) are most commonly seen with perforating wounds and subsequent iris prolapses.

Other signs of chronicity or **equine recurrent uveitis** include cataracts (*q.v.*), which may be focal or generalized, lens luxation, and persistent corneal edema. Chorioretinal scarring may also be seen, and the typical "**butterfly**" **lesion** of depigmentation and atrophy medial and lateral to the optic disk may be considered a sign of equine recurrent uveitis. Having said that, it would be unwise to fail a horse at pre-purchase examination (*q.v.*) because these butterfly lesions were seen in a case where no other signs of uveitis were present. Recent research associating these lesions with equine herpesvirus infection underlines the possibility that they may occur without uveitic change. Generalized retinal atrophy may follow severe inflammation. Glaucoma can be a complication but generally **phthisis bulbi** (*q.v.*) is a more frequent result of chronic or severe inflammation.

A particularly severe form of uveitis, referred to as **keratouveitis**, is accompanied by a non-ulcerated keratitis, usually characterized by a fleshy corneal infiltrate and marked corneal neovascularization.

Diagnosis

Although a morphologic diagnosis of uveitis may be easy to make based on clinical signs, it is often difficult to ascertain the etiology. **Fluorescein** should be applied to the cornea to rule out ulceration. Systemic involvement should be evaluated by a general physical examination, CBC and serum chemistry panel. Tests for specific etiologic factors, such as conjunctival biopsies for onchocerciasis and serology for viral or bacterial agents, must be interpreted with care, as many normal horses may have *Onchocerca* (*q.v.*), or positive serology titers. Especially in recurrent cases, the episode of uveitis may occur long after the initial infection and an elevated serum antibody titer may not be seen. Extremely high or rising paired sera antibody titers may be supportive of a diagnosis. Comparison of affected horses with normal stablemates may

be useful. Elevated aqueous antibody titers are diagnostic, although collection of the aqueous sample will exacerbate the uveitis.

Treatment

Many cases of uveitis will not have a cause determined and therefore are treated symptomatically. Uveitis should be treated with **anti-inflammatory agents** and **mydriatics/cycloplegics** for symptomatic therapy. In cases where a specific etiology is identified or suspected, specific therapy should be instituted. However, in onchocerciasis, anthelmintic therapy may **exacerbate the inflammatory response** if anti-inflammatory therapy is not adequate.

Initial therapy should be aggressive, and reduced as clinical signs subside. **In the absence of corneal ulcers, topical corticosteroids** are extremely useful. Prednisolone acetate 1% or dexamethasone 0.1% are the drugs of choice, and should be given every 1–6 h, depending on the severity of the uveitis. Frequent therapy may be facilitated by a subpalpebral or nasolacrimal lavage system, which may be used with or without a perfusion pump. **Subconjunctival corticosteroids** are useful to supplement topical therapy if frequent applications are not possible. Methylprednisolone acetate (10–40 mg), triamcinolone acetonide (10–40 mg) or betamethasone (3–5 mg) can be used. Injection volumes should not exceed 1 mL, and may be repeated q 1–4 wk as required.

Systemic corticosteroids may also be beneficial. Dexamethasone may be used at doses up to 20 mg/500 kg PO b.i.d., but prednisone used at 0.8–1.5 mg/kg may be as efficacious, with less risk of corticosteroid-induced side effects. NSAIDs are also very useful. Flunixin meglumine (1 mg/kg IV, IM, PO) or phenylbutazone (3–6 mg/kg IV or PO b.i.d.) is useful in active uveitis. Aspirin (30 mg/kg PO s.i.d.) may be useful in reducing episodes of equine recurrent uveitis. Topical NSAIDs are also available. Suprofen 1% and flurbiprofen 0.03% are potent anti-inflammatory agents and can be used concurrently with topical corticosteroids to achieve an additive effect. Their use in corneal ulceration is controversial.

Atropine is the mydriatic/cycloplegic of choice. Topical or subconjunctival therapy should be aggressive until mydriasis is achieved, at which time it should be reduced to a maintenance level. Mydriasis may persist for several weeks after discontinuing therapy. **Intestinal motility** should be closely monitored if higher dosages are used, as systemic effects have been reported. Although not a useful mydriatic in the normal eye, topical phenylephrine may augment the mydriasis in eyes refractory to dilation.

Any case of uveitis is **potentially blinding**. In cases of equine recurrent uveitis, the prognosis is generally poor, due to the chronic, recurrent nature of the disorder. Cases of acute uveitis may have a fair to good prognosis depending on the cause and severity of the uveitis. Keratouveitis (*q.v.*) generally has a poor prognosis.

Intravitreal implants containing **ciclosporin** in a slow-release formulation have been reported to be efficacious in down-regulating the inflammatory effects of recurrent uveitis but clearly such medication has to be repeated and can only be considered as a control measure and not a cure.

Surgical vitrectomy, on the other hand, has recently been reported to be a useful therapeutic option with long-term resolution of episodic recurrence. Other workers have not had particular success with the technique, but this

difference may be explained by the fact that the German ophthalmologists, who first reported success with the technique, designed and constructed a specific lengthened probe for both mechanical vitrectomy and cataract phacoemulsification. Attempting vitrectomy with a probe designed for the human or small companion eye is doomed to failure since complete removal of all vitreous humor is not possible using equipment designed for smaller eyes. The exact mechanism by which vitrectomy prevents recurrence of intraocular inflammation is still somewhat unclear: it may be that sequestered leptospiral antigen is thus removed, or that the inflammatory "soup" of cytokines and resident immune competent cells in the vitreous is removed.

Hyphema

Anterior chamber hemorrhage may be associated with blunt or penetrating trauma, chronic uveitis with iridal neovascularization, neoplasia or bleeding disorders (*q.v.*). Non-specific treatment includes stall rest and symptomatic uveitis therapy (*q.v.*). Non-clotted blood will clear from the anterior chamber within a few days. Clotted blood may take a few weeks to resorb. Surgical intervention is not indicated in non-clotting hyphema, and only in clotted hyphema if complications such as glaucoma (*q.v.*) are occurring. Tissue plasminogen activator or urokinase may be used to lyse the clot. Prognosis for hyphema in the absence of severe ocular disease is generally good. The presence of persistent hyphema may be a poor prognostic sign in trauma cases.

GLAUCOMA

INTRODUCTION

Glaucoma is an ocular condition characterized by an elevation in intraocular pressure (IOP) that is associated with **optic nerve damage** and eventual **blindness**. The elevation in IOP in most cases is thought to be due to an inability of the aqueous humor to exit the globe. Glaucoma in the horse is considered by some to be rare, but the initial clinical signs are so subtle that the actual incidence of this disease is not known. Equine glaucoma is an **insidious**, **progressive disease** that produces significant optic nerve damage without overt clinical signs until late in the disease.

ANATOMY AND PHYSIOLOGY OF AQUEOUS HUMOR PRODUCTION AND DRAINAGE

Aqueous humor is produced in the ciliary epithelium by energy dependent and independent mechanisms. The carbonic anhydrase and Na^+K^+ ATPase enzymes are involved in aqueous production. Aqueous humor passes into the posterior chamber, through the pupil into the anterior chamber, and then exits through the iridocorneal angle (conventional pathway), or through secondary (unconventional) outflow pathways, such as the iris vasculature or supraciliary space. Obstruction at the pupil, iris face, iridocorneal angle or any other part of the outflow pathway can result in an increase in IOP. One theory concerning the

apparent low incidence of glaucoma in the horse is that, in spite of the extensive anterior segment alterations that occur in equine recurrent uveitis (*q.v.*), the unconventional outflow pathways are quite extensive and allow for substantial aqueous drainage despite damage to the conventional pathways.

ETIOLOGY AND DIAGNOSIS

Primary glaucoma, a result of biochemical alterations in the iridocorneal angle, has not been definitively diagnosed in the horse. Glaucoma secondary to obstruction of outflow pathways with vascular membranes, inflammatory cells and debris, or tumor cells is more commonly reported.

Horses with **early glaucoma** present with more subtle clinical signs than horses with advanced disease. Early glaucoma has been diagnosed in Quarter Horses, Thoroughbreds, Arabians, Warmbloods, Appaloosas, Tennessee Walking Horses and Welsh ponies. The most commonly reported early signs are generalized corneal edema, deep linear corneal band opacities, and a fixed, dilated pupil. The affected eye is rarely painful or blind. Topically administered corticosteroids can cause the edema to resolve, suggesting an inflammatory component to equine glaucoma, but the IOP remains elevated. The corneal band opacities are found in horses without glaucoma, thus their relationship to the glaucoma is confusing.

Advanced cases of equine glaucoma may have extensive corneal edema, buphthalmos, blepharospasm, and exhibit signs of blindness due to optic nerve damage (*q.v.*).

The normal IOP of the horse ranges from 16 to 32 mmHg with an average of 24 mmHg. **Electronic applanation tonometers** are the most reliable means of determining the IOP in the horse, although digital tonometry can provide rudimentary IOP levels. Auriculopalpebral nerve blocks should be done prior to tonometry to prevent artificially high readings due to pressure on the eyelids during tonometry.

TREATMENT

Therapy is directed at lowering IOP to maintain vision for as long as possible by decreasing aqueous humor production, increasing aqueous humor outflow, and suppressing any inflammation associated with the glaucoma. Medical therapy in cases of early glaucoma in the horse is difficult to manage, and particularly frustrating in the **Appaloosa** breed, which has a particularly aggressive form of glaucoma.

Outflow can be increased with topically administered **parasympathomimetics**, such as 0.03% echothiophate iodide (b.i.d.), or 0.25% demecarium bromide (b.i.d.). These drugs can exacerbate iridocyclitis (*q.v.*) and should be used with caution if inflammation is present. Aqueous humor production can be lowered with 0.5% timolol maleate. Topical 0.03% sodium flurbiprofen and corticosteroids and systemically administered NSAIDs are also beneficial. Topical carbonic anhydrase inhibitors and prostaglandins will be available in the near future for cases of equine glaucoma.

Atropine may be useful in glaucoma in the horse. This is somewhat ironic, given that in all other species the drug is contraindicated in glaucoma.

As noted above, the horse appears to have an unusually high proportion of aqueous outflow through the unconventional outflow pathway—through choroidal spaces rather than the iridocorneal angle—and this outflow is increased by pupillary dilation. Given the secondary nature of most equine glaucoma with iridocorneal angle blockage through inflammatory debris or peripheral anterior synechiae (*q.v.*) closing the angle, increasing this unconventional outflow is a valuable treatment option, although IOP should be monitored during treatment to ensure that atropinization does not increase it.

Surgical therapy may be necessary to control the IOP in refractory cases. Damage to the ciliary body caused by nitrous oxide (cyclocryotherapy) or laser energy (cyclophotocoagulation) is necessary to reduce the aqueous production and lower the IOP in some cases. This may be the therapy of choice in early cases of equine glaucoma. Filtration gonioimplant surgeries to increase outflow of aqueous humor are experimental in the horse. Chronically painful, blind buphthalmic eyes, or eyes in which the glaucoma is caused by an intraocular tumor, should be enucleated or eviscerated with placement of an intraocular silicone prosthesis. In some cases injection of intravitreal gentamicin may be considered but this pharmacoablation of the ciliary body can result in substantial intraocular inflammation and thus is not recommended in most horses.

THE LENS

ANATOMY

The lens is a spheroidal, transparent, refractive structure suspended from the ciliary body behind the iris by zonular ligaments. The zonule inserts into the equatorial region of the lens capsule, which surrounds the entire lens. The inner surface of the anterior part of the lens capsule is lined by a single layer of lens epithelium. The lens substance comprises lens fibers laid down in concentric layers like the layers of an onion. The fibers are formed by elongation of lens epithelial cells at the lens equator. New fibers are continually formed around the periphery of the lens throughout life, compressing older fibers in toward the center of the lens. The outer area of lens is the cortex, the inner and older region the lens nucleus. The lens undergoes minimal change in refractive power during accommodation in the horse.

CONGENITAL ANOMALIES

Congenital abnormalities of the lens in the horse are rare with the exception of cataract. **Microphakia** refers to a congenitally small lens, which may be seen in association with other developmental abnormalities of the eye. **Coloboma**, or an absence of part of the lens and associated zonule, may also infrequently occur.

CATARACT

Cataracts, or opacities in the lens, are the most common abnormality of the lens. They may be found in foals at birth or be acquired at any age throughout life. **Congenital cataracts** are the most common congenital ocular anomaly in

the horse. They are often bilateral and can be associated with other abnormalities, including microphthalmia and aniridia (*q.v.*).

The cause of cataracts in the horse is rarely determined but the most likely etiologies include heredity, trauma or uveitis. **Focal cataracts** may be seen at the tips of the lens sutures in a Y-shaped configuration, or at the posterior capsule on the central lens axis associated with persistent hyaloid artery in the vitreous. Congenital cataracts may involve only the lens nucleus or be mature and total opacities of the whole lens. **Acquired cataracts**, such as those caused by trauma or uveitis (*q.v.*), may involve any focal area of the nucleus or cortex, and may progress to become total mature cataracts.

Congenital nuclear cataracts rarely progress to become total cataracts after birth. The progression of acquired cataracts in older horses cannot be predicted with any certainty. The discovery of a focal cataract in a previously normal lens is reason for concern about probable progression and deterioration of vision.

Clinically, cataracts can be diagnosed after applying a **topical mydriatic** to the eye. Tropicamide (Mydriacyl, Alcon) 1% applied to the conjunctiva will dilate the pupil in 20 min and enable examination of the lens with either a focal oblique light source or slit beam. The location of most cataracts can easily be determined in this way. Cataracts secondary to trauma or uveitis will have other signs of ocular inflammation—conjunctival injection, corneal edema, aqueous flare, fibrin or hyphema, and in chronic or quiescent cases pigment on the anterior lens capsule or posterior synechiae between the iris and lens (*q.v.*).

The extent of **visual impairment** is proportional to the volume of the lens that is cataractous, and, to some extent, the location of the cataract within the lens. Focal cataracts involving a small area of the lens, suture line cataracts or hyaloid-associated cataracts do not impair vision to a significant extent and require no treatment. Horses affected with cataract may only begin to show visual impairment when large areas of the lens are affected. Horses with congenital nuclear cataracts may have severe visual deficits, especially when the pupil is constricted in bright light. Total mature cataracts cause blindness in the affected eye.

Nuclear cataracts with a peripheral ring of clear cortex impair vision with a small pupil. Application of topical 1% atropine to the affected eye q 72–96 h will maintain mydriasis and often enable useful vision around the edges of the cataract. At present there is no effective medical therapy that will cause regression of cataracts.

The only effective therapy for total mature cataracts is **surgical removal**. Selection of suitable cases is extremely important in improving the chance of a successful surgical outcome. Inherited, congenital or acquired cataracts are the best surgical candidates. Cataracts secondary to previous ocular trauma may be surgical candidates provided there is no evidence of active ocular inflammation prior to surgery. Horses with cataracts secondary to equine recurrent uveitis (*q.v.*) are not candidates for cataract surgery and can be guaranteed to have severe problems after surgery unless vitrectomy is performed as detailed above.

In horses <6 mo of age the cataract can be removed by discission and aspiration of the lens cortex and nucleus after removing the anterior lens capsule. In older horses, the technique of choice for cataract removal is extracapsular with removal of a portion of the anterior lens capsule followed by **phacofragmentation** (the use of ultrasound energy) and aspiration of the cataract. The equipment required for phacofragmentation is available to

many veterinary ophthalmologists, although **special phacofragmentor needles** are needed to cope with the size of the equine eye. This technique uses a small incision at the limbus, which is less traumatic than opening the eye through 180°. Coupled with the use of both systemic and topical NSAIDs and topical corticosteroids, cycloplegics and mydriatics, this technique has improved the success rate for cataract removal in horses. Even with this technique, the proportion of animals with long-term maintenance of vision is significantly lower than with the same technique in dogs. The effects of cataract surgery on vision in the horse are unknown, although owners should be warned that caution is needed if the horse is used for activities such as jumping which involve reasonable visual function.

Complications of cataract extraction in the horse include corneal ulceration, severe chronic uveitis and retinal detachment (*q.v.*). Glaucoma does not appear to be a common complication in this species.

LENS LUXATION

Lens luxation occurs congenitally associated with other ocular anomalies, or secondary to equine recurrent uveitis (*q.v.*) or ocular trauma. Luxations due to equine recurrent uveitis occur after chronic recurrent bouts of disease, and signs of chronic uveitis are always evident. Traumatic luxations require considerable force to break the zonule and dislocate the lens. Other signs of severe ocular damage will also be present. The lens may be luxated anteriorly into the anterior chamber or posteriorly into the vitreous. Anterior lens luxations may be referred to a veterinary ophthalmologist for removal by an intracapsular approach with reasonable results. A posteriorly luxated lens is more difficult to remove surgically and may as well be left in situ.

THE POSTERIOR SEGMENT

ANATOMY

The posterior segment consists of three layers, the retina being innermost, the middle choroid that includes the tapetum fibrosum, and the sclera providing the outer protective coat. The ocular fundus, that portion of the posterior segment that can be viewed by ophthalmoscopy, consists of tapetal fundus, non-tapetal fundus, retinal blood vessels and the optic disk or papilla. The retina consists of the neurosensory retina (the inner 9 layers) and the outer single layer of retinal pigment epithelium (RPE). The photoreceptors within the neurosensory retina are predominantly rods with a ratio of 1 cone to 20 rods.

The horse retina has two areas of increased cone density and visual perception: the "area centralis" for forward binocular vision and the "visual streak" for monocular lateral vision that are 15 mm and 8 mm dorsolateral of the optic disk, respectively.

With large, laterally positioned globes, large oval corneas, horizontal pupils, and a large lens with limited or no accommodation, the horse eye has evolved to provide primarily panoramic views. The horse is thought to see green and yellow colors, but has poor vision for red.

VARIATIONS OF THE NORMAL FUNDUS

Tapetal fundus

The **tapetum fibrosum layer**, consisting of organized lamellae of collagen fibers with their long axes parallel to the retina, can be observed by ophthalmoscopy through the transparent neurosensory retina and RPE. The tapetal fundus is an irregular triangular area in the upper two thirds of the ocular fundus. Its horizontal base is immediately above the optic disk or papilla. Distributed evenly throughout the tapetal fundus are minute black spots ("**stars of Winslow**") that mark the penetration of individual choriocapillaries through the tapetum fibrosum.

The tapetal fundus color ranges from yellow-green to green-blue. **Partial albinism** of the tapetal fundus occurs occasionally in gray, palomino, light chestnut and Appaloosa horses and frequently with partial iridial heterochromia (*q.v.*). Partial albinism may be demonstrated in the tapetal fundus as yellow areas with red "stars of Winslow". In some light gray horses the tapetum is hypoplastic or sometimes completely absent, and is often combined with incomplete pigmentation of the non-tapetal fundus permitting direct observation of the underlying choroidal vasculature. Multiple foci of fairly uniform pigmentation occur occasionally in the tapetal fundus and converging lines of pigmentation signal the origin of the vortex venous drainage system.

Non-tapetal fundus

The non-tapetal area occupies the ventral fundus and completely surrounds the tapetal fundus. The normal dark brown-black non-tapetal fundus results from the densely pigmented RPE. At the junction of the tapetal and non-tapetal fundi, the transition of pigmentation of the RPE is often irregular. In the non-tapetal fundus immediately above the optic disk, pigmentation is often limited and irregular, permitting direct visualization of the deeper choroidal vasculature and occasionally the sclera. In lightly pigmented horses with palomino, gray and white haircoats and in the Appaloosa breed, the non-tapetal fundus may have limited pigmentation permitting direct observation of the deeper choroidal vessels against the white scleral background. The periphery of the retina may be seen on ophthalmoscopy at its junction with the ciliary body (the **ora serrata**).

Retinal vasculature

The equine ocular fundus has a **paurangiotic retinal vasculature** pattern consisting of approximately 40–60 small blood vessels that branch dichotomously and extend from the optic disk for only 2–3 disk diameters. Because of the small diameters of these blood vessels, the arteries cannot be distinguished from the veins ophthalmoscopically, but can be separated by high-speed fluorescein angiography. The arteries, which are branches from the short ciliary arteries, are confined to the inner retinal layers and provide the blood supply to only the immediate peripapillary retina and the optic disk. Hence, the majority of the neurosensory retina must exchange its metabolites and oxygen across the RPE from the deeper choroidal vasculature.

Optic disk/papilla

The round to oval optic disk or papilla is situated within the non-tapetal fundus just below the tapetal junction. Its color ranges from red to pale orange to a pale pink. Its surface is irregular, containing limited numbers of small tortuous blood vessels. The edges are usually easily distinguished from the surrounding non-tapetal fundus and occasionally a ventral notch is present. Sometimes, a white scleral rim is seen, usually at the dorsal edge of the optic disk, arising from a lack of the RPE and choroidal vessels. This rim is traversed by the normal peripapillary vasculature. The peripapillary retina may appear thicker and slightly translucent because of its increased thickness. Infrequently medullated nerve fibers emerge with the ventral peripapillary retinal blood vessels, appearing as white to gray irregular tufts or streaks, and must be differentiated from retinal edema and peripapillary chorioretinitis (*q.v.*). The optic nerve exits the eye through a collagenous meshwork in the sclera, the lamina cribrosa.

EXAMINATION OF THE OCULAR FUNDUS

Abnormalities of the equine ocular fundus occur in approximately 10% of the general horse population. The equine ocular fundus is examined most often by direct and indirect ophthalmoscopy; other procedures that can be employed include fluorescein angiography, A- and B-scan ultrasonography, electroretinography, and slit lamp biomicroscopy. The ocular fundus is best examined in a darkened room, with the pupils dilated with 1% tropicamide, and the horse restrained gently but firmly.

DISEASES OF THE RETINA AND CHOROID

Congenital anomalies

Congenital diseases of the ocular fundus include typical and atypical **colobomas** (defects in or absence of tissue due to improper development), and **night blindness** in the Appaloosa. Large typical colobomas involving the optic disk and non-tapetal fundus (at the 6 o'clock position) are associated with failure of the fetal fissure to close, and have been reported in the horse in association with uveal, retinal and lens defects, and blindness. These colobomas contain foci of hyperplastic and dysplastic retina.

Atypical colobomas, affecting the retinal pigment epithelium, affect the ocular fundus in areas other than the 6 o'clock position. They occur infrequently in the non-tapetal fundus and appear as single or multiple foci of reduced pigmentation with sharply defined borders, often in the peripapillary region. Similar RPE defects occur rarely in the tapetal fundus and appear as single to multiple areas of **intense pigmentation**. Vision in affected horses appears unimpaired. There is no treatment.

Congenital night blindness in the **Appaloosa** horse is characterized by visual impairment in reduced illumination as early as 1 mo of age. Day vision is infrequently impaired. Affected animals are unwilling to enter unfamiliar environments with reduced illumination and often injure themselves. The ocular fundi are normal by ophthalmoscopy but electroretinography can

confirm the disease. Breeding of affected animals or their parents is not recommended as the condition may be inherited as a recessive trait.

Inflammatory disorders

Inflammation of the ocular fundus may involve the retina, the choroid and/or the optic disk. The inflammatory process may originate from the optic nerve, the peripapillary retinal and choroidal blood vessels or extend posteriorly from inflammation in the anterior uvea and vitreous. The retina, as modified neural tissue, often shares diseases common to the CNS; the posterior uvea or choroid may be affected with infections of hematogenous origin. Inflammations of the retina and/or choroid have been reported with **equine recurrent uveitis**, various septicemias and bacteremias, toxoplasmosis, Borna disease, trypanosomiasis and onchocerciasis (*q.v.*).

Equine recurrent uveitis (*q.v.*) may have multiple etiologies that include *Leptospira* spp., and is characterized as multiple recurrent bouts of anterior and posterior uveitis. While the anterior segment abnormalities often prevent detailed inspection of the ocular fundus, fundic lesions may appear in as many as 25% of horses affected with equine recurrent uveitis. Often the "butterfly" peripapillary chorioretinitis or chorioretinopathy is associated with the anterior segment inflammation. Confusion occurs when only unilateral or bilateral "butterfly" peripapillary lesions are present. While peripapillary chorioretinitis or chorioretinopathy has been associated with the equine recurrent uveitis complex, it may also occur as a distinct disease. An assessment of *Leptospira* titers (*L. pomona, L. icterohaemorrhagica, L. hardjo* and *L. autumnalis*) in horses with peripapillary lesions revealed that the majority of horses with increasing titers to *L. autumnalis* developed peripapillary chorioretinopathy within 6–12 mo. The peripapillary lesions have also been produced in ponies inoculated experimentally with *L. pomona*. Similar lesions have been produced by experimental intranasal inoculation with equine herpesvirus type 1 (*q.v.*), and thus peripapillary lesions may be related to herpetic infection and not equine recurrent uveitis.

Active chorioretinitis in the tapetal and non-tapetal fundi appears funduscopically as slightly raised grayish foci with indistinct edges. Inactive chorioretinitis or chorioretinopathy appears as foci of either reduced or increased pigmentation and in the tapetal fundus areas as either increased or reduced tapetal reflectivity. In the peripapillary region, the retinal vessels in the active phase of inflammation may appear more prominent and raised; in the inactive phase there may be a paucity of vessels. Unless considerable ocular fundus is involved or the optic nerve is affected, visual impairment is not usually demonstrable. Horses with **peripapillary chorioretinopathy** in the absence of anterior segment disease should be carefully monitored for significant changes to the optic disk. Treatment with systemic antibiotics and/or corticosteroids has not demonstrated efficacy for this condition.

Trauma and retinal detachments

Trauma to the head and/or eye is most apt to affect the anterior segment causing anterior uveitis, hyphema and corneal abnormalities. Trauma in foals may

result in **complete retinal detachments**, often complicated by disinsertion at the ora serrata. The condition is usually unilateral and affected foals are usually presented with visual impairment limited to the affected side. The retinal detachment is visible by ophthalmoscopy and appears as a gray translucent membrane extending from the optic disk into the ventral vitreous. Occasionally vitreous hemorrhage is also present. Treatment is not successful.

Neoplasms

Intraocular neoplasms (*q.v.*) affecting the ocular fundus usually originate from the anterior uvea or posteriorly from the optic nerve. Both **malignant melanomas** of the anterior uvea and optic nerve **medulloepitheliomas** occur but are rare in the horse. Both present as space-occupying masses and are usually detected by slit lamp biomicroscopy, ophthalmoscopy and ultrasonography. These conditions are treated by enucleation and exenteration, respectively.

Miscellaneous retinopathies

Funduscopic changes of generalized retinal degeneration (pigmentary retinopathy) occur in the horse and signal complete blindness. Scattered throughout the tapetal fundus are dark irregular pigmented foci; despite several reported cases, microscopic examination of the affected eyes has not been reported. **Glaucoma** (*q.v.*) in the horse is being recognized more frequently with the routine **use of applanation tonometry**. Increased intraocular pressure causes degeneration of the retinal ganglion cells, and cupping and atrophy in the optic disk. **Retinal detachments** in horses are also associated with ocular congenital anomalies and fundic inflammation; reattachment of the detached retina secondary to inflammation may follow successful resolution of the initial condition. Small subretinal and/or choroidal hemorrhages in the tapetal fundus are not uncommon in equine neonates and usually resolve quickly without treatment. These hemorrhages may signal trauma or transient hypoxia during parturition.

DISEASES OF THE OPTIC DISK AND NERVE

Several conditions can affect the optic disk and nerve of the horse. Unilateral optic nerve disease may be revealed as slight mydriasis (dilation of the pupil), monocular visual impairment or blindness, occasional stumbling (primarily on turning), and reduced or absent light-induced pupillary light reflexes. Since 80% of the optic nerve fibers in the horse decussate, the indirect or consensual light pupillary reflex occurs but is usually slower and less complete. When both optic nerves are affected, marked visual impairment or blindness is usually present.

Congenital anomalies

Congenitally blind foals may present with bilateral optic nerve hypoplasia, with or without colobomas and other ocular anomalies (*q.v.*). In either case, the optic nerve can be significantly hypoplastic. Funduscopically the **hypoplastic**

optic disk appears white, reduced in size, and depressed below the surrounding retina. Few or no retinal vessels are present. When **colobomas** (*q.v.*) are present, both the optic disk and ventral non-tapetal fundus may be involved; within these excavations the underlying sclera is visible and pigmented membranes of hyperplastic and dysplastic retina extend forward into the vitreous.

Inflammatory disorders

Inflammation of the optic disk and nerve in the horse has been associated with many diseases including equine recurrent uveitis, systemic leptospirosis, *Onchocerca cervicalis* and toxoplasmosis (*q.v.*). A specific **exudative optic neuritis** occurs in horses in Europe, often with a history of trauma, hemorrhage or colic, and often sudden blindness. Both optic disks may be affected; the disk appears raised with indistinct margins and frequently has hemorrhages on its surface. **Optic atrophy** may occur several months later. The cause or causes for exudative optic neuritis have not been established. Treatment with systemic antibiotics and/or corticosteroids appears ineffective.

Trauma

Optic nerve inflammation and subsequent atrophy may follow skull trauma, usually associated with injury to the head by rearing and hitting overhead objects. Even without obvious orbital and skull fractures and any changes to the optic disk, avulsion and pressure on the optic nerve within the optic nerve canal and the optic chiasm should be suspected. **Orbital hemorrhage and/or edema** may also compress the long optic nerve. The disease is often unilateral. Loss of vision, the direct light-induced pupillary reflex and menace response occurs, as does mydriasis. Early funduscopic findings may include a normal disk or hyperemic disk with peripapillary hemorrhages or edema. Several weeks later, **optic atrophy** can occur with a depressed white optic disk and loss of the peripapillary blood vessels. Other neurologic signs (*q.v.*) such as focal muscle atrophy, proprioceptive deficits and lameness may eventually become apparent. The prognosis for this condition should always be guarded. Treatment with high doses of systemic corticosteroids (10–20 mg dexamethasone daily) and phenylbutazone (1–2 g daily) immediately after the injury may be effective in some cases. Affected optic nerves and even the optic chiasm examined at necropsy may demonstrate focal swelling and constrictions that microscopically are foci of cavitation (liquefactive necrosis), fibrovascular bands, and astrocytic gliosis characteristic of axonal swelling and myelin degeneration.

Ischemic optic neuropathy

Ischemic optic neuropathy occurs in the horse associated with **vessel ligature** of the large arteries (internal and external carotid arteries and palatine artery) for **guttural pouch disease** and the prevention of recurrent hemorrhage. The equine fundus, except for the immediate peripapillary region, is dependent on the underlying choroidal vessels and may be predisposed to hypoxia. The choroidal vessels receive their primary blood supply from the 4–6 short posterior ciliary

arteries that are branches of the external ophthalmic artery. The two long posterior ciliary arteries may also provide some branches laterally and medially to the choroid. In approximately 50% of affected horses the exterior and internal ophthalmic arteries exchange anastomotic branches. Unilateral visual impairment to blindness and mydriasis (*q.v.*) are the usual presenting signs occurring soon after the surgery. Funduscopically the optic disk appears swollen, hyperemic and contains several raised white myelin-like excrescences that extend into the adjacent retina and vitreous. The edema from the optic nerve ischemia may acutely extrude the myelin and ruptured nerve fibers into the peripapillary retina and vitreous. **Unilateral blindness** results from this condition.

Post-hemorrhagic neuropathy

Optic disk and nerve atrophy and retinochoroidopathy occur in the horse following profound hemorrhage postoperatively or occasionally after injury. In many species the retina, optic nerves, and the brain vasculature possess autoregulation. The choroidal vessels have high flow rates, no autoregulation, and are highly permeable, permitting the exchange of metabolites to the neurosensory retina and RPE. With the highest metabolic rate and limited storage of oxygen and glycogen, the equine retina may be **very susceptible to ischemia**.

Clinically the condition most often follows **castration** complicated with extensive postoperative hemorrhage. The horse may become recumbent, and visual impairment or blindness is noted several days post hemorrhage. **Bilateral mydriasis** (*q.v.*) is usually present, with negative light pupillary and menace reflexes. Ophthalmic findings are limited to the ocular fundus and optic disk, and may not be apparent until several weeks to a few months after the initiating event. The blindness appears directly related to the **optic nerve atrophy**; the optic disks appear depressed and white, with absence of the peripapillary vasculature. Numerous tapetal and non-tapetal lesions are concentrated at the posterior pole and consist of clumps of intense pigmentation and reduced pigmentation that mimic the distribution of the underlying choroidal vessels. Focal raised yellow-white exudates may appear on the disk's surface and edge. Microscopic examinations of affected eyes reveal focal full thickness retinal destruction with RPE hyperplasia and migration into the remaining retina. There is also generalized degeneration and loss of the retinal ganglion cells. The optic disk and generalized optic nerve atrophy are characterized by the widespread loss of myelin and axons, and the replacement by gliosis. Treatment with high doses of systemic dexamethasone has been unsuccessful.

Neoplasia

Primary and secondary neoplasms of the optic nerve are very rare in the horse. Medulloepitheliomas have been reported, which presented as space-occupying orbital masses. Benign gliomas, astrocytomas and schwannomas may also occur in the optic nerve head but have not been associated with visual compromise.

Proliferative optic neuropathy

Proliferative optic neuropathy occurs in older and aged horses, usually as a **unilateral** condition **without visual impairment**. It is usually detected during routine ophthalmic examinations. Funduscopically, proliferative optic neuropathy appears as a small single nodule or, rarely, multiple nodules on the edge or surface of the optic disk extending into the vitreous and usually the same color as the adjacent disk. The ocular fundus and peripapillary retinal and optic disk vasculature are usually normal. Microscopically, proliferative optic neuropathy has been classified as astrocytoma, granular (Schwann) cell tumor, and xanthoma. Treatment of the condition has not been attempted.

Miscellaneous

Cupping and excavation of the optic disk occur with glaucoma (*q.v.*). Funduscopically, the optic disk is markedly depressed and gray to white; its surface may be smooth with baring of the lamina cribrosa and loss of the peripapillary blood vessels.

NEOPLASIA OF THE EYE AND ADNEXA

INTRODUCTION

When presented with a horse possessing an ocular and/or periocular mass, signalment, haircoat and skin coloration, husbandry practices, geographic location, rate and location of lesion development, and previous treatment may help in the logical differential diagnosis. Squamous cell carcinoma (SCC), sarcoid, papilloma, melanoma and nerve sheath tumors, in descending order of prevalence, are the most common neoplasms of the equine eye and adnexa. Squamous cell carcinoma, sarcoid, papilloma and melanoma also commonly affect other anatomic regions of the horse; thus, a **complete physical examination** should always be performed in conjunction with the ophthalmologic examination.

If the horse is fractious or in pain, some form of chemical restraint may be required such that a thorough clinical examination and adequate sample collection can be safely obtained in an efficient manner. In addition to systemically administered analgesics and sedatives, topical anesthesia and auriculopalpebral and/or local eyelid nerve blocks may be necessary.

Routine blood tests and conventional skull or thoracic radiography may be indicated if local invasion of the orbit or metastasis is suspected. Special imaging techniques that may yield additional information, especially regarding intraocular or orbital disease, include B-scan, dimensional ultrasonography, dacryocystorhinography and computed tomography.

Biopsy and **histopathologic examination** are required for definitive diagnosis and selection of an appropriate mode of treatment. Excisional biopsy is usually performed on a mass that is readily accessible, localized and relatively small. In contrast, an incisional (wedge) biopsy is generally obtained when a lesion's location impedes easy access (e.g. the orbit) and when lesions are invasive, multiple or large. Fine needle aspiration biopsy (*q.v.*) can be useful as a first step before a more invasive technique is used.

SQUAMOUS CELL CARCINOMA

Squamous cell carcinoma (SCC) is the most common tumor of the eye and its adnexa in horses. The globe, adnexa and/or orbit can be affected; however, the nictitating membrane, nasal canthus, limbus and eyelid are most frequently involved. The cause is not known but **non-pigmented adnexa** and exposure to **intense solar radiation** are associated with an increased prevalence. In addition, an increase in age, the breed (draft horses, Appaloosas, American Paints and Pintos), and gender (geldings more than stallions and mares) appear to be associated with a greater likelihood of SCC development. Ocular SCCs usually slowly enlarge, are locally aggressive and rarely metastasize. If metastasis does occur, the regional lymph nodes and salivary glands are generally affected.

Clinical signs and diagnosis

The gross appearance of SCC is dependent upon its anatomic location and stage of development. Early neoplastic change may cause a localized, low grade inflammatory response. A hyperplastic plaque or papilloma-like growth may subsequently develop, undergo further metaplastic change and become an SCC, which can be circumscribed if discovered early in its development. If unhindered growth takes place, the tumor may become invasive, irregular and necrotic in appearance. Histologic confirmation of presumptive ocular/adnexal SCC should always be obtained since its clinical appearance can resemble sarcoid, papilloma, cutaneous habronemiasis, foreign body granuloma, *Onchocerca*-induced keratoconjunctivitis and other less common neoplastic or inflammatory processes (*q.v.*).

Treatment

Treatment of SCC is dependent upon tumor size and anatomic location, the presence or absence of distant metastases, the clinician's expertise, availability of equipment, and the owner's financial limitations. **Routine tetanus prophylaxis** (*q.v.*) should be administered before any invasive procedure.

SCC of the eyelid may be completely removed by **excision** alone. However, if the mass is large, surgical reduction and adjunctive **cryotherapy**, **brachytherapy** or localized hyperthermia are recommended. Cryotherapy is a rapid, inexpensive and repeatable procedure. Two or three rapid freeze (to a tissue temperature of −20 to −25°C) and slow thaw cycles should be performed. A 5–10 mm zone of normal tissue beyond the grossly evident tumor should also be frozen. When eyelids are frozen, depigmentation of the skin is usually transient, whereas whitening of the hair is permanent. Although liquid nitrogen is a stronger cryogen, the use of nitrous oxide may provide better control of freezing cycles when dealing with the relatively delicate ocular adnexa. Excessive cryotherapy of the eyelid can cause marked contracture and subsequent distortion of the eyelid aperture.

Brachytherapy with iridium wires or strontium-90 beta irradiation may be applicable with the former implanted in deeper lesions while the latter can be used after debulking of a more superficial neoplasm.

Localized hyperthermia (50°C for 30 s) is effective when used to treat ocular/adnexal SCCs that are superficial and have a small tumor volume. In contrast, interstitial radiotherapy (e.g. caesium-137 and cobalt-60) has been

successful in the treatment of large, non-resectable eyelid tumors, but the impractical logistics (expense, necessary expertise and potential danger) of this treatment modality limit its availability.

Treatment modalities available for SCC involving the **nictitating membrane** include partial or complete nictitating membrane resection and surgical cytoreduction with adjunctive cryotherapy. Strontium-90 beta irradiation (approximately 90–120 Gray [100 rads]) and carbon dioxide laser ablation may also yield excellent results, but these modalities are not readily available.

Limbal SCC can be effectively treated by superficial keratectomy/conjunctivectomy alone or in combination with localized hyperthermia. Despite the potential for persistent corneal scarring and conjunctival depigmentation, localized hyperthermia is an inexpensive, rational therapeutic modality. **Strontium-90 beta irradiation** and **carbon dioxide laser ablation** are also effective in the treatment of limbal SCC, but expense limits availability.

SCC that goes unnoticed, or recurs despite treatment, may eventually affect the orbit. Orbital SCC should be aggressively treated by **exenteration**. Adjunctive cryotherapy of suspicious, non-resectable orbital tissues has been used in selected cases with success.

Prognosis

Because of slow tumor growth and rare metastasis, ocular/adnexal SCC is associated with a good overall prognosis in horses. However, tumor location may influence the prognosis. Eyelid or orbital involvement is associated with the poorest prognosis, whereas involvement of the nictitating membrane typically has an excellent prognosis. In addition, tumor size is inversely related to survival, and one or more recurrences appear markedly to reduce survival time.

SARCOID

Sarcoid (*q.v.*) is the second most common equine periocular tumor. Two **viruses**, bovine papillomavirus and a C-type retrovirus, have been incriminated as causes of these benign, fibroblastic tumors that affect the skin of horses, donkeys and mules. Although sarcoids in the periocular region are usually less aggressive than those appearing in other anatomic locations, they may be resistant to treatment.

Clinical signs and diagnosis

Sarcoids usually develop in younger horses (<7 yr) and have considerable variation in their clinical appearance. These bizarre dermatologic growths have been divided into three morphologic types: (1) **verrucous** or wart-like sarcoids are generally <6 cm in diameter, dry, hairless and cauliflower-like; (2) **fibroblastic** sarcoids are larger and resemble granulation tissue; (3) **mixed** sarcoids are a combination of the verrucous and fibroblastic types. Reasonable differential diagnoses include SCC, papilloma, nerve sheath tumors, cutaneous habronemiasis, phycomycosis and granulation tissue (*q.v.*). Because no pathognomonic clinical characteristics exist and treatment regimens for these similar diseases differ greatly, histologic confirmation of a presumptive sarcoid should always be made.

Treatment and prognosis

Sarcoids can be extremely difficult to treat. Surgical resection alone often results in recurrence. Small sarcoids may be cured with localized hyperthermia (to 50°C) or cryotherapy (to −20 to −25°C). Radiation therapy, if available, may be extremely efficacious: **iridium wire implantation** is the most effective treatment option. **Cisplatin** (*q.v.*) is effective against most types of sarcoids. However, periocular sarcoids may also be successfully treated by intralesional inoculation of cell walls of **bacillus Calmette–Guérin (BCG)** suspended in oil (*q.v.*). Following surgical cytoreduction, tumor saturation with the BCG vaccine stimulates an active immune response. Treatment must be repeated if the tumor persists after the inflammatory reaction subsides. In general, 1–6 BCG treatments are needed to effect complete regression. Immunotherapy with BCG does not result in excessive scarring or altered function of the treated eyelid tissue and the prognosis is generally good. Complications such as nonhealing fistulas can, however, occur even when all tumor has been obliterated by the ensuing inflammatory reaction. See also Chapter 5, page 379.

PAPILLOMA

Papillomas, also called **warts**, are common, benign cutaneous tumors caused by either an equine papillomavirus or non-infectious irritants. The infectious, multicentric variety is referred to as **papillomatosis** (*q.v.*). Once a premise is infected by a papillomavirus, the disease may become a herd problem and recur on a yearly basis affecting new offspring.

Clinical signs and diagnosis

Papillomas frequently affect the muzzle, eyelids and ears of young horses. Papillomas are usually keratinized masses with fronds and may exist in clusters. Diagnosis can generally be inferred from the clinical characteristics.

Treatment and prognosis

Equine infectious papillomatosis is a self-limiting disease but the duration varies considerably, from 1 to 6 mo. Medical or surgical intervention is not necessary unless the lesions are cosmetically objectionable. **Cryotherapy** and **intradermally administered autogenous vaccines** have been effective.

Prevention

Affected foals should be isolated from susceptible foals. In addition, administration of a commercially prepared vaccine to foals 2–3 mo of age may prevent wart development in high-risk environments.

MELANOMA

Horses with gray or white haircoat colors have an increased prevalence of cutaneous (including the eyelid) and intraocular melanoma (*q.v.*). A disturbance in melanin metabolism, and thus an increased likelihood of tumor formation, may be associated with aging and graying in the horse.

Clinical signs and diagnosis

In general, equine **ocular/adnexal melanomas** are slow-growing, pigmented, localized neoplasms that do not metastasize and may affect the eyelid, bulbar conjunctiva and/or sclera, and the anterior uveal tract. Arabian, Lippizaner, Percheron and related breeds have an increased risk for cutaneous melanoma. Epibulbar melanocytomas are rare in horses and should be differentiated from congenital dermoids. Melanomas are the most common equine intraocular tumors. **Intraocular melanomas** are generally locally expansive and destructive, suggesting malignancy, but an absence of metastasis and their histologic appearance imply a benign biologic behavior.

An **anterior uveal melanoma** may present as a slowly or rapidly expanding, darkly pigmented, dense mass with secondary pupil distortion, or possibly obliteration of the anterior chamber. Marked uveal involvement may also cause uveitis and cataract (*q.v.*).

Anterior uveal cysts may resemble an intraocular melanoma. Uveal cysts usually appear as spherical to ellipsoidal, dark brown to black, smooth bodies in older horses. Anterior uveal cysts may become detached and float freely within the globe or they may spontaneously rupture. Heavily pigmented cysts may prevent transillumination by a focal beam of light. In contrast, some uveal cysts may appear thin-walled and translucent.

Hypertrophic and cystic change of the corpora nigra, or granula iridica, may also be difficult to differentiate from melanoma.

Treatment and prognosis

Surgical debulking and adjunctive cryotherapy is an effective treatment scheme for eyelid and epibulbar melanomas. **Complete excision** (sector iridectomy or iridocyclectomy) is the treatment of choice for intraocular melanoma in horses. However, risks inherent in the surgical procedure, tumor size and expense often eliminate the possibility of surgical management for intraocular melanoma. These cases are usually monitored, treated symptomatically and, when painful or secondary complications develop, the affected globe is enucleated. **Exenteration** should be reserved for those cases with extraocular extension. Aggressive surgical management should yield a good prognosis.

NERVE SHEATH TUMORS (NEUROFIBROMA AND SCHWANNOMA)

Nerve sheath tumors arise from perineural fibroblasts and nerve sheath or Schwann cells. The initiating cause of nerve sheath tumors is unknown.

Clinical signs and diagnosis

Neurofibroma of the upper and lower eyelid appears to be a specific entity in the horse. Eyelid neurofibromas occur subcutaneously as single or multiple, small, circumscribed lesions that increase in size up to 1 cm in diameter.

Treatment

Because of local extension, recurrence is common following attempted surgical removal. Cryotherapy, BCG immunotherapy and interstitial radiotherapy

are alternative and possibly more effective treatment modalities for large nerve sheath tumors.

OTHER OCULAR/PERIOCULAR TUMORS

Many other, less common, ocular, adnexal and orbital tumors have been reported in horses. More information is needed such that natural behavior, preferred treatment modalities and prognosis can be established for these uncommon neoplasms. Some of these rarer tumors involving the equine ocular/periocular tissues are discussed below. Since the first attempt at treatment has the greatest chance of resulting in a cure, an aggressive therapeutic regimen should be utilized when a tumor of which little is known is diagnosed.

Eyelid

Adenocarcinoma, adenoma, basal cell tumor, fibroma, hemangiosarcoma, lymphosarcoma, mast cell tumor and sebaceous adenoma have been documented affecting the equine eyelid. Some eyelid adenocarcinomas have been reported to metastasize following incomplete excision. Equine basal cell tumors are usually solitary, slow-growing, benign lesions that can be successfully removed via surgery. Lymphosarcoma of the eyelids may be primary or secondary. Multicentric lymphosarcoma is presently not treatable via practical means. Equine mast cell tumors do not readily metastasize and may respond to surgery alone or in conjunction with cryotherapy.

Nictitating membrane

Except for SCC, tumors of the nictitating membrane are very rare. The following neoplasms have been reported involving the nictitating membrane of the horse: basal cell tumor, hemangiosarcoma, papilloma, lipoma, lymphangiosarcoma, neurofibroma, primary lymphosarcoma and sebaceous adenocarcinoma. Metastasis has been documented in horses with lymphangiosarcoma and sebaceous adenocarcinoma of the nictitans.

Cornea and sclera

Analogous to neoplasia of the nictitating membrane, except for SCC, tumors of the cornea, bulbar conjunctiva and/or sclera are rare. Histologically confirmed neoplasms include angiosarcoma, hemangioma, hemangiosarcoma, lymphosarcoma, mastocytoma, melanocytoma and papilloma.

Intraocular tumors

Medulloepitheliomas are rare, congenital, neuroepithelial tumors that usually arise from the ciliary body but have been reported to originate from the retina and optic nerve. These tumors are generally non-pigmented, vascularized and slow growing. The characteristic biological behavior of these tumors is unknown; therefore, affected globes should be enucleated once secondary complications or growth are documented. In contrast, a rare, benign proliferation of the optic papilla and adjacent retina has been described in the horse and named

proliferative optic neuropathy. Affected horses are usually aged and asymptomatic. The unique proliferative process affects one globe, protrudes into the vitreous, and is well circumscribed, whitish-gray to pink, and non-progressive. Thus, an affected eye should be retained unless complications are noted upon periodic re-examination.

Orbit

Orbital neoplasia, primary or secondary, is uncommon in horses. Secondary orbital tumors may be the result of metastasis from a distant primary site or local extension from adjacent tissue. Reported equine primary orbital tumors include undifferentiated adenocarcinoma, carcinoma of neuroepithelial origin, lipoma, medulloepithelioma, melanoma, meningioma, multilobular osteoma (chondroma rodens), neuroepithelial tumor of the optic nerve and granulocytic sarcoma.

Orbital tumors are usually slowly progressive and non-painful. The only exception to this is the marked lymphomatous deposit that can cause exceptional chemosis and exophthalmos in cases of leukemia, but such cases are rare. Marked **exophthalmos** may cause lagophthalmos and concomitant exposure keratitis. Orbital tumors may also cause periorbital swelling, shallowing of the supraorbital fossa, protrusion of the nictitating membrane, strabismus, and resistance of the globe to retropulsion. Scleral deformation and retinal detachment, or inflammation and pressure atrophy of the optic nerve may decrease or eliminate vision.

Diagnosis of orbital disease can be difficult because a thorough diagnostic work-up is expensive and may require special techniques, instrumentation or expertise. **Exophthalmos** (*q.v.*) is caused by a space-occupying lesion and must be differentiated from **buphthalmos**, in which the globe is enlarged as a consequence of chronic glaucoma (*q.v.*). Differential considerations for an orbital, space-occupying mass should include tumor, cyst, granuloma, abscess and cellulitis (*q.v.*). Orbital cysts are exceedingly rare. A granuloma, abscess or cellulitis may be caused by a migrating foreign body, guttural pouch mycosis or extension of a suppurative disease from the frontal or maxillary sinuses. Biopsies, and possibly tissue cultures, are necessary to definitively diagnose an orbital disease.

If an orbital tumor is well circumscribed and small, an exploratory orbitotomy may result in complete excision and retention of the eye. Extensive, infiltrative disease usually mandates orbital exenteration. If allowed to progress without some form of intervention, orbital tumors may enter the calvaria, or dome of the skull, and result in neurologic manifestations (*q.v.*). Primary neoplastic disease of the sinuses that has subsequently invaded the orbit is seldom amenable to treatment and the prognosis is poor.

OCULAR TRAUMA

INTRODUCTION

The horse by its nature and lifestyle seems inordinately prone to ocular injuries. Kicks from other horses or sudden head movements in enclosed

spaces can result in considerable force being applied to the orbital area. A closed bony orbit, while protecting against minor blows, may be fractured, entrapping the eye or adnexal structures. The prominence of the eye predisposes itself to both blunt trauma and sharp penetrating injuries. The **prognosis** for saving a traumatized eye and maintaining vision is related to the type of trauma. Sharp penetrating or perforating injuries in general carry a better prognosis than blunt trauma that causes either **contrecoup reactions** (bruising of brain tissue) or ocular rupture. Perforating injuries of the cornea alone tend to have a better prognosis than those that extend into the scleral coat of the globe.

OCULAR EXAMINATION

The most important and urgent question to be answered when examining a horse with ocular trauma is the extent of globe involvement. If the eyeball has been damaged, expeditious medical or surgical treatment is essential. An attempt should be made to assess whether the affected eye has vision using the **menace response** as a guide.

Most horses with eye injuries are in **pain**. Xylazine administered at 0.4 mg/kg IV provides adequate sedation for ocular examination. The direct pupillary light reflex (PLR) should be evaluated if the anterior chamber is clear. A miotic (constricted) pupil most likely indicates iridocyclitis and is a better prognostic sign than mydriasis (reflex pupillary dilation), which suggests damage to the parasympathetic innervation of the iris. If **hyphema** (*q.v.*) is present, the iris and posterior segment may not be seen. If the consensual PLR is present in the normal eye when a bright light is shone into the injured eye, this is an indication that retinal and optic nerve function are still present on the injured side.

To examine the globe, it is essential that **regional motor nerve blocks** (*q.v.*) are used. Failure to do this may result in considerable pressure being exerted on the globe. The auriculopalpebral nerve is blocked with 1–2 mL 1% lidocaine along the dorsal aspect of the zygomatic arch halfway between the lateral canthus of the eye and the base of the ear.

The eyelids, conjunctiva, nictitating membrane, cornea and sclera are examined for contusions, abrasions and lacerations. The anterior chamber is examined for aqueous flare, fibrin, hemorrhage or the presence of a dislocated lens. The posterior segment (vitreous and retina) is examined by ophthalmoscopy for hemorrhage or retinal edema or detachment, and the optic nerve is examined for signs of hemorrhage or optic atrophy.

ORBITAL FRACTURES

Fractures of the ventral orbital wall and zygomatic processes of the orbital bones are relatively common in the horse. Ocular tissues, including extraocular muscles, may be entrapped, and subconjunctival and retrobulbar hemorrhage may occur. Corneoscleral lacerations and uveitis may be present and should be treated independently. Radiography of the orbit can be attempted but positioning and interpretation is often difficult, the lateral oblique view usually giving most information.

Fractures need not be treated immediately, and more attention should be paid to the eyeball initially. If **entrapment** of ocular tissue is considered likely,

however, the fractures should be treated immediately. Initial therapy should consist of cold compresses, dimethyl sulfoxide (DMSO), NSAIDs and systemic corticosteroids to reduce swelling, and systemic antibiotics if fractures are compound. Topical **artificial tears** and petrolatum ointment should be used to avoid corneal exposure if swelling limits eyelid closure. Fractures with minimal displacement may not require surgical treatment. If the cosmetic appearance is affected, displacement is severe or compound fractures occur, surgical repositioning of bones and fragments should be attempted.

EYELID INJURIES

Trauma may result in eyelid contusions or lacerations. Eyelid and conjunctival edema (**chemosis**), conjunctival hemorrhage and reduced eyelid motility are typical signs. Contusions are treated with cold compresses, DMSO applied to the lids, and systemic NSAIDs such as flunixin meglumine 1 mg/kg IV or PO daily. Severe eyelid and conjunctival swelling will result in conjunctival and corneal exposure. **Artificial tears** and **lubricating petrolatum ointment** should be applied to the conjunctiva and cornea to keep these moist until swelling around the eye has subsided.

Lacerations of the eyelids should be repaired surgically. Small lid lacerations involving only the skin can be sutured with 4-0 silk. Complicated, full thickness lacerations of the eyelid should be repaired in two layers. The inner tarsoconjunctival layer of the eyelid is sutured with absorbable 5-0 to 6-0 polyglactin 910, and the skin layer with 4-0 silk. Suturing must begin at the eyelid margin for both layers. A cruciate (figure of eight) suture pattern provides best apposition at the eyelid margin in the outer skin–orbicularis muscle layer. The rest of the laceration is sutured with a simple interrupted pattern. Post-surgical medications should include topical antibiotic ointment, systemic NSAIDs and antibiotics and tetanus prophylaxis.

LACERATIONS OF CONJUNCTIVA AND NICTITATING MEMBRANE

Small conjunctival lacerations will in most cases heal without surgical repair. Extensive lacerations can be repaired with 6-0 polyglactin 910, with a simple continuous suture pattern. Even without surgery these will eventually heal. **Topical antibiotics** should be used. Lacerations of the nictitating membrane may require suturing with 6-0 to 7-0 polyglactin 910 using a simple interrupted or continuous pattern in the conjunctiva. Care should be taken not to leave knots or suture material protruding from the bulbar surface of the nictitating membrane to abrade the cornea. A triple antibiotic solution or ointment should be applied t.i.d. to q.i.d.

CORNEAL AND SCLERAL LACERATIONS

Trauma to the cornea may result in superficial abrasions, or penetrating or perforating lacerations. Lacerations may extend into the sclera. **Corneal abrasions** result in a painful, red eye with a miotic pupil due to reflex iridocyclitis. The area around the laceration is edematous and thickened. The extent of the

corneal abrasion is determined by irrigating the cornea with **sodium fluorescein dye**. Abrasions should be treated with topical antibiotics and atropine 1% q 6 h.

Penetrating corneal and scleral lacerations should be repaired under general anesthesia. The laceration is sutured with 7-0 polyglactin 910 using a simple interrupted pattern. Sutures should penetrate the cornea to two-thirds the depth of the stroma and be placed 1–2 mm apart.

Small perforating **puncture wounds** in the cornea may seal rapidly with fibrin from the aqueous humor, and can be treated medically with topical and systemic antibiotics and atropine for the associated uveitis (*q.v.*) provided leakage of aqueous is not detected.

Perforating injuries to the cornea and sclera may present with a collapsed anterior chamber. The lacerations may be plugged with iris. When the cornea is perforated, the blood–aqueous barrier is disrupted. Fibrinogen enters the anterior chamber and polymerizes to fibrin, forming secondary or plasmoid aqueous and along with the iris helps to seal the laceration. Secondary aqueous that leaks through the laceration forms a gelatinous mass that adheres to the edges of the laceration and prolapsed iris. This may give the appearance that the laceration is larger than is actually the case. The secondary aqueous usually obscures the true extent of the laceration. This may be compounded beyond the limbus where scleral lacerations are obscured by edematous conjunctiva.

These lacerations must be repaired under general anesthesia. **Flunixin meglumine** and **systemic broad-spectrum antibiotics** are given IV **before** surgery. The eye should be medicated immediately before or at the time of inducing anesthesia with a topical broad-spectrum antibiotic and atropine. The extent of the laceration should be explored, paying careful attention to potential extension across the limbus into the sclera. Failure to suture any scleral extension of the laceration will result in phthisis of the globe after surgery.

The iris should be gently freed from any adhesions to the edge of the laceration. In injuries <24 h old, the iris can be replaced into the anterior chamber. The anterior chamber is irrigated with **lactated Ringer's solution** or balanced salt solution to remove as much blood and fibrin as possible. If the anterior chamber is difficult to re-form with irrigating solutions, an air bubble will often push the iris and lens away from the cornea while the laceration is repaired. Alternatively, **viscoelastic materials** including sodium hyaluronate or sodium chondroitin sulfate–sodium hyaluronate can be injected through the laceration to re-form the anterior chamber. Viscoelastics have the added advantage of protecting the posterior endothelial surface of the cornea during surgical manipulations, although the cost of volumes large enough to fill the equine anterior chamber may be prohibitive.

If the laceration has been present >24 h, some of the entrapped iris may be devitalized. The protruding iris may be **trimmed** with scissors until hemorrhage is seen or may be **debrided** with a fine cautery and then the remaining iris can be replaced in the anterior chamber. Extensive debridement of the iris is rarely necessary.

The laceration should be sutured with 7-0 to 8-0 polyglactin placed to two-thirds the corneal depth, spaced 1–2 mm apart in a simple interrupted pattern. An air bubble or viscoelastic material can be replaced by lactated Ringer's solution or balanced salt solution prior to placing the last suture provided that the anterior chamber has re-formed.

It has previously been recommended that a subpalpebral lavage be placed in the upper eyelid at the conclusion of surgery in order to medicate the eye effectively in the postoperative period. More recently a medial lower eyelid lavage system has been suggested which is more readily placed and exceptionally well tolerated by the horse. Clearly, in a trauma situation, the placement of such a system will depend on the areas of lid damaged in the trauma. Medications include systemic NSAIDs and antibiotics, topical antibiotics and atropine q 4–6 h.

CORNEAL FOREIGN BODIES

Superficial foreign bodies in the cornea can be removed using sedation, local motor nerve blocks and topical anesthesia of the cornea with proparacaine hydrochloride. Deep penetrating or perforating foreign bodies should be removed under general anesthesia and the injury site sutured. Gunshot in the eye may be removed if accessible in the anterior chamber. Rarely is gunshot in the vitreous accessible for removal. Gunshot in the orbit should be left in situ.

TRAUMATIC UVEITIS

Anterior uveitis or iridocyclitis (*q.v.*) is a common finding in cases of ocular trauma. It may accompany corneal injuries or occur without any corneal lesion being detected. Signs of uveitis include a hyperemic conjunctiva, corneal edema, aqueous flare or hyphema, miosis and swelling of the iris. The eye is painful due to spasm of the ciliary muscle.

Atropine 1–3% is applied topically q 4–6 h for cycloplegia to reduce pain and dilate the pupil to reduce the incidence of posterior synechiae development. NSAIDs are given systemically to provide analgesia and reduce intraocular inflammation and miosis. Drugs chosen may include **flunixin meglumine** 1 mg/kg administered IV or PO, aspirin 25 mg/kg b.i.d. for 3–5 days and then 30 mg/kg once daily as long as needed, or phenylbutazone 2 g/kg once daily. Topical NSAIDs are also useful. Although not licensed in the horse, topical flurbiprofen (0.03%) can be applied q 6 h while other NSAIDS such as ketorolac can be equally useful. Dexamethasone 0.1% suspension or prednisolone acetate 1.0% should be used q 4–6 h unless corneal ulceration is present or supervenes.

The prognosis should be guarded, especially when the lens cannot be seen. Anterior segment hemorrhage and fibrin will be cleared from the eye via the aqueous outflow pathways and by phagocytosis within a few days of the injury in most cases that receive adequate therapy.

LENS TRAUMA

Trauma to the eye may result in **rupture of the lens**. This is especially likely in cases of sharp perforating injuries through the cornea or sclera. When the lens capsule is disrupted, lens protein released into the eye causes an immunologic reaction with development of severe uveitis. Clinical signs are those of **severe uveitis** (*q.v.*), which shows a poor response to therapy within the first few days. Hazy lens contents may be seen, mixed with fibrin protruding from the

lens surface. Medical therapy alone is not adequate to control the inflammation and in many cases the injury may be of such magnitude that the eye cannot be saved. If the horse still has any vision on the affected side and evidence of a consensual PLR to the other eye the prognosis may be improved. The ruptured lens contents must be removed surgically. This requires referral to an ophthalmologist. The lens material can most easily be removed by phacofragmentation and aspiration. The laceration is repaired at the same time and the eye treated intensively for uveitis.

Lens dislocation can occur in cases of blunt trauma. The zonules that support the lens behind the pupil are quite resistant to breaking in the normal horse, and the magnitude of trauma required to dislocate a normal lens is usually great enough that other signs, including **intraocular hemorrhage** and **retinal detachment**, are also present. The lens may be dislocated into the vitreous or into the anterior chamber. It may often be seen with a focal light source or its position verified if the cornea is opacified by ultrasound. The dislocated lens can be removed by an ophthalmologist, although the prognosis is guarded to poor.

VITREOUS HEMORRHAGE

Hemorrhage into the vitreous may occur with blunt ocular trauma or after rapid decompression of the eye by a perforating injury. Vitreous hemorrhage usually resorbs over several weeks. Therapy is aimed at any coexistent uveitis or retinitis.

RETINAL EDEMA AND DETACHMENT

In cases of blunt trauma, posterior segment inflammation may occur. This is detected by ophthalmoscopy. **Retinal edema** may be seen as gray lines in the tapetal or non-tapetal fundus that may radiate from the optic nerve. The optic nerve may appear edematous, or hemorrhage may be seen in the vitreous. Systemic corticosteroids and NSAIDs should be administered to treat traumatic posterior segment inflammation.

Retinal detachment may occur with ocular trauma. The retina may be detached from the retinal pigment epithelium by edema, or tears may occur, often in the peripheral retina. The affected eye will have visual loss that parallels the extent of the detachment. Total retinal detachment presents with blindness. The PLR may be present initially although this is eventually lost. The retina may be seen with a light source or by ophthalmoscopy as a gray sheet behind the lens in the vitreous. The tapetum may appear more reflective than usual, although this is not a marked finding in this species. Bullous retinal detachments should be treated in the same way as **retinal inflammation** although the prognosis is usually very poor. Surgical repair of rhegmatogenous detachments (where vitreous enters the subretinal space) is not as yet practical in the horse.

RETINAL ATROPHY

Radiating light-colored lines or spots with a pigmented center may be seen several weeks after ocular trauma in the retina. These may be focal or generalized

and be associated with ocular trauma and possibly severe blood loss. The tapetum may undergo color change and appear more reflective than usual.

OPTIC NEUROPATHY

Horses that receive blows to the back of the head when rearing or falling backwards may stretch the optic nerve at the optic foramen as the eye moves forward in the orbit. The affected horse may appear **blind immediately** after the injury or within a few days. Examination of the nerve may show areas of peripapillary edema initially, occasionally with hemorrhage and later signs of optic atrophy. The atrophic nerve is pallid and has a reticulated pattern where the lamina cribrosa of the sclera is seen through the degenerating neurons. Most horses thus affected lose and never regain vision despite therapy. Similar findings have been reported in horses that experienced excessive blood loss. Therapy in the immediate period after the injury should include systemic NSAIDs and corticosteroids.

FACIAL NERVE TRAUMA

Fractures of the zygomatic arch and other bones along the course of the auriculopalpebral branch of the facial nerve may result in **facial paralysis**. Apart from drooping of the lid, the horse is unable to blink and has reduced tear production. Corneal ulceration (*q.v.*) is a common sequel due to exposure of the cornea. Inability to blink can be determined by stimulating the periocular region. Recovery after facial nerve trauma is unusual and the eyelid and lacrimal deficiencies often result in corneal ulceration. Immediate therapy should comprise application of topical **artificial tears** and **petrolatum ointment**. Topical antibiotics should be used if corneal ulceration is present. Permanent lateral and medial tarsorrhaphies will help reduce corneal exposure and drying. **Parotid duct transpositions** can be performed in the horse to increase corneal wetting in the long term.

NEURO-OPHTHALMOLOGY

NEUROANATOMY

Neuro-ophthalmic examination permits evaluation of cranial nerves (CN) II, III, IV, V, VI, VII, and to some extent VIII. The axons of the retinal ganglion cells make up the optic nerve (CN II), and form the afferent pathway of the PLR, and for vision. The optic nerve becomes myelinated after traversing the lamina cribrosa. The nerve crosses the orbit to exit through the optic foramen. The two nerves meet at the optic chiasm, where 10–20% of the nerve fibers remain on the ipsilateral side and 80–90% cross over to the contralateral side. Beyond the chiasm, the nerve fibers serving vision continue via the optic tracts to the lateral geniculate body. Vision fibers project through the optic radiations to the cerebral cortex. Lesions at these levels will cause loss of vision, but not loss of PLR. Pupillomotor fibers project to the pretectal nucleus. From this nucleus, fibers again decussate to the parasympathetic

nucleus of CN III (Edinger–Westphal nucleus). The nerve fibers travel to the ciliary ganglion, where post-ganglionic neurons supply the iris sphincter.

The **menace response** is a cortical blink response to a visual stimulus. The efferent pathway travels via the internal capsule and pons to the nucleus of the facial nerve. Motor innervation to the eyelids is provided by the auriculopalpebral branch of the facial nerve. Cerebellar interaction is required for function, and severe cerebellar lesions may therefore cause loss of the menace response in a visual eye with an intact facial nerve.

Sympathetic upper motor neurons arise in the hypothalamus, midbrain, pons and medulla and descend through the spinal cord to the anterior thoracic segments. Preganglionic fibers run cranially in the cervical sympathetic trunk with the vagus nerve to the cranial cervical ganglion adjacent to the guttural pouch. Post-ganglionic sympathetic fibers supply a number of tissues, including the iris dilator muscle.

In addition to the autonomic component of the oculomotor nerve, it also innervates the dorsal, medial and ventral rectus muscles, as well as the ventral oblique extraocular muscles. Loss of the innervation creates **ptosis** (drooping of the upper eyelid), **lateral strabismus** (abnormal alignment of one or both eyes) and inability to rotate the globe in the direction of the affected muscles.

The trochlear nerve, CN IV, supplies the lateral rectus and retractor bulbi muscles. Paralysis is manifested by a medial strabismus and inability to retract the globe.

REGIONAL NERVE BLOCKS

The **auriculopalpebral nerve** may be blocked at two sites. A depression is palpable caudal to the posterior border of the ramus of the mandible at the level of the temporal position of the zygomatic arch. A 2.5 cm needle is inserted to the hub in the depression, directed slightly dorsally, and 5 mL lidocaine 2% injected. This usually produces a total motor block, although some horses will maintain control of the lower eyelid due to secondary innervation from the buccal nerve. The ipsilateral ear will also droop.

The **palpebral branch** can be blocked as it crosses the zygomatic arch. The accompanying vessels are palpable at the highest point of the dorsal border; 2–3 mL lidocaine are deposited just below the dorsal border.

Sensory innervation to the eyelids is provided by various branches of the trigeminal nerve, CN V. The medial and middle thirds of the upper eyelid and much of the forehead are supplied by the frontal nerve. This nerve travels through the supraorbital foramen, which can be palpated in the supraorbital process at the point where it begins to widen. A 1.5 cm 25 gauge needle is directed perpendicular to the bone, and slightly medially. One to 2 mL lidocaine are injected at this depth, and another 1 mL is injected as the needle is withdrawn through the foramen. Another 1–2 mL is injected SC over the foramen.

The lacrimal nerve supplies the lateral portion of the upper eyelid. The nerve can be blocked by injecting 2–3 mL lidocaine beneath the dorsal rim of the orbit approximately 1 cm medial to the lateral canthus. The infratrochlear nerve supplies the medial canthal area. This nerve can be located by palpating the notch in the dorsal orbital rim, approximately 1–2 cm lateral to the medial canthus, and injecting 2–3 mL lidocaine deep and slightly rostral to the notch.

The zygomatic nerve supplies much of the lower eyelid, and can be blocked by injecting along the ventral orbital rim, approximately 1–2 cm medial to the lateral canthus.

Alternatively, the eyelids may be blocked by **local infiltration**. The cornea and conjunctiva require **topical anesthesia**, unless a retrobulbar block is performed.

NEUROLOGIC DISORDERS

Various neurologic lesions may be localized by identifying the cranial nerves involved in the deficits. Lesions of the retina and optic nerve are discussed in their own section (*q.v.*).

ABNORMAL PUPILLARY RESPONSE

Mydriasis

Pupil size and mobility depend on sympathetic and parasympathetic innervation. A decreased response, or **increased pupil size**, may be due to fright, creating a transient sympathetic overload, pharmacologic blockade (e.g. due to atropine), iris atrophy, synechiae formation, glaucoma, retinal or optic nerve atrophy (*q.v.*), as well as internal ophthalmoplegia, i.e. loss of parasympathetic innervation. Primary neurologic causes are not common and may be located in the pretectal or Edinger–Westphal nuclei, or in the oculomotor nerve. Lesions involving the oculomotor nerve may show an accompanying "down and out" strabismus (*q.v.*) due to loss of innervation to extraocular muscles. Additional neurologic signs are frequently present. Parasympathetic denervation may be confirmed by demonstrating hypersensitivity to pilocarpine instilled into the affected eye compared with the normal eye.

Miosis

Miosis, or a **failure to dilate**, may be related to the presence of uveitis or ocular pain, posterior synechiae formation, or pharmacologic stimulation of the iris sphincter, e.g. due to pilocarpine or organophosphates, as well as neurologic disease either centrally or associated with Horner's syndrome (*q.v.*). Bilateral miosis can be a sign of acute, severe central lesions, and may be of little localizing value. Miosis in these cases is a more favorable prognostic sign than mydriasis.

Horner's syndrome

Lesions causing Horner's syndrome (*q.v.*) may be central, pre- or postganglionic. Etiologies include spinal cord injury, cranial thoracic tumors or trauma, surgery or injections in the neck, including **jugular intravenous injections**, causing interference with the vagosympathetic trunk, as well as guttural pouch disease.

Clinical signs include increased skin temperature and sweating of the ipsilateral face and ear, miosis, ptosis, prolapse of the nictitating membrane and enophthalmos. **Ptosis** (*q.v.*) is most easily assessed from the front of the animal by determining the angle of depression of the eyelashes on the affected side.

The lesion responsible for the syndrome may be localized through pharmacologic tests. Central and preganglionic lesions will allow the affected pupil to respond to **1% hydroxyamfetamine**, causing mydriasis. Post-ganglionic lesions will not respond. However, post-ganglionic lesions will cause the effector cells to be super-sensitized to **phenylephrine**, resulting in rapid mydriasis. Central and preganglionic lesions will not respond to phenylephrine.

Treatment is aimed at the initiating cause, if it can be identified. Palliative therapy consists of topical epinephrine (adrenaline) or phenylephrine, used as required. Clinical signs tend to resolve over time.

Facial nerve paralysis

Damage to the facial nerve is frequently the result of trauma, although polyneuritis, meningitis or middle ear infections (*q.v.*) should be considered. Clinical signs include loss of the blink reflex and lagophthalmos (where the eye cannot close completely), inability to flare the ipsilateral nostril, flaccid lips and facial contracture toward the normal side. Proximal injuries will also show a paralyzed ear. **Keratoconjunctivitis sicca** (*q.v.*) may occur, due to loss of parasympathetic innervation to the lacrimal glands, which travels with the facial nerve. Skull radiographs may be required to determine the cause.

Treatment consists of systemic corticosteroids or NSAIDs in the acute case. Local massage and warm compresses may also be of benefit. Ophthalmic ointments should be used to protect the cornea. The eye should be protected by a temporary tarsorrhaphy if exposure keratitis or KCS is a problem, or a permanent tarsorrhaphy in cases with permanent paralysis. The horse should not wear a halter, to prevent further trauma to the nerve.

Recovery may occur in 3–4 wk, or may be prolonged. The paralysis may be permanent.

Nystagmus

Nystagmus is an involuntary ocular movement that can be induced in the normal horse by moving the head from side to side or up and down. The eye movement has a rapid phase in the direction of the head movement, with a slow phase in the opposite direction, with both eyes moving simultaneously. This system requires function of the vestibular system, the medial longitudinal fasciculus, and CN III, IV and VI.

Abnormal nystagmus may be the result of head trauma, guttural pouch or sinus infections, or CNS inflammatory disease (*q.v.*). In **vestibular disease**, the eyes tend to deviate ventrally on head extension, especially the eye ipsilateral to the lesion. Peripheral lesions are associated with a horizontal or rotary nystagmus, with direction of the rapid phase away from the side of the lesion. Central disorders may show **vertical nystagmus**, or nystagmus that changes with the position of the head. Ataxia and head tilts may also be present.

Skull radiographs may be of benefit in diagnosis, with particular attention paid to the tympanic bullae and the petrosal portion of the temporal bone.

Treatment usually consists of antibiotic and anti-inflammatory therapy. Prognosis is guarded. Initial response may be promising, but complete recovery may be prolonged. A residual deficit may persist.

Chapter 20

Oncology

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Chapter contents

INTRODUCTION

The **prevalence of tumors in horses is increasing**, partly related to animals living to older ages but also to better preventive and therapeutic medical practices. As a result, veterinarians are called upon more frequently to diagnose and manage horses with tumors. Horse owners are more aware of progress in cancer treatment and are becoming more demanding in seeking care for their horses.

More than 80% of tumors in horses affect the **skin and subcutaneous tissues**. Because lesions involving the skin are easily seen by the owner and so are often rapidly brought to the attention of the veterinarian, the vast majority of equine tumors should be caught early and be highly curable. Unfortunately, mismanagement of equine tumors due to lack of knowledge of the disease process and misuse of conventional treatments may result in euthanasia.

In this chapter the principles of oncology as applied to the equine patient are presented. The intent is to provide equine practitioners an overview of the principles and practices of cancer diagnosis, and treatments. Readers should refer to the Index and the systematic chapters for details of diagnosis and treatments of specific tumor types and locations.

There are five rules for successful tumor management (Box 20.1).

A **correct assessment of the treatment goal** is critical to select the optimal treatment or treatment combination. Overly aggressive treatment plans can expose animals that are not curable to **needless morbidity** or to prolonged

Box 20.1 Rules of tumor management

1. Establish a diagnosis
2. Stage the disease, i.e. to assess tumor size and extent (local invasion and metastasis)
3. Assess the general health status of the patient
4. Discuss treatment goals with the owner
5. Formulate the treatment plan

and expensive treatments. On the other hand, therapeutic decisions that are too pessimistic deprive the animal of a chance for cure.

ASSESSMENT OF THE CANCER PATIENT

THE BASIS OF THE ASSESSMENT

Each affected horse has a **unique set of clinical problems** that should be completely identified by the historical and physical examinations and recorded in the animal's medical record for future reference. In many cases, the **clinical presentation of skin mass** will enable a tentative clinical diagnosis to be made. However, there are occasions when the neoplastic nature of a problem is not obvious. In either case, a **systematic approach** to the case will increase the likelihood of curative management.

HISTORY

The history should establish relevant long-term information about the animal, such as previous disease or illness, and treatments. A complete history should include date of onset of any visible tumor, the rapidity of growth, any change in size, shape and/or color over time and the appearance of new lesions in the same location or at a distance.

Particular attention should be paid to the results of any previous diagnostic tests, diagnoses and attempts at treatment for the presenting problem, and whether any measures have had significant effects on the course of the condition.

PHYSICAL EXAMINATION

Before proceeding to a detailed assessment of a tumor, it is essential to examine the **whole animal**. A **complete physical examination** will alert the clinician to other masses that may not have been noticed by the owner and will also allow an appraisal of any concurrent disease.

Although the incidence of **metastatic disease** for malignant tumors in the horse is only 25%, many tumors (including equine sarcoid [*q.v.*], squamous cell carcinoma [*q.v.*], and melanoma [*q.v.*]) frequently arise in **multiple sites** on the same horse.

For **deep-seated tumors**, the clinician relies upon clinical manifestations of the disease resulting from a mass effect leading to obstruction or compression, bleeding, and effusion or endocrine syndromes associated with **hyperfunctional tumors**. Frequently, indirect systemic effects of cancer, known as **paraneoplastic syndromes**, including cachexia, fever not associated with infection, hypercalcemia, hematologic–hemostatic abnormalities and hypertrophic osteopathy are the first manifestations of an occult tumor.

For superficial or accessible tumors such as cutaneous and endocavitary tumors, the majority of the physical examination can be performed by **direct visual assessment** and **manual palpation**. Cutaneous and subcutaneous tumors such as sarcoid tumors, squamous cell carcinomas, basal cell carcinomas, adenocarcinomas (sweat gland), squamous papillomas, melanomas and dermal melanomatosis, cutaneous lymphomas, soft tissue sarcomas including fibrosarcomas, schwannomas, hemangiosarcomas, liposarcomas, lymphangiosarcomas, hamartomas and mast cell tumors (*q.v.*) should be examined with respect to their appearance (mass or ulcer, symmetry, contour), color, number, size, location, consistency, presence or absence of fixation to underlying tissue, and whether the overlying skin is ulcerated.

The **growth pattern of the lesion**, i.e. any irregular growth and contour, should be carefully assessed. Based on appearance, the biological behavior of the lesion, and risk factors including age, breed/skin pigmentation, exposure to contributing agents such as viruses, sun exposure, chemicals and trauma, a tentative diagnosis of "tumor" can be made.

DIAGNOSIS

Although the clinical manifestations or appearance, location and growth pattern of a lesion may give the veterinarian a high degree of suspicion as to the type of tumor involved, it is imperative that a definitive diagnosis be attained so as to plan treatment properly and discuss prognosis with the owner. The most common diagnostic procedures are **cytology** and **tissue biopsy.**

Aspiration cytology

Aspiration cytology is simple procedure requiring only a 22 G, 25 mm (1 inch) needle and a 6 mL syringe for superficial lesions or 22 G, 65 mm (2.5 inch) spinal needle with stylet for deeper lesions.

The technique can be used for tissues (**fine needle aspirate**) or body cavity fluid. The site is cleaned with a surgical scrub and alcohol if an abdominal cavity is to be entered. Usually there is no need for sedation or local anesthesia. Topical anesthetic (lidocaine 2.5% and prilocaine 2.5%) may be used on a shaved skin but local anesthesia takes approximately 15 min for mucosa and 30 min for intact skin. The sample is obtained by **gentle aspiration**, as the needle is advanced through the tissues in several different locations.

All negative pressure must be released before the needle is withdrawn from the tissue. The syringe is detached and the aspirated cells are then expelled onto a **microscope slide** with a frosted end. A second slide is placed flat on the first and the two are gently slid apart to spread the aspirate. The slide is then allowed to air-dry. If larger volumes of fluid sample are obtained, a small drop

can be smeared in a similar manner. Information regarding patient and aspiration site should be written with a pencil on the frosted end.

Separate needles are used for sampling **multiple sites**. Multiple slide preparation with standard fixative should be made when possible and the cellularity of the specimen should be evaluated prior to submission to a diagnostic laboratory by microscopic examination of a stained slide preparation to ensure sample quality. The air-dried slides are then shipped by courier or mail to a diagnostic laboratory in a polypropylene slide mailer with a snap top lid or Styrofoam container to protect the glass slides.

Fine needle aspirate cytology is a **screening tool** to differentiate neoplastic from inflammatory lesions. Cytology often helps differentiate between epithelial and connective tissue tumors. Several tumors such as melanomas, lymphomas and mast cell tumors (*q.v.*) can be accurately diagnosed cytologically. In most cases a positive cytologic finding can only give a tentative diagnosis and a negative cytologic finding should be treated as inconclusive. Aspiration cytology cannot be a substitute for histopathology because it does not provide any information about the biological behavior of the tumor.

Biopsies

Procurement and interpretation of a biopsy specimen is perhaps **the most important step** in the management of all tumors. Not only will the biopsy provide a definitive diagnosis, it may also be used to predict the biologic behavior of the tumor, which aids in selecting the type and extent of treatment and determining prognosis. It is important to provide the pathologist with a well-fixed (1 part tissue volume to 10 part fixative volume) tissue specimen large enough to represent the **disease process**. Fixative solutions (10% buffered neutral formalin) are provided in containers of different sizes by diagnostic laboratories upon request. Fixed samples are kept at room temperature and shipped to the local veterinary diagnostic laboratory.

As a rule, any active lesion (growth, appearance change, new lesions) **that is not responding or temporarily responding to medical treatment** should be biopsied.

There is no evidence that a biopsy can negatively affect the outcome of a patient as long as it is followed by definitive treatment if the diagnosis is tumor. Moreover, in the human and veterinary literature there is no suggestion of tumor transformation or an increased risk of metastasis after a planned biopsy. The advantages of an accurate diagnosis far outweigh the theoretical risk of enhancing metastasis or the unproven risk of transforming a benign lesion into a malignant one. Thus there is no medical reason for not performing a biopsy, and if a client brings an active lesion to a veterinarian's attention it is worth taking a biopsy. If a veterinarian recommends a biopsy for a suspicious lesion and the client declines the procedure, the reasons for not performing the biopsy should be documented in the medical record for legal purposes and a plan for follow-up established.

The only contraindication for biopsy of an accessible lesion is the lack of commitment of the owner to pursue treatment for financial or emotional reasons because the trauma caused by the biopsy can **trigger tumor proliferation**

of an otherwise slow-growing tumor and precipitate its local evolution. The non-medical reasons for not performing a biopsy should be documented in the medical record and a plan for follow-up established.

An accurate diagnosis should be obtained prior to surgery if the type of treatment or extent of the treatment depends on the tumor type or when the owner's decision to treat depends on prognosis. Large lesions or lesions in unfavorable locations should be biopsied **before any treatment** attempt.

The most common techniques of tissue procurement prior to surgery are needle core biopsy, punch, pinch and incisional biopsies (*q.v.*). All biopsy tracts should be positioned in such a manner that the tracts they create can be excised in continuity with the primary tumor at surgery to prevent tumor seeding. In other words, prior to performing a biopsy, the veterinarian must assume the lesion is a tumor and determine an appropriate surgical approach. Keeping this in mind, the veterinarian must then plan the biopsy sites and tracts within the planned surgical field.

Needle core biopsy

Needle core biopsies of soft tissue tumors may be obtained with **Tru-Cut** or **ABC needles**. Palpable lesions may be fixed in place manually and biopsied blindly. Deep-seated lesions must be biopsied under **ultrasound guidance**. Bone lesions and bone marrow biopsies may be performed with a **Jamshidi needle** or **Michelle trephine**.

After sterile skin preparation with surgical scrub, 3–5 mL of buffered lidocaine (3 mL of 2% Xylocaine plus 1 mL of sodium bicarbonate 8.4% added immediately before injection) is injected using a 25 G needle in and around all of the tissues that extend from the skin to the lesion. A small stab incision is made in the overlying skin, and through the same skin hole several needle cores are removed from **different sites**. Tissue samples recovered from the instrument are **fixed in formalin** solution.

The biopsy procedure is usually done in the conscious animal using sedation, e.g. detomidine 0.01 mg/kg IV plus butorphanol 0.1 mg/kg IV, or xylazine 0.5 mg IV plus butorphanol 0.1 mg/kg IV, if necessary.

In spite of a small sample size, the structural relationship of the tissue and tumor cells can be determined histologically. The technique is relatively atraumatic but care must be exercised to avoid large blood vessels.

Bone marrow aspiration and biopsy

Bone marrow aspiration, and less commonly biopsy, is an essential procedure for determining cytologic abnormalities of the bone marrow caused by a wide variety of neoplastic and myelodysplastic conditions. It is used for the diagnostic and staging of **hematopoietic malignancies** (lymphomas and leukemias [*q.v.*]). A bone marrow biopsy is used when bone marrow aspiration does not yield enough tissue for diagnostic.

The preferred site for bone marrow aspirates is the **sternum** (ventral midline between front legs) because hematopoietic activity persists throughout life, and it provides an easy access. Other sites include tuber coxae or proximal ribs. The hair is clipped, and the bone marrow aspiration site is prepared with a surgical

scrub. Using a 25 G needle, approximately 3–5 mL of buffered lidocaine (3 mL of 2% Xylocaine plus 1 mL of sodium bicarbonate 8.4% added immediately before injection) is injected in and around all of the tissues that extend from the skin where the bone marrow needle is to be introduced to the bone.

The 12 mL collection syringe and bone marrow needle is rinsed with **EDTA** before the procedure to reduce clotting of the bone marrow sample. The biopsy area is scrubbed a final time and, using sterile technique, the skin is stretched between the thumb and index finger and a small stab incision of the blocked skin is made with a no. 11 surgical blade. The bone marrow needle (50 mm/2 inches long, Illinois or Rosenthal bone marrow needle) with the stylet in place is advanced through the stab incision and through the skin and subcutaneous tissue, down to the bone. With the stylet in place, the bone marrow needle is advanced into the bone, using a corkscrew motion (clockwise and counterclockwise) while applying firm and steady pressure. The instrument should not be allowed to wobble. When the needle is firmly fixed in the bone, the stylet is removed and the syringe is affixed.

The bone marrow sample is **aspirated briskly** into the 12 mL syringe; usually, 1 mL of marrow is adequate. If a sample is not obtained, the stylet is replaced in the bone marrow needle, and the instrument is then advanced further into the bone for a second attempt at aspirating marrow contents. Once marrow has been obtained, marrow can be spread on a glass slide with a frosted end into a monolayer like an ordinary blood smear and air-dried. Sample shipment and identification are the same as for any aspiration cytology sample.

Punch biopsy

Tissue sampling of a relatively flat lesion of skin or mucosa such as an early epithelial or dermal tumor can be done with a **punch biopsy** tool holding a circular blade (2–8 mm in diameter). The tissue specimen is shorter but wider than that obtained with needle biopsy. Preparation of the patient and of the site are the same as for core biopsies (*q.v.*). Once the punch instrument has cut into the tumor, the core is gently lifted and the base of the core is cut off with scissors and fixed in formalin solution.

Incisional biopsy

Incisional biopsy refers to the removal of a small wedge of tissue procured with a surgical blade. It is often used when neither cytology nor core biopsy yields diagnostic material, and the procedure is preferred for the diagnosis of large ulcerated and necrotic masses that require major surgical procedures for excision.

After appropriate sedation, local anesthesia and surgical preparation of the site using the same protocol as for a needle biopsy (*q.v.*), a wedge of viable tumor tissue is procured from the **junction of normal and abnormal tissue**. Care should be taken to choose a location for the biopsy that will not compromise subsequent curative resection. The incisional biopsy tract must be positioned in such a way that it can be removed in continuity with the tumor at subsequent resection because it will have been contaminated by tumor cells. It is important not to open widely any uninvolved tissue planes that could become contaminated with released tumor cells.

The biopsy incision should be orientated to cause the least amount of tension on the skin, which will make the subsequent definitive procedure easier.

Pinch biopsy

Pinch biopsy of lesions affecting natural cavities or a hollow lumen (such as oral and nasal cavities) can be done under direct visualization through endoscopic systems with round-tip biopsy forceps. The technique suffers from limited biopsy sample size and there is a danger of false negative results. This technique is of value for the diagnostic of carcinomas and lymphomas affecting the oropharyngeal, laryngeal and nasal cavities (*q.v.*).

Excisional biopsy

Excisional biopsy is used for small operable lesions for which treatment would not depend on tumor type, and removal may not compromise definitive treatment. The term "excisional biopsy" refers to the removal of the **entire suspected tumor** tissue with little or no margin of surrounding normal tissue. It is more frequently carried out than may necessarily be indicated, but when used on properly selected cases it can be both diagnostic and therapeutic as well as cost effective. A good example would be the removal of a small skin lesion that can be removed with minimal skin tension.

The biopsy site should **never be drained** because the drain tract may be contaminated with tumors if the lesion resected turns out to be a tumor. After an excisional biopsy, the entire tissue should be submitted for histopathologic examination in 10% neutral buffered formalin for diagnosis (and evaluation of surgical margins if it is a neoplastic process) to determine the completeness of the resection.

WORK-UP

After a diagnosis has been reached, a careful physical examination and ancillary diagnostic tests may be undertaken to stage the disease before embarking on treatment. Staging describes the extent of any primary tumor (size, invasion of adjacent tissues, involvement of nerves, blood vessels or lymphatic tissues), site, evidence and sites of metastases (regional, systemic), and the general health status of the patient.

Diagnostic imaging

For tumors surrounded by or attached to critical normal tissues, including bone, blood vessels, nerves, **diagnostic imaging** (*q.v.*) will assist in assessing tumor extent and invasion. This information will help decide whether to pursue treatment or not, and how best to plan surgery and additional treatments. When compared to exploratory surgery, the technique will not have a negative impact on subsequent treatment.

The most common imaging techniques used are plain **radiographs**, **endoscopy**, **ultrasound**, **scintigraphy** and **computed tomography** (CT). **Endoscopy of guttural pouches** (*q.v.*) in horses with melanoma (*q.v.*) allows visualization of the number and size of melanoma masses in the throat area.

Ultrasound images provide information on soft tissue architecture, invasiveness (Doppler) and size that survey radiography can not. For tumors associated with a high risk of metastasis (e.g. lymphomas, carcinomas, melanomas, [*q.v.*]), quality **thoracic radiographs** and **abdominal ultrasound** examination should always be performed before definitive treatment to rule out widespread metastases.

In addition to ultrasonography, **scintigraphy** is now available at most universities and many private referral hospitals. The procedure requires special gamma cameras and the injection of radioactive materials into the bloodstream. The principle of nuclear scintigraphy then lies in increased uptake of specific radioisotopes in **hyperfunctional tumors**. Scintigraphy using **^{99m}Tc pertechnetate** (2.6–3.3 MBq/kg) is commonly used for staging of thyroid tumors (benign and malignant) (*q.v.*). Because of the heavy equipment required and potential radiation hazards, scintigraphy cannot be used in the field.

When available, CT—also known as **computed axial tomography** or "CAT scan"—is ideal for evaluation of tumors of the head and extremities. The procedure requires a dedicated scanner available at most universities and many private referral hospitals with in-house or mobile equipment. The technique allows electronic measurement of the absorption of X-rays by structures within the body and produces images with similar properties to conventional radiographs. It provides images that represent **thin slices** through the body, which eliminates the problem of superimposition of structures that affects conventional radiographs and allows distinction between areas of similar attenuation that would appear the same in conventional radiographs. CT is very accurate for the evaluation of **tumor invasion in bone**. To evaluate soft tissue tumors of the head, **contrast-enhanced CT** (1400–1500 mg of iothalamate/kg, IV) affords sufficient contrast to visualize tumor and normal surrounding tissues, providing information on size and invasiveness.

Clinical laboratory

Routine hematologic, serum biochemical evaluations and urinalysis do not reveal any abnormalities in most horses with cutaneous or subcutaneous tumors that are otherwise healthy. However, laboratory screens are useful to estimate patient tolerance of general anesthesia, extensive surgery or chemotherapy, and to recognize the presence of paraneoplastic syndromes (such as cachexia, anemia, leukocytosis, hyperproteinemia, fever, ectopic hormone production [hypercalcemia] or neurologic abnormalities secondary to endocrine, fluid and electrolyte imbalance). A screen is recommended, particularly for **older horses** with **concurrent disease** (**such as chronic renal or gastrointestinal disease**, *q.v.*) and horses with tumors affecting the endocrine, gastrointestinal and hematopoietic systems.

Careful examination of **peripheral blood** count and cell morphology as well as **bone marrow** cytologic evaluation is of particular importance to rule out systemic or visceral dissemination of **lymphomas** (*q.v.*). **Bone marrow aspiration** or biopsy is very important in clinical staging of horses with lymphoma to rule out systemic or visceral dissemination and in horses with hematologic abnormalities such as anemia, lymphocytosis, peripheral lymphocyte atypia or other peripheral cytopenias (*q.v.*).

PRINCIPLES OF TREATMENT

The stage of the disease, treatment cost and availability, and veterinarian's skills must be taken into account before formulating the treatment plan and goals. The clinician should know his or her competence and offer the client a referral to a specialist center if one is within reasonable access. Unless the primary tumor can be removed in toto, it is usually preferable to perform a biopsy of the site (*q.v.*), visualize the extent of the tumor, and then consider the treatment options with the help of a specialist. The clinician should always refrain from undertaking heroic procedures that could compromise the efficacy of other treatments.

Treatments can be broadly grouped into **ablative** (surgery, laser vaporization, cryotherapy), **cytotoxic** (radiation therapy, chemotherapy) and **biologic** (immunotherapy) modalities. Treatments directed at the primary tumor mass include ablative treatments, radiation therapy and local chemotherapy; those directed at the tumor and metastases or multicentric tumors include systemic chemotherapy and immunotherapy.

ABLATIVE TREATMENTS

The goal of ablative treatments is to remove **all tissues** that may contain tumor cells. The treatments are not selective because a cuff of surrounding normal tissue containing microscopic disease is removed with a cold blade or destroyed physically or chemically.

Surgery

Introduction

Surgery has a central role in the diagnosis, treatment and reconstruction of anatomic defects after other treatment modalities. It may be curative, used alone or in combination with other (adjuvant) treatments; it may also be palliative in some cases. Complete surgical removal of localized tumors cures more patients than any other form of treatment. The **first surgery** has the best chance of cure because recurring tumors often appear histologically and biologically more aggressive, and they require wider excision than for the initial tumor.

The surgical technique to be used depends on the tumor volume, histology and location. Surgical failures occur because, despite the most radical procedures, not all microscopic disease is removed or because there is poor surgical technique, i.e. tumor cells may be shed into the operative field from the tumor itself or from the surgeon's gloves or instruments.

Basic principles

The **basic principles** of oncologic surgery include minimal tumor manipulation, en bloc resection of gross tumor mass, early vascular ligation, flushing of the operative wound with warm saline (to wash away exfoliated cells), and frequent changes of gloves and instruments.

Radical operations may eliminate **tumor microextensions** but the price may be **anatomic deformity** and perhaps **physiologic impairment**. It also

must be remembered that there may not be a surgical advantage in excessive removal of surrounding normal tissues that may not contain any tumor. On the other hand, partial removal (**debulking surgery**) of a tumor achieves little because it does not bring residual disease to the microscopic level. It should be remembered that removing 99.9% of a 1 cm tumor (1×10^9) still leaves a large number of tumor cells behind (1×10^6). Grossly **incomplete resections** may actually reduce the efficacy of adjuvant treatments.

Cold blade excision

Standard **cold blade excision** remains the treatment of choice for the majority of equine accessible solid tumors. However, a clinician can never be certain of an incomplete excision and after an **apparent complete resection** it is critical that the surgical margins be submitted for **histopathologic evaluation**. It is best if the surgeon marks the specimen (fine suture on questionable edges) or submits margins in a separate container to help the pathologist identify and evaluate the surgical margins to determine the completeness of the surgical resection. A **detailed history** should always accompany the biopsy specimen and it is useful if the clinician **maps the specimen** if it has been procured from an anatomically complex area.

Adjuvant treatment or re-operation of the entire previous surgical site is warranted when evidence of **microscopic residual disease** (close or positive surgical margins) is present. Adjuvant treatment after histologically complete surgical resection may be recommended when the risk of local recurrence is high after surgery (30% for sarcoids [*q.v.*] and other soft issue tumors) and when tumor recurrence may be difficult to manage because of tumor location.

Cryotherapy and laser surgery

Alternate modalities including **cryotherapy and laser surgery** have **no oncologic benefits** over a well-planned conventional surgery. Cellular death results from the controlled use of cold temperature with cryotherapy while it is induced by heat with laser surgery. Both treatments should not be used in the treatment of tumors because both heat and cold **diffusion is very limited** in living tissue, and target temperatures may not be achieved in tumors and tumor margins without producing significant **normal tissue damage**. These treatments do not allow histopathologic evaluation of surgical margins to assess the quality of the procedure. In addition, **excessive scarring** or healing delay following treatment may delay objective diagnosis until obvious tumor recurrence.

CYTOTOXIC TREATMENTS

Antineoplastic chemotherapy

Introduction

Until recently, the use of antineoplastic agents found limited applications in equine oncology, primarily due to drug cost and potential toxicity. However, access to low cost generic drugs and the development of new routes of administration designed to increase the therapeutic benefit have resulted in new

treatment options. Treatment using antineoplastic drugs can be divided into **local** and **systemic** chemotherapy. Local chemotherapy, including topical and intratumoral chemotherapy, has been developed to improve drug therapeutic index and decrease treatment costs for horses with accessible tumors.

Local chemotherapy

Topical application of ointments containing antineoplastic or caustic drugs has limited applications because of:

1. The **significant biohazard** by contact or inhalation associated with repeated applications by the owner or veterinarian
2. **Poor diffusion and inadequate distribution** of currently available drugs from the surface to the deep margins of a tumor
3. **Poor cosmetic and functional results**.

Because drugs do not diffuse more than 5 mm in normal or tumor tissues before they are reabsorbed in the bloodstream, topical administration of antineoplastic drugs often results in a tumor-free surface, giving the **false sense of efficacy**, which is followed by **tumor recurrence** from the deep margins of the tumor.

Intratumoral treatment

Intratumoral chemotherapy has been developed to improve drug distribution in the tumor and tumor bed and eliminate the risk of biohazard. Treatment is safe to attendants because the drug is administered directly into the tumor, and it is safe for the horse because the doses administered are approximately one fiftieth of the systemic dosage.

Several drugs have shown activity against specific tumor types. A slow-release formulation of *cis*-diaminedichloroplatinum (**cisplatin**) in a viscous–fluid oily formulation (3.3 mg cisplatin per mL of mixture) is the **most effective** against all cutaneous tumor types including **sarcoid of all clinical types**, **carcinomas**, **fibrosarcomas** and most **soft tissue sarcomas**, and **solitary melanomas and lymphomas** (B and T cell) (*q.v.*). Medical grade or chemically pure cisplatin is widely available. The treatment consists of four intratumoral administrations at 2 wk intervals. It is most effective when used **in combination with surgery**. It can be used in horses, donkeys and mules, and is safe for use in stallions and pregnant mares. To administer the drug, a 22–25 G needle mounted on a Luer-lock syringe is inserted to the desired length into tissue, and the drug is injected at a **constant flow** while the needle is withdrawn to provide uniform dose distribution in the target volume.

The target volume of tissue to be treated includes **all visible tumor** and a **margin of normal tissue** of 1–2 cm (as a function of tumor type and tumor size). It is critical to treat a margin of normal tissue both laterally and at a depth to kill microscopic deposits of tumor cells extending into apparently normal tissue surrounding the tumor. The volume of tissue to be treated around the gross tumor, i.e. the **biologic margin**, is the same as would have to be resected to obtain a histologically complete surgical resection.

The planning of the pattern of injections (0.6–0.8 cm apart) is **critical** to achieve uniform dose distribution. Depending on the shape and accessibility of the lesion, the target volume is injected via multiple sites using a **parallel-row**

technique or **field-block technique.** Multiple planes of injections may be needed for large tumor volumes using parallel or orthogonal axes of injection. The treatment field size should always remain the same during the course of treatment and the volume of tissue treated should not be decreased if a reduction in tumor size is observed.

Systemic chemotherapy

Most **systemic chemotherapy** protocols in horses rely on the use of a single agent. The benefit of using **combination chemotherapy** protocols has been shown in people and small animals. However, combining drugs at their maximum tolerable dose is still in its infancy in equine oncology. Drugs used as single agents include steroids, doxorubicin, L-asparaginase (400 IU/kg), cyclophosphamide and cytosine arabinoside. Glucocorticoid hormones and synthetic derivatives (prednisolone, dexamethasone) are used at high doses for their immunosuppressive properties (*q.v.*).

Immunosuppression (*q.v.*) is the basis for treatment of various lymphoproliferative diseases (*q.v.*). **Dexamethasone** (starting dose of 50 mg/day, tapering dosage over 2 wk) is used for **multiple cutaneous lymphomas** during an active growth phase (which is often seasonal). **Doxorubicin** (60–80 mg/m^2, 6 cycles at 3 wk intervals) is used alone for **advanced carcinomas** or in combination with **prednisolone** for **multicentric lymphomas** and **leukemias** (*q.v.*).

The only **combination drug protocol** used commonly for **metastatic lymphoma** and **lymphocytic leukemias** is known as **COAP**: **cyclophosphamide** (200 mg/m^2, IV weekly, ×4–6 weeks), **vincristine** (0.75–1 mg/m^2, IV weekly, ×6 weeks), **cytosine arabinoside** (100 mg/m^2, slow IV/6–12 h, 3 times a week, ×6 weeks) and **prednisolone** (1 mg/kg, PO every other day, ×2 weeks). Use of these drugs requires appropriate medical training for drug preparation and administration, and management of drug toxicity in horses.

Radiotherapy

Radiation therapy is the use of ionizing radiation in the treatment of **localized tumors**. It was first described for the treatment of equine cutaneous tumors in 1906. Radiotherapy techniques vary considerably based on the tissue involved and adjacent normal structures. Radiation therapy is currently only available at referral practices, e.g. at universities and large referral private practices, because of the cost of equipment, potential radiation hazards and requirements for a radiation use license.

There are two methods of irradiation available for large animals: teletherapy (also called external beam therapy) and brachytherapy.

Teletherapy

Teletherapy is a technique in which the **source of radiation** is at some distance (80–100 cm) from the target tissue. The distance allows the delivery of homogeneous doses of radiation to **large and deep-seated tumors**. However, the technique also results in similar doses being applied to surrounding normal tissues in the path of the radiation beam. The higher the energy of the radiation, the more significant is the sparing of superficial structures (i.e. skin and subcutaneous tissues) and the deeper is the penetration of the beam.

High energy radiation, including X-rays produced by linear accelerators and gamma-rays produced by telecobalt units, is used for treatment of extensive or **deep-seated tumors** and **tumors invading bone**. The total radiation dose is given as a series of small, equally sized doses termed **dose fractions** to spare normal tissue in the radiation path.

All treatments are done while the horse is under **short-term general anesthesia**, which enables accurate positioning and immobilization. Anesthesia protocols are undertaken according to preference and equipment, but a safe protocol for a series of anesthesias (8–12) in an 11 month period might include: premedication with xylazine (0.3–1 mg/kg, IV), induction with ketamine (2.2 mg/kg) plus diazepam (Valium) (0.1 mg/kg) and maintenance with a chemical anesthetic (triple drip, guaifenesin-ketamine-xylazine or GKX) or inhalant anesthetic (isoflurane).

The total dose of radiation (42–48 Gy; 1 Gy = 100 rad) is given in 7–12 dose fractions of 4–6 Gy given two or three times a week over 3–4 wk.

The increased availability of high energy radiation therapy units in veterinary medicine has expanded the use of teletherapy in equine oncology. Teletherapy is very effective for tumors of the **oral and nasal cavity** with bony involvement. Other tumors that can be successfully treated include **inoperable cutaneous and subcutaneous tumors** of the extremities affecting critical tendons, blood vessels or nerves (e.g. squamous cell carcinoma, angiosarcoma, sarcoid [*q.v.*]) and tumors involving large areas or multiple lesions present at the same time in a small area.

Brachytherapy

Brachytherapy is a technique in which **sealed** radioactive sources are **applied directly** to the area to be treated. The short distance between the source of irradiation and the tumor provides a high radiation dose to the tumor-bearing structures while sparing uninvolved adjacent normal tissues because of the rapid decrease in dose as distance from the radiation source increases.

When radioactive sources (usually **iridium-192 in seeds or wire**) are **implanted directly** into the tissues, the treatment technique is called interstitial brachytherapy or **curietherapy**. Remote afterloading of the radiation sources entirely eliminates radiation hazards to personnel and shortens treatment times.

Treatments are performed on an outpatient basis in referral specialist centers, and there is no residual radiation when the horse is discharged. The radiation dose is usually delivered in 2–4 dose fractions at 1 wk intervals while the horse is under general anesthesia.

Brachytherapy is used successfully for any **cutaneous lesion that cannot be completely excised**. Treatment is most suitable for **squamous cell carcinomas**, **sarcoids** and **soft tissue sarcomas** of the head, distal extremities and genitalia.

Plesiotherapy

When radioactive sources are applied onto the tumor surface, the technique is called surface brachytherapy or **plesiotherapy**. Using an ophthalmic applicator, radioactive strontium-90 is mounted on a stainless steel shaft fitted with a Lucite beta shield to emit a high energy beam of electrons (maximum range in

tissue: 3 mm). One application (200 Gy) while the horse is anesthetized or heavily sedated is usually sufficient.

Treatment is often curative for **superficial lesions of the skin**, including **carcinoma** in situ and early **squamous cell carcinoma,** and tumors of the **eyelid conjunctiva** and **corneoscleral tissues**, including squamous cell carcinomas and melanomas (*q.v.*).

Side effects

Side effects associated with radiotherapy are usually mild and self-limiting and range from **local alopecia** to **erythema** and **minor erosion** of the skin. In horses treated with high radiation doses to the skin or mucous membranes, more severe and **extensive skin reactions** including moist desquamation and necrosis may occur. Management of these reactions is largely symptomatic but should include cleansing the tissue with a 1.5% solution of hydrogen peroxide, systemic antibiotics (trimethoprim–sulfamethoxazole) and flunixin to minimize infection and inflammation.

BIOLOGIC TREATMENT (IMMUNOTHERAPY)

General

Immunotherapy refers to treatments that alter the host–tumor relationship and improve the ability of the host to reject the tumor. Antitumor effects are produced primarily through restoration or **stimulation of immunologic activity**. The only attempt at **restorative immunotherapy** is the use of **cimetidine** for **melanomas** (*q.v.*). Unfortunately, cimetidine treatment has shown modest to no therapeutic benefit and at a dosage of 5 mg/kg t.i.d. has been shown to have little if any effect.

Stimulation of the host's intrinsic immune system can be achieved either through non-specific immunostimulation or through immunization against tumor-associated antigen present on tumor cells. Many **non-specific immunostimulants** have been evaluated in horses including microorganisms (bacillus Calmette–Guérin, *Propionibacter acnes*) and their purified cell wall products (cell wall skeletons and extracts), and plant extracts (acemannan). These products have no direct cytotoxic effects but tumor cells are killed as bystanders at the site of inflammation associated with the delayed type hypersensitivity to the microorganism antigens.

Certainly, convincing results have been shown with the **bacillus Calmette–Guérin (BCG) derivative** (*q.v.*). Treatment consists of **multiple injections into the tumor mass** and tumor bed to ensure complete infiltration of the target volume. The number of treatments ranges from 1 to 6, given at 1–2 wk intervals. Treatment with live freeze-dried BCG is not recommended because side effects from administration of live BCG, including anaphylaxis, fever, diarrhea, laminitis, nodular lymphangitis and death, outweigh the therapeutic benefits and alternative treatments are available. **BCG cell wall extracts** are less toxic and have been shown to be effective against small (<2 cm) **periocular sarcoids** (*q.v.*) in immunocompetent horses. The potential for significant adverse reactions should, however, always be considered before embarking on BCG immunotherapy.

Active tumor-specific immunotherapy

Active tumor-specific immunotherapy consists of immunization with **tumor-specific antigens** or tumor cells carrying these antigens. Partial tumor response to autologous vaccines using antigen-augmented live tumor cells has been documented in horses with **lymphoma** and **melanomas** (*q.v.*). Treatment includes a series of 6–12 intradermal injections of gamma-sterilized autologous tumor cells at 1–2 wk intervals. A polyvalent allogeneic antigen-supplemented vaccine prepared from highly immunogenic melanoma cell lines has shown encouraging results in horses with **multicentric melanomas** (*q.v.*).

Chapter 21

Anesthesiology

R. S. Jones (Consultant Editor)

Chapter contents

INTRODUCTION

When considering anesthesia in domestic animals it is well known that horses, of all of the common species, have by far the **highest morbidity and mortality rates**. While mortality rates appear to have been reduced over the last 30 years, when reasonably accurate records have been kept, from approximately 5% to a current figure of 1.6%, it is unlikely that any further significant reduction will occur in the near future due to a number of factors, which include the conduct of more complex surgery and the associated longer duration of anesthesia. Recent figures show an overall mortality rate of 1.8%, but when colic surgery and emergency obstetric procedures were excluded mortality rate fell to 0.8%. However, the mortality for colic surgery remains in the region of 8%.

Anesthetic risk is increased by a number of factors that include, in addition to colic surgery, extremes of age, increased duration of anesthesia, and those occasions when procedures are performed outside what is considered to be normal working hours. The major causes of death are **cardiac arrest** (*q.v.*) or **postoperative cardiovascular collapse**, and fractures with myopathy. Abdominal conditions, respiratory obstruction and spinal cord malacia (*q.v.*) are lesser causes.

GENERAL CONSIDERATIONS IN ANESTHETIZING HORSES

Horses present **special problems** for general anesthesia due to their weight, breed, temperament and specific anatomy and physiology. Size determines the ease with which horses can be handled both in the conscious and anesthetized states. Breed and temperament are often interrelated. This is well illustrated by a comparison of the nervous young Thoroughbred with the larger and more phlegmatic draft breeds.

Horses are relatively heavy when compared with most of the other domestic species. While the average Thoroughbred weighs approximately 450 kg, it is not uncommon for equines weighing up to 800 kg to be presented for anesthesia. It is very rare for even very large draft horses to weigh >1000 kg. Heavyweight horses are more difficult to position both for surgery and to recover from anesthesia. The greater the **weight**, the greater the predisposition to muscle and/or nerve damage associated with general anesthesia.

Post-anesthetic myopathy (*q.v.*) is produced by **inadequate perfusion** of muscle resulting in ischemia. It is a multifactorial condition and its etiology is not completely understood. However, its incidence can be reduced by:

1. Ensuring that the **duration of anesthesia** is kept to a minimum commensurate with the performance of the procedure
2. Maintaining the **mean arterial pressure** >70 mmHg
3. The choice of suitable material for **padding** of the operating table surface
4. **Careful positioning** of the patient.

Treatment of myopathy is mainly symptomatic with analgesia and sedation plus adequate fluid intake and careful nursing.

Post-anesthetic neuropathy is produced by pressure on the nerve, stretching of the nerve, trauma and ischemia. It occurs in a number of superficial nerves including the facial, femoral and radial. Prevention and treatment are similar to that for myopathy although complete recovery may be prolonged. Euthanasia may be indicated.

In addition to causing musculoskeletal problems, the combination of recumbency and general anesthesia has profound effects on the **cardiovascular** and **respiratory** systems. **Dorsal recumbency** is the most undesirable position but pragmatism dictates that it is often essential to place anesthetized horses in that position for the performance of abdominal surgery.

The **arterial partial pressure of oxygen** is influenced by the size and position of the animal but is relatively uninfluenced by the respiratory depression associated with general anesthesia. Horses are likely to develop **alveolar–arterial (A-a) gradients** during general anesthesia, and these appear to be more marked with inhalational agents. A-a gradients occur when there is a difference between the oxygen tensions (pO_2) in the lung alveoli (**A**) and the arterial circulation (**a**). A-a gradients are the result of a number of factors. The degree of A-a gradient does not appear to differ in those animals that breathe spontaneously compared to those that are subjected to intermittent positive pressure ventilation (IPPV). Factors that may contribute to the development of A-a gradients include pulmonary diffusion defects, progressive atelectasis, right to left intrapulmonary vascular shunts, redistribution of pulmonary blood

flow relative to ventilation and a reduction in cardiac output without a reduction in tissue oxygen consumption.

Pulmonary diffusion impairment is not considered to be a cause of hypoxemia in anesthetized horses but it does develop in the dependent areas of the lungs. Venous admixture is probably due to a mismatching of ventilation and perfusion of the lungs. Normally **cardiac output** is reduced under general anesthesia but oxygen consumption remains relatively unaltered and so it is unlikely to contribute to the A-a gradients.

PREPARATION FOR GENERAL ANESTHESIA

A full and thorough **clinical examination** is essential before administering a general anesthetic to a horse. It should preferably be carried out **at least 24 h** prior to anesthesia to enable any further tests and laboratory examinations to be performed before induction. A full and accurate **history** must be obtained, although this can be difficult, particularly when horses are transported to referral centers, often by a third party.

There are a number of findings that require particular attention. The relatively high incidence of **equine polysaccharide storage disease** (*q.v.*) in the draft breeds increases the risk of postoperative myopathy and this will require further dialogue with the person responsible for the horse. This can, of course, be done during the full discussion of the risks of the procedure and of general anesthesia when obtaining consent. **Informed consent** is crucial before anesthetizing any horse and should only be neglected in an extreme emergency even though it may be necessary to defer a non-urgent procedure.

A thorough investigation of any concurrent or proposed medication is necessary, and any potential drug interactions should be considered. **Oral medication** should never be administered after pre-anesthetic drugs have been given as some medications, particularly of the **paste formulation**, may be retained in the oropharynx or the esophagus. There is then a strong likelihood that they will be regurgitated and/or pushed into the trachea during induction of anesthesia and endotracheal intubation.

Aminoglycoside antibiotics such as gentamicin or neomycin may produce **neuromuscular blockade** and depress pulmonary ventilation and should not be administered immediately prior to or during anesthesia. Particular caution is needed with gentamicin in renally compromised animals. The **IV injection of penicillin** can cause **hypotension** and should also be avoided before or during anesthesia.

While **non-steroidal anti-inflammatory drugs (NSAIDs)** (*q.v.*) have a number of undesirable side effects, particularly when administered over a prolonged period, they are used extensively in equine anesthesia and at other times to provide analgesia (*q.v.*). NSAIDs are best administered by slow IV injection. Side effects can include gastric ulceration, diarrhea and potentiation of protein bound anesthetic drugs by displacement of these agents from their protein binding sites.

General bodily condition should be considered as obesity can influence respiratory movements, and both obesity and extreme thinness may interfere with the disposition of drugs in the body. A history of **recent trauma** should

be thoroughly investigated and during physical examination special attention should be directed to the possible presence of such common conditions as diaphragmatic or bladder rupture and to hemorrhage. **Hemorrhage**, particularly when it is from the nose or associated with trauma and accompanied by tachycardia, will suggest that it is severe and usually will necessitate treatment with **circulatory blood volume expanders** (*q.v.*).

Horses with **chronic lung disease** should have a thorough physical examination of the thorax and any diagnostic aids such as radiography or ultrasound should be utilized when considered appropriate and available. Horses with respiratory infections should be treated with vigorous antibiotic therapy and appropriate ancillary therapy. Anesthesia should be delayed for **not less than 3 weeks** unless emergency surgery is indicated.

Cardiovascular disease (*q.v.*) is an extremely important consideration when assessing anesthetic risk and fitness to undergo general anesthesia. It is of extreme importance when it is severe enough to **restrict exercise tolerance** (*q.v.*) and/or accompanied by **cardiac dysrhythmias** (*q.v.*). All of these animals will require full and further investigation utilizing such diagnostic aids as electrocardiography and echocardiography.

The proposed anesthetic technique may well need to be modified to suit the condition of the patient. In some instances it will be necessary to **defer anesthesia** to initiate suitable therapy in order to improve the patient's condition.

When presented with a horse as an emergency with an **acute gastrointestinal condition**, the relief of pain is often the prime consideration. Analgesia and analgesic drugs are discussed elsewhere (*q.v.*). These animals may also be at risk from **endotoxic shock** (*q.v.*) and from **impaired ventilation** due to the **abdominal distension**.

Pre-anesthetic assessment should include measurement of packed cell volume (PCV) and total protein (TP) plus blood gas analysis.

It is often a matter of fine judgment as to how long anesthesia and surgery should be delayed while an attempt is made to correct any serious abnormality and improve the patient's condition. Except in an emergency it is desirable to **starve** horses of food for 12–18 h before anesthesia, and **water** should be withheld for 2 h. It is still a matter of debate as to whether **horses in training** should be "let down" for a period of 7–10 days before anesthesia. The general consensus is that it should be done wherever possible. The **shoes** should be removed before anesthesia and the **mouth flushed with water** to remove any solid food material. A **padded head collar** should be used to reduce the risk of damage to the poll and the facial nerves.

Horses should be **weighed** wherever possible but formulae and tape measures may be used in the absence of a weigh scales and provide a reasonably accurate estimate of a horse's weight. (See also page 173.)

PREMEDICATION, SEDATION AND CHEMICAL RESTRAINT

DEFINITIONS

A number of drugs are available for the purposes of premedication, sedation and restraint but, as there is some confusion over the terminology used to

Box 21.1 Doses of sedative drugs and their combinations with opioids

Acepromazine	0.03–0.1 mg/kg IV or IM
Detomidine	0.005–0.002 mg/kg IV or IM
Diazepam	0.01–0.02 mg/kg IV only
Romifidine	0.01–0.02 mg/kg IV or IM
Xylazine	0.25–1.1 mg/kg IV or IM

All can be combined with the following opioids:

Butorphanol	0.02–0.03 mg/kg IV or IM
Methadone	0.1 mg/kg IV or IM
Morphine	0.05–0.2 mg/kg IV or IM
Pethidine	1–5 mg/kg IM only

describe the various classes of drugs and their effects in horses, the following definitions are used here. A **hypnotic** depresses the central nervous system and tends to produce sleep; these agents are rarely used in horses. A **sedative** is a drug that relieves anxiety and produces a state of drowsiness. Many drugs appear to be both **hypnotic and sedative** with dose related effects. Chloral hydrate and xylazine are typical examples in the horse. A **tranquilizer** or ataractic drug is one that relieves anxiety and produces a variable degree of sedation. Three categories of tranquilizer are described: **hypnotic/sedatives, antipsychotics** and **anxiolytics**. Benzodiazepines are both anxiolytics and sedative/hypnotics. Antipsychotics are also known as neuroleptics and are typified by the butyrophenones and the phenothiazines.

Four main groups of drugs are used to premedicate and sedate horses (Box 21.1). These are phenothiazines, benzodiazepines, α_2-adrenoceptor agonists and anticholinergics.

PHENOTHIAZINES

There are a number of compounds in this group but only **acepromazine maleate** is generally licensed for use in horses. Acepromazine (ACP) is available as an injectable form (10 mg/mL), as a paste, and tablets (25 mg). It has a wide spectrum of effects in horses.

The response to a given dose of ACP is somewhat **unpredictable** but, in general, a low dose will produce tranquilization or a calming effect while higher doses are required for sedation. It is recognized that sedation only occurs in 60–70% of horses. Larger doses tend not to increase the degree of sedation but to prolong the duration of action. In clinical doses there is very little effect on respiration but **hypotension** does occur. While this may be of minor significance in normal animals, it should be avoided, or the dose reduced significantly, in hypovolemic animals.

ACP produces muscular relaxation, which appears more marked when it is given IV. In males this produces **relaxation of the retractor penis muscle** and hence protrusion of the penis. The penis is normally flaccid but there have

been a few reports of **priapism** (sustained erection) (*q.v.*). **Penile protrusion** is normally of short duration but if it is prolonged it should be treated by massage, compression and lubrication. It is extremely important to avoid damage to the penis, and support should be provided to keep the penis as close to the body wall as possible.

BENZODIAZEPINES

The use of benzodiazepines for sedation in adult horses is limited. However, they do produce sedation in foals and are used at induction of anesthesia, particularly with **ketamine** (*q.v.*). They tend to produce excitement when they are used as sole agents, but have minimal cardiovascular and respiratory effects. The most commonly used agent is **diazepam** (Box 21.1)**.**

α_2-ADRENOCEPTOR AGONISTS

There are three drugs in this group that are used in horses. They are xylazine, detomidine and romifidine and they all have common properties but different durations of action. For dose rates, see Box 21.1.

One of the most important actions of these drugs is on the cardiovascular system. **Cardiac output** is reduced and a few minutes after IV injection there is a transient rise in arterial blood pressure, which then falls to below the original resting level. The duration of this effect is drug and dose dependent. The response to the hypertension is a **profound bradycardia**, which is accompanied by atrioventricular and sinoatrial block (*q.v.*). Heart block is at its most intense in the first few minutes after IV injection and tends to disappear as the heart rate increases. However, these effects are variable and depend on a number of factors including the drug, its route of administration and the individual animal. Respiratory effects are minimal in normal healthy animals.

The main effects on the central nervous system are analgesia and sedation. They produce an **increase in urine production** mainly due to inhibition of antidiuretic hormone and probably by hyperglycemia.

All three agents produce an increase in **uterine contractions** and in intrauterine pressure although firm evidence on the significance of these actions is lacking. It appears that the degree of these effects varies between agents and possibly between individual animals. As a precaution it is strongly recommended that the drugs should **not** be administered during the last 3 mo of pregnancy.

They produce hypothermia, which is only of significance in **foals,** but they also produce sweating in some animals.

There have been reports that the administration of **detomidine** in conjunction with **potentiated sulfonamides** caused death in horses but precise information on the possible mechanism is not clear. It is therefore advisable not to use any of the drugs in conjunction with potentiated sulfonamides.

Xylazine hydrochloride is the oldest of the drugs in this group. It can be administered either IM or IV, and after IV injection the effects are evident within 2 min. The head is lowered and the eyelids and lips droop. While horses may sway on their feet, cross their legs and knuckle on their forelimbs, they usually remain standing and do not exhibit any signs of panic. Sedation reaches a maximum within 5 min and lasts 30–60 min. Xylazine has good

analgesic properties, which can be particularly useful in horses with colic. The animals remain very **sensitive to touch** and will often respond by kicking even though they appear to be heavily sedated.

Detomidine hydrochloride is a very potent agent and can be administered by both the IM and IV routes. The nature of the sedation is very similar to that produced by xylazine but of longer duration, 90–100 min.

Romifidine has similar properties to the other two agents with a duration of action of up to 2 h. It is suggested that the head does not droop so low and that there is less ataxia with this drug than with the other two.

Drugs in this group have also been administered by the **epidural route** (*q.v.*) to provide analgesia, either alone or in combination with lidocaine or morphine.

A number of α_2-adrenoceptor antagonists are available but none is licensed for use in horses. The most commonly used agent is **atipamezole hydrochloride**. Reversal is not usually necessary in horses except when adverse reactions occur or excessive ataxia is produced. Atipamezole will antagonize the actions of all of the drugs in the group by displacing them from the receptors. A dose of 50 μg/kg is administered slowly IV and may need to be repeated. Slow administration is essential as a rapid injection rate may produce a sudden hypotension and reflex bradycardia. The drug is unlikely to be abused in competition horses as the effects are unlikely to affect performance

Analgesia and the analgesic drugs have been discussed elsewhere (*q.v.*). Analgesic drugs are often used in conjunction with α_2-adrenoceptor agonists to improve the quality and reliability of sedation. The most commonly used opioids for this purpose are **butorphanol** and **methadone**. Acepromazine is sometimes added to the combination in relatively small doses. The doses and routes of administration are discussed in Box 21.1. The most commonly used combinations are either of the above drugs with the α_2 agent of choice, depending mainly on the duration of action required.

ANTICHOLINERGIC DRUGS

Anticholinergic drugs are not used routinely in equine anesthesia. They may be used occasionally during anesthesia to treat **profound bradycardia** (*q.v.*), and either **atropine** (0.01–0.02 mg/kg IV) or **glycopyrrolate** (0.005–0.01 mg/kg IV) is the drug of choice. Atropine has a prolonged duration of action of many hours in the horse and may produce gastrointestinal problems such as impaction colic, particularly of the cecum. Some reports suggest close monitoring of the patient at a heart rate of 20 bpm and if it falls further atropine is given at 0.001 mg/kg (0.5 mg for a 500 kg horse).

INDUCTION OF ANESTHESIA

GENERAL PRINCIPLES

Following suitable preparation and premedication, a catheter is inserted into the jugular vein. The catheter may also be inserted before the horse is premedicated. It is important to observe strict aseptic precautions when inserting

catheters into veins. A fine gauge needle or a dental syringe is used to place a small "bleb" of local anesthetic solution into the skin over the area of the vein where the catheter is to be inserted. A number of different types and sizes of catheters are available, but it is usual to select a 12 or 14 gauge 10 cm long "over the needle" catheter for the induction of anesthesia and for fluid therapy.

Catheters are introduced into the vein in either an upward or downward direction. The upward direction is usually easier to place, reducing the risks of technical problems such as air embolism. Care must be taken not to introduce the catheter into the **carotid artery**. Catheters are normally fixed in position by sutures or with "superglue". Once the catheter is in place it should be flushed with **heparinized saline** and the end occluded with either a three-way tap or a cap. It should also be flushed after each injection.

An ideal method of induction of anesthesia has not yet been described and a technique should be selected on the basis of a number of factors including the size of the horse, its temperament, the available facilities and, most importantly, the indication for general anesthesia. It is not advisable to anesthetize any horse without facilities for resuscitation being readily available, with particular emphasis on **oxygen** and a means of administering it, and drugs commonly used for **cardiac resuscitation** such as epinephrine (adrenaline) and lidocaine.

Facilities for induction of anesthesia can vary from the very basic to sophisticated tilting tables. Until relatively recently it was common to anesthetize horses in open fields or paddocks but with the development of more advanced surgical techniques, some of which are of long duration, this is no longer the case. It is still acceptable for simple and short-duration procedures to be performed in the open provided that **adequate facilities** are available for anesthesia, resuscitation and recovery.

When a significant number of horses are being anesthetized, it is appropriate for induction to be performed in a **padded box**, which also serves as a recovery area. The **restraint** applied to a horse at induction of anesthesia will often be governed by the available facilities. When the horse is allowed to fall to the floor or ground at induction, it is normal practice to have one or two people with rope(s) attached to the head collar to control the fall by keeping the head low and gently pushing the horse backwards. In a padded box, the rear end of the horse may be placed against a wall or in a corner, allowing the animal to slide down the wall to the floor. Padded gates are sometimes available in induction boxes and facilitate the restraint of the horse during induction. When **tilting tables** are used, the premedicated horse is stood and restrained against the vertical table; the induction agents are injected IV and the table rotated to the horizontal position.

Normally anesthesia is induced in horses using an IV technique, commonly based on the combination of a sedative followed by a barbiturate or a dissociative agent. In addition, a drug that provides muscular relaxation such as **succinylcholine** or **guaifenesin** may also be used. A variety of drug combinations have been described and the choice is often a matter of personal preference. The various combinations of drugs in common usage, with their dosages, are shown in Box 21.2.

Following the injection of the induction agent it is important to restrain the head, as described above, to prevent it being raised and the horse falling over backwards.

Box 21.2 Doses of some common premedicant and induction agents

Acepromazine 0.05–0.1 mg/kg IM	then	thiopental 10 mg/kg IV
Xylazine 1 mg/kg IV	then	thiopental 10 mg/kg IV
Detomidine 0.01 mg/kg IV *or* romifidine 0.08–0.1 mg/kg IV	then	ketamine 2.2 mg/kg IV
Xylazine 1 mg/kg IV	then	guaifenesin infused until ataxia
Detomidine 0.01 mg/kg IV	then	thiopental 5 mg/kg IV *or*
Romifidine 0.08–0.1 mg/kg IV	then	ketamine 1.5 mg/kg IV

THIOPENTAL SODIUM

Thiopental is commonly used to induce anesthesia in horses. The dose depends on the degree of sedation produced by the **premedication** (*q.v.*) and on any adjunctive agents such as guaifenesin that may be used.

Recovery from thiopental anesthesia is more dependent on its redistribution within the body than its elimination from it. Hence, in general, the lower the dose, the better the quality of recovery.

Following **acepromazine premedication**, thiopental will produce recumbency in 25–30 s, and recovery to the standing position will occur in 35–40 min. **α_2-Adrenoceptor agonists**, such as detomidine or xylazine, will enable a reduced dose of thiopental to be used and will slow the induction time. Recovery time will be similar to that with acepromazine but the quality of the recovery will usually be better.

Thiopental is often administered with the centrally acting muscle relaxant **guaifenesin**. After premedication, guaifenesin is infused IV until the horse becomes ataxic, at which stage a bolus of thiopental is given to induce anesthesia. Under some circumstances a mixture of the drugs can be infused but this provides less control over the induction. For dose rates, see Box 21.2.

KETAMINE HYDROCHLORIDE

Ketamine is a **dissociative agent** that produces profound analgesia combined with a "light sleep" and tends to produce stimulation of the central nervous system and muscle rigidity when it is administered alone. Suitable drugs must be used for **premedication** to offset these latter effects. Drugs of choice are the α_2-adrenoceptor agonists and/or the benzodiazepines. Ketamine should never be given alone.

Commonly, **xylazine** or one of the other drugs in the group is administered IV and there is a time lag until signs of sedation are obvious, around 5 min. **Diazepam** is then injected, followed immediately by a **ketamine bolus**. Induction of anesthesia and recumbency follow in 2–3 min. The technique normally produces an excellent and well-controlled induction, and while recovery can be **abrupt** it is usually of good quality. Ketamine may also be used with **guaifenesin** in a similar manner to thiopental. For dose rates, see Box 21.2.

INDUCTION IN FOALS

Anesthetic induction in foals is normally performed with a volatile anesthetic agent (*q.v.*). Halothane or isoflurane is vaporized with oxygen or oxygen/nitrous oxide and administered by facemask, by an endotracheal tube introduced nasally, or by nasal insufflation with a narrow bore tube. In the vast majority of animals manual restraint is often sufficient to enable the procedure to be performed. However, small doses of **xylazine** or **pethidine** may be administered IM to produce sedation. In the vast majority of cases the mare should be sedated and kept with the foal until induction of anesthesia is complete.

MAINTENANCE OF ANESTHESIA

INTRODUCTION

Anesthesia in horses is maintained with either **inhalational** or **total intravenous anesthesia (TIVA)**.

In order to maintain a clear airway during anesthesia and to administer oxygen it is essential to **intubate the trachea**. Normally this will be by the oral route and is a relatively straightforward procedure provided anesthesia is deep enough and the mouth can be held open either manually or by a gag placed between the incisor or molar teeth. The lubricated tube is passed blind through the larynx into the trachea. If any difficulties are encountered they can usually be overcome by altering the angulation of the head and neck and using gentle pressure to push the tube into the larynx and on into the trachea.

INHALATIONAL ANESTHESIA

Inhalational anesthetic agents are normally administered with 100% oxygen as a carrier gas. Large circle absorbers and to-and-fro circuits have been developed for use in horses. Ventilators are also used in conjunction with circle systems to deliver IPPV.

Halothane was introduced into equine anesthesia some 40 years ago and can be said to have revolutionized equine anesthesia. It produces a dose dependent reduction in arterial blood pressure and cardiac output in horses. While the facility to measure end-tidal concentrations enables the anesthetist to control the inhaled amount of an agent, this facility is not generally available due mainly to the cost of the equipment. In practice it is usual to maintain anesthesia with delivered concentrations of 2–4% halothane in oxygen. The time from the cessation of the administration of halothane to standing is between 30 and 60 min. It is mainly dependent on which other sedatives and anesthetic drugs have been administered for premedication and induction and on their duration of action.

Isoflurane has been used in horses for approximately 15 years and its properties are similar to halothane, as is the response of animals to its administration. It has a lower blood solubility, which means that the induction of and the recovery from anesthesia can be rapid. Isoflurane produces a lesser fall in cardiac output during anesthesia than halothane but the degree of **respiratory depression** is greater, particularly in the absence of surgical stimulation necessitating the use of IPPV.

Sevoflurane is a recently introduced volatile agent that is currently considered to be too **expensive** for routine clinical use. It has a low blood solubility, which facilitates rapid changes in anesthetic depth and in recovery from anesthesia.

It is well known that horses can exhibit sudden movements during general anesthesia associated with rapid changes in depth of anesthesia, usually in response to a **painful stimulus**. A number of agents are used to provide **additional analgesia**. These include **butorphanol** 0.02 mg/kg and **morphine** 0.1–0.2 mg/kg, although the role of opioids in this situation is still unclear. Small **bolus doses** of thiopental of up to 1 g and ketamine 0.1–0.2 mg/kg are also used. More recently, **infusions** of low doses of ketamine 40 μg/kg/h have been used and this technique merits further investigation.

TOTAL INTRAVENOUS ANESTHESIA

Total intravenous anesthesia (TIVA) has been used in horses for many years, but the results have been variable. Originally, single bolus doses of either thiopental or pentobarbital were used to prolong the duration of anesthesia. Later, combinations of thiamylal or thiopental and guaifenesin or chloral hydrate were used, but they produced prolonged recoveries. More recently a number of other combinations using ketamine, guaifenesin and either xylazine or detomidine have been described. They incorporate 1 g **ketamine** with either 500 mg **xylazine** or 10 mg **detomidine** mixed with 500 mL of 10% **guaifenesin**. When this combination is used for TIVA, guaifenesin should not be used as part of the induction technique to reduce the total dose of this long-acting drug in an attempt to improve the quality of recovery. The combination should be infused at a rate of 1 mL/kg/h but the rate should be based on the **clinical assessment** of anesthetic depth. A more rapid rate may be required during the early part of a procedure and at the time of maximum surgical stimulation and a slower rate toward the end of the procedure.

NEUROLEPTANALGESIA

A technique involving the IV administration of **etorphine** (2.45 mg/mL) and **acepromazine** (10 mg/mL) in combination has been used to produce a state of neuroleptanalgesia for the conduct of short procedures in Equidae. A dose of 0.5 mL/50 kg is recommended and the actions of the etorphine can be reversed by the IV administration of a similar volume of **diprenorphine** (3 mg/mL). In order to reverse the results of any accidental injection in humans, **naloxone** should be available. This combination is no longer available for use in horses or donkeys.

COMPLICATIONS OF GENERAL ANESTHESIA

Complications during general anesthesia in horses generally involve the cardiovascular or respiratory systems.

Hypoxia is very difficult to treat, particularly in animals that are extremely sick with such conditions as endotoxemia associated with colic (*q.v.*). The

administration of **100% oxygen** is not a very effective treatment but it is often used. **Clenbuterol** has been used at a dose of 0.8 mg/kg IV but there is debate regarding its efficacy. **IPPV** may be of some value in the treatment of hypoxia although its effectiveness is still under debate. In order to be effective, a mechanical ventilator is essential, and a rate of **6–10 per minute** and a tidal volume of **10–15 mL/kg** are employed.

Hypercapnia occurs commonly in anesthetized horses. **IPPV** is the rational treatment but it will cause an **increase in intrathoracic pressure** that can have deleterious effects on the cardiovascular system, particularly in the presence of **hypovolemia** (*q.v.*).

Hypotension and hypovolemia are relatively common in horses under general anesthesia. **Hypovolemia** can be prevented and treated by the IV infusion of large volumes (20–30 L) of **balanced electrolyte** solution (Plasmalyte). If this is unsuccessful then **hypertonic saline** solution should be administered at a rate of 4 mL/kg IV. However, its effect may be relatively short lived and **large volumes of electrolyte solution** (20–30 L) should also be infused at the same time or immediately afterwards.

Hypotension, with a mean arterial blood pressure <70 mmHg, is undesirable and should be treated as it is likely to lead to complications such as **myopathy** (*q.v.*) Sympathomimetic drugs such as dobutamine are recommended for the treatment of hypotension but it is often preferable to reduce the depth of anesthesia to a level commensurate with the execution of the surgical procedure and to infuse adequate volumes (up to 10 mL/kg) of electrolyte solution before resorting to drug therapy. The sympathomimetic drug of choice for the treatment of hypotension is **dobutamine**, which should be given IV at a rate of 1–5 μmg/kg/min. In some horses, especially those with **endotoxic shock** (*q.v.*), it will not be effective. Dobutamine does not increase the arterial blood pressure but may produce tachydysrhythmias (*q.v.*). In such situations **phenylephrine** may be administered IV at a rate of 0.2–2 μmg/kg/min, or a single dose of **ephedrine** (0.03–0.06 mg/kg IV) may be given.

RECOVERY

Horses should be allowed to recover from anesthesia in a **padded, dimly lit box** with the minimum of disturbance. If a stormy recovery is anticipated then a small dose of **xylazine** IV (up to 100 mg depending on size, temperament, previous medication etc.; normal sedative dose, 1.1 mg/kg) should be given at the end of anesthesia. Manual assistance at recovery may be justifiable under some circumstances, such as after orthopedic surgery. It is important to emphasize that, while the safety and welfare of the horse is important, the **safety of personnel is paramount** and no unnecessary risks should be taken.

Oxygen (100%) should be administered through the endotracheal tube until the animal begins to swallow and the tube is removed. Nasal insufflation of oxygen is then continued until the animal begins to attempt to stand. After a prolonged period of anesthesia, particularly with the horse in dorsal recumbency, edema of the nasal mucosa may produce **respiratory obstruction**. The passage of a **narrow bore endotracheal tube** up a nostril usually relieves the

problem. The tube should be **well secured** to prevent its aspiration or falling out during recovery. **Phenylephrine** has been used as a nasal spray to reduce nasal edema and facilitate tube entry.

Adequate analgesia should always be provided, either preemptively and/or at the end of anesthesia by the administration of **opioids** such as morphine 0.1–0.2 mg/kg IV and/or **NSAIDs** such as flunixin 1.1 mg/kg IV.

It is essential for animals to be kept under **continuous observation** until they regain their feet and are able to stand and to move in a coordinated manner. Any problems related to the respiratory or locomotor systems should be dealt with rapidly and effectively, hence it is essential to be able to obtain effective assistance should it be required. Normally, under hospital conditions, the animals would be returned to their own box some 20–30 min after regaining their feet. Arrangements should be made for **regular observation** of the patient and the administration of **analgesic drugs** as required.

LOCAL AND REGIONAL ANESTHESIA

LOCAL ANESTHESIA

Three solutions are used commonly to produce **local and regional anesthesia** in the horse. These are bupivacaine, lidocaine and mepivacaine. **Lidocaine** is used most frequently in practice.

Regional anesthesia of the limbs is discussed in Chapter 15 (*q.v.*), where details of forelimb and hindlimb regional and intrasynovial analgesia are provided (see Table 15.1, page 875). A number of regional nerve blocks are also used on the head of the horse. Auriculopalpebral, lacrimal and supraorbital blocks for **ophthalmic procedures** are discussed in Chapter 19 (*q.v.*) (see page 1208).

The rostral part of the infraorbital nerve supplies the upper lips, nostril and related skin of the face. The more caudal part of the nerve, which is situated in the canal, supplies **the teeth** (*q.v.*) to the level of the first molar and the skin of the face. It can be blocked as it leaves the foramen or a needle can be inserted through the foramen into the canal. The mental nerve supplies the skin of the lower lip and can be blocked as it emerges from the foramen. The mandibular nerve supplies the canine and incisor teeth and may be blocked on the medial aspect of the mandible although this is technically very difficult and not used very often.

EPIDURAL ANESTHESIA

Epidural anesthesia has a number of indications in the horse and these include surgery of the anus, perineum and vulva (*q.v.*) plus the prevention of straining during **obstetrical procedures** (*q.v.*). In the horse **posterior anesthesia** is almost invariably used as the interference with locomotion almost totally precludes the use of the anterior technique.

Absolute cleanliness is essential when using the epidural technique. After surgical preparation of the site a **wheal of local anesthetic** solution is placed at the site of the needle insertion using a fine needle. A 20 G, 10 cm needle is most commonly used and it is inserted into the **first inter-coccygeal space**.

One of two techniques is used for insertion of the needle: (1) at right angles to the general contour of the croup until it strikes the floor of the neural canal and is then withdrawn 0.5 cm; (2) at the caudal part of the inter-coccygeal depression, directed at 30 degrees to the horizontal and inserting it to its full length.

Until recently lidocaine was the agent of choice for epidural anesthesia. However, opioids (*q.v.*) and α_2-adrenoreceptor agonists (*q.v.*) have also been used. It is important to use **preservative-free solutions**. The most common combination is probably lidocaine and xylazine.

EUTHANASIA

INTRODUCTION

Euthanasia is often defined as a quiet and gentle death but it is probably better to refer to it as a quick and painless death. Euthanasia of horses is carried out by veterinarians under three different circumstances:

1. At sporting events when it is not feasible or possible to treat a particular injury such as compound fractures and fractures of the higher long bones of the limbs (*q.v.*)
2. When horses have reached the end of their useful and productive life and are suffering from crippling, debilitating or untreatable conditions (*q.v.*)
3. When incurable conditions are discovered during surgery and the animal is not allowed to recover from anesthesia.

These three situations each require a different approach.

It is important to ascertain whether the animal **is insured** and wherever possible to seek **permission from the insurance company**. If the owner of the horse or a responsible agent is available it is best to secure their agreement to carry out euthanasia. In an emergency and in the absence of the owner or agent it is strongly recommended that a **second veterinary opinion** as to the indications for euthanasia be obtained. Under most circumstances it is preferable to obtain written consent although under certain circumstances verbal agreement, in the presence of a reliable witness, is adequate. **Written records** of the procedure should be kept, and whenever possible a post mortem examination carried out.

TECHNIQUES

Horses can be humanely destroyed using either drugs or physical methods that damage the brain. Irrespective of the technique, the aim is to stop the flow of oxygenated blood to the vital tissues and produce death. The drugs used to produce euthanasia are of two distinct types, i.e. those that produce hypoxia and those that depress the central nervous system.

Hypoxic agents should never be used as sole agents. Muscle relaxants (*q.v.*) may be used in combination with a barbiturate (*q.v.*). They produce **muscle paralysis without anesthesia** and their use as a sole agent is **inhumane**.

Central nervous system depressants that produce cardiac and respiratory arrest are the **agents of choice** for euthanasia in horses. Due to the physical size of horses, the use of a number of agents is impractical. **Barbiturates** (*q.v.*)

are probably the drugs of choice although chloral hydrate, magnesium sulfate and potassium chloride have been used. For doses, see below.

In some countries, shooting with a free bullet has been employed, often with an attached silencer. When using a gun it is important to place the muzzle in the correct position at a site **just above the intersection** of the imaginary lines drawn from the base of the ear to the orbit on the opposite side of the head (Figure 21.1). Captive bolts are not advisable for use in the horse, as if the head moves the bolt may bend and become unusable in the event that a second shot is needed.

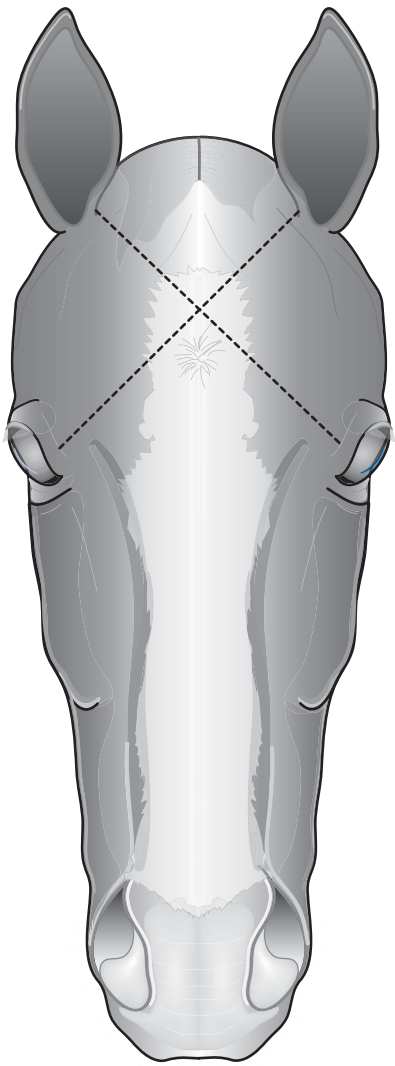

Figure 21.1 A front view of the head of a horse showing the two lines joining the base of the ears and the centre of the orbit on the opposite site. The site of entry of the bullet should be just above the point of intersection of these two lines. Reproduced with permission from Jones, R.S. (1992) Euthanasia in horses, *Equine Veterinary Education* 4: 154–157.

Recommended techniques

One technique that has found universal favor is the use of 10 g **thiopental sodium** (*q.v.*) dissolved in 60 mL of water administered IV through a 14 G catheter followed immediately by 100 mg **succinylcholine** (*q.v.*). If death does not occur within 2–3 min then 50 mL of **triple strength pentobarbital** (200 mg/mL) should be administered IV.

The use of α_2-adrenoceptor agonists (*q.v.*) to produce sedation is not recommended as they slow the circulation and the horse tends to fall over backwards.

An injection of 200 mL of **triple strength pentobarbital** followed by **succinylcholine** administered IV has also been recommended.

In some countries a mixture of **secobarbital** and **cinchocaine hydrochloride** (a local anesthetic) is available (e.g. as Somulose) and widely used for euthanasia in horses. A dose of 5 mL/50 kg is recommended to be administered IV through a catheter over a 12–15 s time period. The use of α_2-adrenoceptor agonists is not recommended except in a fractious horse or when sedation is essential for assessment prior to euthanasia. This combination solution has the advantage of small volume and a relatively rapid rate of action. In the UK, it is subject to the Misuse of Drugs Act (1971) and is subject to special prescription and record keeping but not to custody requirements. Other restrictions may apply elsewhere.

Chapter 22

Fundamentals of the equine pre-purchase examination

L. M. Van Hoogmoed (Consultant Editor)

Chapter contents

INTRODUCTION

The pre-purchase examination is a procedure unique to the equine industry and places the veterinarian in a rather peculiar position compared to his or her standard practice of animal husbandry. In no other area are veterinarians consistently called upon to act as objective "consultants" for a buyer before a horse is sold. It would be unusual, for example, for someone to consult with an expert before buying a car, furniture, or other sports equipment. Except in unusual circumstances, pre-purchase examinations are rarely performed in acquiring other species such as companion or food animals. It is also apparent that veterinarians do play a significant role in the outcome of the sale based on their findings during the examination. Beyond the sale, the **reputation of the horse** in the show world and in the next pre-purchase examination can also be affected if the horse did not sell.

Given the competitive nature of equestrian events and the rising costs of maintaining and training these athletes, buyers are pursuing pre-purchase examinations potentially in order to **avert acquiring a problem**. The examinations are an important facet of the equine industry for both owners and veterinarians and can establish new clientele for the veterinarian, provide

significant revenue for the clinician's practice, and provide a beneficial exposure for clients to the veterinary profession.

The veterinarian's examination is critical since many **transfers of ownership** are heavily based on the outcome of the pre-purchase examination, and the decision to buy the animal or not frequently hinges on details revealed during the course of the examination.

While there are many potential benefits to both the client and the veterinarian, the examinations may also pose some **liability concerns** for the veterinarian. This may occur if a lesion is missed during the examination or if a clinical finding such as a radiographic change is misinterpreted. For these reasons, some veterinarians avoid pre-purchase examinations or are extremely conservative in their interpretations of the findings. However, as long as the potential buyer is educated about the objectives and the limitations of the examination, many of these reservations can be reduced or eliminated.

COMMITMENT AND UNDERTAKING

One of the difficulties with pre-purchase examinations is the expectation by the prospective buyer that the veterinarian can **predict and/or guarantee future soundness**. This predicament for the veterinarian becomes even more difficult when the examination is clouded by a mild lameness or mild response to a flexion test in the presence of radiographic changes. Occasionally radiographic changes may also be present in the absence of clinical signs such as degenerative changes at the tarsus or remodeling of the subchondral bone such as the trochlear ridges of the stifle or tarsus. For this reason, practitioners have moved away from declarations of "pass" or "no pass". Instead it is more typical to summarize for the potential buyer the **significant findings** of the examination and the radiographic survey with the understanding that this examination is **simply a snapshot in time and not a prediction of the horse's future athletic career**.

Generally, unless qualified to do so, **veterinarians should not comment on the price** or assist in the negotiation of the purchase price of the horse. It is important for clinicians to inform potential buyers that while they can make an assessment of the horse's overall physical well-being, there are limitations to the pre-purchase examination.

HORSES FOR COURSES

Occasionally, specific details of the pre-purchase examination are dictated by the client's financial ability, expectations, facilities available and the intended use of the animal. In horses intended for a **specific purpose**, such as Western pleasure or endurance, there may be some areas that are more relevant to the prospective buyer than others. For example, the potential endurance prospect may be more likely to receive an upper airway endoscopic examination than a Quarter Horse intended for Western pleasure/show classes. This may also increase the **emphasis of scrutiny in specific areas**. For example, in horses intended for cutting or reining, excessive forces are exerted at the hocks and lower joints so these areas must be especially evaluated to look for any lesion or evidence of an impending problem, most commonly via palpation and radiography.

Given that **navicular degeneration** (*q.v.*) can be common in Quarter Horses, the feet are also examined carefully with special attention to the heel area. It is generally accepted that no horse is "perfect", especially if it has been competing consistently in some athletic event. Therefore, it becomes a question of what flaws and how many the potential buyer is willing to accept. Again, this question is one that can only be answered by the buyer.

Veterinarians must be aware of their own limitations and refer the horse to specialists if needed. For example, not all veterinarians may be qualified to perform a pre-purchase examination on a **gaited horse** such as a Tennessee Walking Horse. The role of veterinarians in pre-purchase examinations requires examiners to "recognize the seeds of soundness as much as the seeds of disease".

Pre-purchase examinations are not always strictly confined to determining whether the horse is **currently** sound or not. Many owners may expect veterinarians to provide personal opinions about the horse's conformation and if it is capable of withstanding its intended use. For example they may question if the musculoskeletal development is appropriate given the horse's age, whether the horse too small, or fine boned, etc. Generally, **overall balance and conformation** evaluation are important considerations since discrepancies from normal can predispose the horse to future problems. For example, horses with a **toed-in conformation** may be at an increased risk of developing **pastern ringbone** (*q.v.*) or **lateral suspensory branch desmitis** (*q.v.*), and horses with **elongated pastern bones** may develop **flexor tendon sheath effusion** (*q.v.*).

In some cases the pre-purchase examination is highly tailored to the type of horse and its intended use. For example in **polo horses**, palpation of the flexor tendons and suspensory ligaments in addition to fetlock joint flexion can comprise up to 80% of the examination. While attempts have been made over the years to standardize the pre-purchase protocol, it still remains, and likely always will, at the discretion of the veterinarian and the parties involved.

The variables that should be evaluated in a pre-purchase examination should be modified according to the specific parties involved, the clinician's experience, the intended use of the horse and the owner's expectations.

HISTORY

It is advantageous for the veterinarian examining the horse to have some information about the horse's career **prior to the examination**. For example: Have the potential buyers ridden the horse before? How long have they known the horse? What has the horse been used for in the past? Has there been any history of lameness or illness?

Commonly, the buyer will have had only limited exposure to the horse, and information regarding the lameness history or medical problems is scant. Horses that have been retired from one career to start another should have a **good history** and **physical examination**. For example, Thoroughbreds that have been "retired" from racing and are being purchased as prospects for dressage should be evaluated closely for signs of injury **related to the racetrack**. The flexor tendons should be inspected carefully for any sign of **tendinitis** (*q.v.*), and the **joints should be palpated** for any synovitis or effusion that might suggest osteoarthritis or chip fractures (*q.v.*). Horses retired for being too slow and **lacking in "heart"** should also be evaluated for poor performance due to

upper airway conditions such as **laryngeal hemiplegia** or **soft palate displacement** (*q.v.*).

Because of the **potential for litigation** and in an effort to minimize any misunderstandings, it is in the veterinarian's best interest to **document fully the entire examination and conversations with the buyer and the seller**. Some practitioners include a **disclaimer** at the summary of the examination form. In addition, **worksheets** that list the procedures to be performed are routinely used by some clinicians, not as the final report for the buyer, but more as a checklist to ensure that areas are not inadvertently omitted during the course of the examination.

Prior to the examination, it is important to discuss with the owner **the parameters that will be evaluated** to ensure that any diagnostic procedures that the buyer may have expected are not missed and also so that they have an estimate of what the cost of the examination is likely to be. Depending on the intended use of the horse, some buyers will want only a bare examination, while others will expect a very thorough diagnostic evaluation.

PHYSICAL EXAMINATION

BASICS

A **complete physical examination** should be performed as a standard procedure in all cases regardless of the selling price. The basic temperature, pulse and respiration are taken before initiating exercise.

The **perineal** region should be examined while inserting the thermometer for any abnormality such as **melanoma** (*q.v.*) in gray horses or an **excessively sloped conformation** (*q.v.*) in mares. This also allows for a brief assessment of **tail tone**. Other areas of increased incidence of melanoma such as the parotid region and peripheral lymph nodes should also be evaluated.

HEART

Cardiac auscultation (*q.v.*) is important to detect any subclinical abnormality such as atrial fibrillation or heart murmurs. While horses have been known to compete successfully even in strenuous careers with cardiac abnormalities such as low grade murmurs, the heart should be evaluated with ECG and ultrasound if there is a concern about future performance.

Auscultation alone cannot differentiate between **physiologic flow murmurs** (which are common and not usually clinically relevant) due to flow of blood through large vessels and murmurs due to **underlying cardiac disease** (*q.v.*) such as mitral regurgitation**.**

Depending on the abnormality, **cardiac disease is usually progressive**. In a study to determine the incidence of various heart murmurs and their effect on performance in Thoroughbred racehorses, heart murmurs were detected in 81.1% of horses, with the most common type being the **systolic murmur over the heart base** (43.1%). **Systolic murmurs over the mitral valve** region were detected in only a small percentage of the horses (3.8%). In reviewing the race records of these horses, it was concluded that there was **no significant association between murmurs and performance**.

EYES

It is important to undertake a thorough examination of the eye. This should involve an evaluation of the **menace response**, evaluation of any **corneal defects** (*q.v.*) using a transilluminator where possible, and observing the **retina** using an ophthalmoscope.

If any significant defects or abnormalities are identified, the horse should be referred for a specialist ophthalmic evaluation. It is worth being aware that in some equine disciplines, horses are allowed to compete with only one visual eye. Details of eye problems in horses are given elsewhere in the book. (See Chapter 19, page 1157.)

LUNG FIELDS

The lung fields are evaluated by ausculting the chest with and without the use of a **rebreathing bag**. The procedure is often facilitated by placing a large plastic bag over a muzzle that keeps the bag from being drawn into the nostrils.

The throat latch area should be palpated for any **thickening or sensitivity** and to detect whether a **cough** is easily elicited. Both jugular veins should be palpated for any evidence of **thrombosis** or other swelling that might indicate frequent or recent injections.

The coat is also evaluated for any sign of dermatitis, sarcoids, melanomas (especially in gray horses in the perineal region), old scars and unusual sweat patterns (*q.v.*).

LIMBS

The limbs are also palpated from proximal to distal with special emphasis on the **joints and flexor tendons**.

The **digital pulses** to the feet should be evaluated, preferably **before initiating any exercise**. Hoof testers are applied to all four feet, usually before the horse is exercised. **Bony exostoses** or splints (*q.v.*) may be present and should not be sensitive to palpation. If there is a concern, a radiograph may be indicated to determine if the exostosis is due to a previously fractured splint bone and to ascertain the size of the callus to see whether it is **impinging on the suspensory ligament** as may happen if it extends to the caudal aspect of the limb. If the suspensory ligament is sensitive to palpation near the bony exostosis, then ultrasound is indicated to determine if there is a desmitis associated with proximity to the splint.

Areas of **unusual hair pattern and/or discoloration** should be inspected closely as they may represent an area that has had previous blistering or treatment for a tendon problem.

The **flexibility and range of motion** of the limbs should be evaluated. The fetlock and carpus should easily flex with no restriction. The front limb should be picked up at the carpus and advanced forward and backward with no resistance. The back and lumbar region should be palpated along the entire length for any irregularity or excessive sensitivity to touch. This includes the tuber sacrale, sacrum and pelvis.

In sport horses, particular emphasis should be placed on an examination of the flexor tendons and suspensory ligaments of the front and hind limbs.

Any abnormality such as thickening or sensitivity should be evaluated with **ultrasound** if there is a concern. Healed lesions on the superficial digital flexor tendons can occasionally be seen in sport horses, especially since many Thoroughbreds retired from the racetrack are given a new career in jumping or dressage. Generally these old healed lesions do not flare again in trained well-conditioned horses, especially if the horse has been competing successfully at the desired level. The semimembranosus and semitendinosus muscles should also be evaluated to determine if there is any thickening or scarring as would occur with a **fibrotic myopathy**.

In young and unproven horses, special attention should be paid to the **joints** such as the hocks, stifles and fetlocks to rule out **developmental disease** such as osteochondrosis (*q.v.*). In older horses that have already been in training or competition, less emphasis is placed on subtle radiographic changes that may be present as these may simply be a function of repeated exercise and stresses but **not necessarily** a career-limiting or -ending finding.

THE VENTRAL MIDLINE

The ventral midline should also be closely palpated for any **evidence of a scar**, which would suggest the horse has had **abdominal surgery**, most likely due to gastrointestinal disease. The history of a horse that has had colic surgery is important, especially if a resection and anastomosis was performed. For example, practitioners may well be concerned about using horses with **large intestinal colopexies** due to displacement or torsion for jumping. The concern is that if these horses are used for rigorous competition, for example challenging high jumps, they may be at greater risk for **tearing the large colon from the body wall** and rupturing the intestine.

Horses with small **ventral midline hernias** have been used in competition with no known deleterious consequences. However because of cosmetic concerns and the potential for incarceration of intestine, most owners elect to repair these defects.

SOUNDNESS EXAMINATION

OBSERVATION

The soundness examination should begin by simply **watching the horse walk** away from and toward the examiner. This allows the clinician to have an assessment of the horse's **demeanor** and look for any **gait abnormalities at a slow speed**, such as interference, landing on the medial or lateral aspect of the foot, and if the horse wings or paddles his limbs.

Certain gait abnormalities, such as **stringhalt** (*q.v.*) and **shivers** (*q.v.*), can also be identified at this time. Horses with these gait abnormalities have been known to compete at high levels of jumping with no apparent difficulty and without an obvious progression of clinical signs.

STRAIGHT LINE TROT, FLEXION TESTS AND LUNGING

The horse is then **trotted in a straight line** and held on a **loose line** so as not to interfere with the movement of the head.

Flexion tests are performed on all limbs in a systematic fashion. The fetlock joints are flexed for 30–45 s followed by the carpus for the same amount of time. On the hindlimbs, the hocks are flexed (**spavin test**) for a minimum of 90 s. Inflammation of the distal intertarsal and tarsometatarsal joints affects a large proportion of jumpers and high level dressage horses, and most will require some treatment to continue competing at these advanced levels. Generally, the clinician can ignore the first several strides as many **sound horses** may be off on the first few steps after flexion. However, if lameness persists beyond that point, it should be considered a positive response. The horse should then be **lunged on a hard surface** in both directions on a loose line. If there is any question or concern, the horse can also be lunged on a softer surface such as a round pen with sand or loose dirt. Generally horses do not need to be ridden, but in some situations it may be advisable for the horse to be observed under saddle and/or performing its intended use such as jumping or dressage.

DIAGNOSTIC PROCEDURES

INTRODUCTION

For the majority of pre-purchase examinations, **radiography** is the most common diagnostic procedure performed. Depending on the owner's wishes, the experience of the veterinarian, and anything else that has come to light during the pre-purchase examination, other procedures may also be performed that are not necessarily routine for every practice. For example these may include radiographs of regions other than the limbs such as the **abdomen** (looking for enteroliths or sand), **nuclear scintigraphy**, **thermography**, **magnetic resonance imaging**, and **ultrasonographic examination of the flexor tendons**, **heart** or other areas.

Horses intended for international competition may need to be tested for various diseases including **piroplasmosis** (*q.v.*), **equine infectious anemia** (*q.v.*), **glanders** (*q.v.*) and **equine viral arteritis** (*q.v.*) in breeding mares and stallions (if indicated). If the clinician has any questions regarding importation and/or transport regulations, the best source is likely to be someone in the horse transportation business or the US Department of Agriculture (USDA) or the appropriate government's regulatory authority.

Some owners, either through personal experience or on the advice of others, may request **specific tests for diseases** that are common in their area or have received recent publicity or notoriety. Specific examples include testing for **equine protozoal myeloencephalitis** (EPM) (*q.v.*) and **Lyme disease** (*q.v.*). Since EPM is endemic in the USA, serologic testing is not always productive since a positive outcome does not immediately confirm disease, but exposure. Of course, a negative response indicates the horse is free of disease. Because of the inherent risks associated with **cerebrospinal fluid (CSF) sampling**, this procedure is not done routinely, but only if indicated by clinical signs such as **neurologic symptoms**. Newer testing techniques such as the **serum indirect fluorescent antibody test** may have greater accuracy compared with traditional Western blot tests.

RADIOGRAPHY

Radiography has for many years been the primary aid used to diagnose **skeletal lesions** in horses. However, the radiographic diagnosis of a specific lesion is truly more effective when combined with another modality such as a **clinical lameness examination** or **nerve blocks** since it is possible that the radiographic finding may simply be an incidental finding.

Radiographic images generated during a pre-purchase examination remain the **property of the clinician** and are part of the medical record. They do not belong to the person who paid for the examination since the fee charged is for the time, expertise and equipment but not the image produced. If the owner asks for the radiographs to be sent elsewhere for a second opinion, then copies can be made and given to the client, or the images can be sent directly to the consulting veterinarian. In the current age of digital radiography, the transfer of radiographs has been simplified since the images can be sent simply via the Internet or copied onto a CD. The veterinarian needs to remain diligent about exercising good judgment and responsibility with this radiographic information.

A complete radiographic study requires several views to ensure subtle lesions are not missed. For the **feet**, the views taken include the lateral, 65° dorsoproximal–palmarodistal, 45° dorsoproximal–palmarodistal, and the skyline flexor view from palmaroproximal to palmarodistal. For the **joints of the distal limb**, the views required include the lateral, dorsolateral–palmaromedial, dorsomedial–palmarolateral, dorsopalmar and flexed lateral (with the exception of the tarsus unless indicated). For the **stifle joint**, the recommended views include the caudocranial, lateromedial, caudolateral–craniomedial and lateromedial patellar.

ENDOSCOPY

Endoscopy should be offered to all clients, especially those who intend to use the horse for **strenuous athletic exercise** such as endurance or jumping. Horses intended for dressage are also encouraged to have an endoscopic examination of the pharynx and larynx since the roaring sound made by a horse with **laryngeal hemiplegia** (*q.v.*) may lead to faults in the show ring. Further, alterations in head carriage in combination with **laryngeal paralysis** may cause restrictions in performance. Horses used as hunters must not make an abnormal noise during work and therefore may be disqualified for the sound even if performance is not impaired.

Gastric endoscopy is performed occasionally for owners concerned about ulceration in performance horses. It is now known that there is a high prevalence of gastric ulceration (*q.v.*) in most types of racing, competition and show horses, including endurance horses, and gastric endoscopy may therefore be increasingly requested.

ULTRASOUND

Owners may also wish to have ultrasound examinations performed on the **flexor tendons** and **suspensory ligaments** to screen for any existing or preclinical problem. Generally, this type of examination is not routinely performed

unless there is an indication such as swelling and/or lameness in the **metacarpal or metatarsal region**.

Ultrasound examinations should be undertaken only by an **experienced operator** competent in performing the examination and interpreting the results. This will help to ensure that **subtle lesions** are not missed and that normal findings are not construed as abnormal findings.

Ultrasound may also be indicated in cases with **excessive swelling of the joint or associated sheath** such as at the level of the digital tendon sheath. This distension may result from chronic inflammation, adhesions, or tearing of the associated structures in the sheath (e.g. deep and superficial flexor tendons).

REPRODUCTIVE EXAMINATION

In horses intended to be used for breeding, reproductive evaluation is also recommended. The specifics of the examination include semen collection and evaluation (*q.v.*) in stallions, and ultrasound of the uterus and ovaries and uterine culture and/or biopsy in mares.

If a mare is to be sold in foal, **ultrasound evaluation of the uterus** is especially relevant to verify the pregnancy and screen for twins. With the proper technique and training, it may also be possible to determine the sex of the fetus if this information is important to the buyer.

GUIDELINES TO VETERINARIANS CONDUCTING PRE-PURCHASE EXAMINATIONS

THE AMERICAN ASSOCIATION OF EQUINE PRACTITIONERS GUIDE

The American Association of Equine Practitioners (AAEP) provides guidelines for veterinarians in conducting pre-purchase examinations.* Generally, recommendations such as these provide common sense information that most practitioners should already be aware of and practice. Some of the major points mentioned in the AAEP Guide include the necessity to provide a **detailed description of the horse for future identification** with the **time and date of the examination**, all abnormalities noted, and the clinician's opinion on the effects any changes may have on the horse's performance.

One important guideline included in the AAEP Guide states that

> The veterinarian should make no determination and express no opinion as to the suitability of the animal for the purpose intended. This issue is a business judgement that is solely the responsibility of the buyer that he or she should make on the basis of a variety of factors, only one of which is the examination and report provided by the veterinarian.

This statement essentially places the burden of making the decision to purchase the horse or not **on the owner** as it should be since he or she will also be assuming the financial, legal and emotional responsibility of owning the

* AAEP (1992) Guidelines for reporting prepurchase examinations approved by the AAEP, *AAEP Report* 6: 3 ISSN 0065-7182.

animal. Maintaining neutrality by the veterinarian minimizes liability should the animal develop a problem after the examination or is found to be unsuitable for the owner's intentions. **Ownership of the horse lies with the buyer**, who should never be in a position to claim that he or she was "talked into the decision to purchase" by the veterinarian.

Another important guideline is that the clinician should qualify any findings to the buyer by **specific reference to tests that were recommended** even if they were not performed, e.g. a **rectal examination** or **blood examination**.

A **drug screen service** can be offered, e.g. for the presence of analgesic and anti-inflammatory agents; such tests are often declined by the buyer. However, the veterinarian should be prepared to provide these types of services, especially in cases where buyers are interested in purchasing a mare primarily as a riding prospect with the option of using her as a broodmare later.

Other national equine veterinary organizations also produce guidelines. Clinicians in the UK, for example, should check the BEVA website for details (www.beva.org.uk).

PREVIOUS INVESTIGATIONS

Studies reporting the results of pre-purchase examinations are sparse. One recent retrospective study of the outcome of 510 examinations over a 10 yr span summarized clinical and radiographic results of pre-purchase examinations and determined whether there was an association between radiographic changes and the lameness outcome. Geldings represented the most common sex. The predominant breed evaluated was Thoroughbreds followed by Quarter-horses. The mean age was 8 years. During the examination, 52.8% of the horses were lame and most of these were valued >$5000.00. Osteochondrosis lesions were identified radiographically in 5.1% of the horses and the majority of these were sold with no apparent lameness on follow-up (47.4%).

The most commonly requested diagnostic procedure was radiography: in 61.6% at least one radiographic study was requested, most commonly of the front feet or tarsi. The navicular bone, coffin bone and the distal tarsal joints were evaluated, graded (range from 0 to 3, with increasing severity of degenerative changes), and attempts were made to correlate the radiographic findings with the soundness examination. Of horses with grade 0 navicular bones, 85.1% were not lame compared with 22.7% that were not lame with a grade 3. The majority of horses with grades 0 and 1 in the navicular bone and coffin bones were not lame compared to those with more advanced changes. For the tarsus, regardless of the grade (0 to 3), the majority of these horses were sound (78.6–79.2%; respectively). On follow-up with the current owner of the horse, 20 of the 21 horses with a grade 3 change in the distal intertarsal and/or tarsometatarsal joint were in active use. The veterinarian examination was also important since the examination had a direct effect on the outcome of the sale (sold or not sold) and on the final price in 80.9% of the cases.

INFORMATION OWNERSHIP

A question that frequently arises relative to pre-purchase examinations is that of information ownership and, specifically, who is entitled to the results of the

physical/soundness examination and any other diagnostic procedure that was performed such as radiography? Typically, the medical record is established under the name of the person paying for the examination, who is usually the buyer. Therefore, the results of the examination are the exclusive property of that person. This can sometimes lead to conflicts when the horse does not sell and another buyer interested in the horse does not wish to buy another set of radiographs when a recent set already exists. Furthermore, the seller may also wish to disclose the results of the examination to another potential buyer. In these cases, the veterinarian should request permission from the original potential buyer to release the information.

THE NEED FOR GOOD COMMUNICATION

One of the most effective and best ways to avoid misunderstandings associated with pre-purchase examinations is good communication. After recording all the information, time is always well spent in discussing the findings with the potential buyer.

The veterinarian has no obligation to discuss the results of the examination with the seller. In conducting a pre-purchase examination, the clinician is retained by, and represents the interests of, the buyer. It is also in the best interest of the veterinarian to make it clear to the buyer **the limitations of the examination** and/or the veterinarian's experience and knowledge. Statements such as "*I do not know*" and "*in my opinion*" should be used when appropriate so the buyer does not have a false sense of confidence. The clinician should recommend a colleague or other appropriate expert if a second opinion is indicated.

THE WRITTEN REPORT

The format of the written report should be divided into several categories, as in Box 22.1 and as recommended by AAEP (*q.v.*).

Box 22.1 The written report of the pre-purchase examination

1. List the horse's identity (name, age, breed, etc.).
2. State that the buyer (include name) is requesting a physical examination on the horse, the intended use of the horse, the site of the examination, and who is present.
3. State any abnormalities detected during the examination of "those organ systems available for examination" in order to make it clear that there will be some areas that cannot be examined. It is also advisable not to make predictions of the horse's behavior unless it is so unmanageable that there is a substantial risk to people involved in the horse's care.
4. Include a summary of the soundness examination (lunging, flexion tests, etc.) and any other diagnostic procedures that were done.
5. Mention those tests that were not performed as well as the reasons for the omission.
6. Summarize the findings, including any disclaimers, and describe any areas of dispute or question.

In cases where a significant problem is identified, such as a lameness, it is for the buyer to determine if the examination should be aborted or further diagnostics performed. If a diagnostic procedure is considered invasive or carries some risk to the horse, the **owner should be contacted** so that he or she is pre-warned and to minimize problems should a complication arise. For example, if a lameness is detected, **diagnostic nerve blocking** should not be performed unless the owner has been contacted in advance and given approval. The seller should also be contacted if the **shoes are to be removed** for diagnostic purposes or for radiographs. It is critical to ensure the shoe is removed carefully to avoid inadvertent hoof wall defects that may make replacing the shoe difficult.

CONFLICT OF INTEREST

One of the most difficult challenges in any pre-purchase examination arises when there is a conflict of interest between the parties involved. This may occur, for example, if the clinician already is **familiar with the horse** or has **knowledge of the animal's medical history** or the seller is a **client of the veterinarian**.

Generally, the best way to resolve such a problem is for the veterinarian to obtain a **written statement** from the seller that all information pertaining to the horse will be disclosed. If the seller does not wish to disclose this information, the clinician should decline the examination. The more open the communication between all parties involved, the less is the potential for conflict later.

Chapter 23

Intensive care medicine

K. G. Magdesian (Consultant Editor)

Chapter contents

INTRODUCTION

Critical care is an exciting area of equine practice that has undergone rapid advancement and increased specialization in recent years. The increasing

pursuit of advanced critical care training and board certification has redefined equine critical care, providing a new focus in the understanding and management of horses requiring intensive care.

The provision of state-of-the-art emergency and critical care is facilitated through the use of an **intensive care unit, or ICU**, with provision of high level monitoring and nursing care, as well as advanced support. Such facilities should have fully trained nursing staff present at all times, with veterinary specialists available 24 h a day.

Critical care medicine is devoted to the comprehensive care of seriously ill horses, which are often suffering from **multiorgan system failure**. A successful outcome requires an **interdisciplinary approach** to the diagnosis, treatment and management of such cases. For example, the horse recovering from colic surgery that develops peritonitis, salmonellosis and renal compromise requires collaborative input from the surgeon, medical internist and critical care specialist. Selection of appropriate antibiotic therapy must address the cause of peritonitis and organisms involved, while balancing the effects of the chosen antimicrobial agents on the *Salmonella* strain, existing gut flora and patient's renal function.

Principles of **infectious disease control** (*q.v.*) must be observed without disrupting primary patient care. The patient must be **isolated** from other susceptible horses, yet maintained in an environment suited to continuous IV fluid administration and frequent monitoring. Additional patient problems to anticipate include electrolyte disturbances associated with **secretory diarrhea**; **catheter-related sepsis** and **venous thrombosis** associated with systemic infection, endotoxemia, prolonged catheterization and rapid fluid administration; **laminitis** due to perfusion deficits and endotoxemia; and negative energy balance resulting from increased energy requirements due to fever, infection, wound healing and decreased feed intake. All aspects of such a case must be addressed **concurrently** and attention focused on monitoring patient trends. Potential complications that could arise while treating existing medical and/or surgical problems must be anticipated.

Excellence of nursing care is the mainstay of any ICU. Critically ill horses are **inherently unstable** and subtle changes in condition must be detected early to allow appropriate changes in therapy. The higher morbidity and mortality rates among critical care patients can become a demoralizing reality. Treatment of seriously ill animals often involves **chronic intensive care**, which is frequently plagued by the development of secondary complications associated with the patient's debilitated state and the need for aggressive and often invasive diagnostic and therapeutic procedures. Nurses working in the ICU must have an understanding of the patient's illness and an appreciation of intensive care therapy to maximize their surveillance capabilities and foster the development of innovative nursing care protocols. Support among co-workers is also vital and helps maintain a positive attitude in the ICU.

Creation of a critical care area within an equine hospital allows trained personnel to monitor and care for a number of seriously ill horses most efficiently. The establishment of a **nursing station** allows for supplies, drugs, delicate instrumentation and monitoring equipment to be centralized. **Recumbency** complicates the care of many horses suffering from neurologic disorders such as rhinopneumonitis and botulism (*q.v.*), or musculoskeletal problems such as

long bone fractures and laminitis (*q.v.*). Stall modifications that facilitate care of critically ill patients include wall-mounted medical gases and suction, padded floors and walls, and ceiling hooks for fluid administration.

Prolonged recumbency is complicated by a variety of secondary problems including decubital sores, self-trauma, gut dysmotility, urine retention and dependent lung atelectasis (*q.v.*). A padded stall equipped with a 2-ton hoist and sling is an invaluable asset when treating such cases.

Deciding which horses to admit to the ICU is termed **triage**, the art of **giving priority to the most critical cases**. Patients should be admitted to the critical care facility based on the intensity of their treatments, the frequency of monitoring required, and the need for special bedding or ICU stall features.

Examples of patient problems that benefit from a critical care setting include the following: **hepatoencephalopathy** (*q.v.*), requiring continuous glucose and fluid infusion, sedation, a padded environment and protective head helmet; **sepsis** (*q.v.*), causing hypotension and organ dysfunction; **renal failure** (*q.v.*), requiring continuous fluid therapy, careful monitoring of fluid administration and urine output, controlled dopamine infusion and diuretic administration; **severe corneal ulcers** (*q.v.*), requiring hourly eye medication via a nasolacrimal or subpalpebral lavage system; **botulism** (*q.v.*), requiring a padded environment to minimize self-trauma associated with recumbency, frequent patient repositioning to prevent dependent lung atelectasis, continuous fluids and enteral nutrition via nasogastric intubation; **severe laminitis** (*q.v.*), requiring padded floors, deep bedding, and supportive care if recumbent; **postoperative colic** (*q.v.*), requiring frequent observation for recurrent pain, gastric decompression via nasogastric intubation, and continuous fluid therapy; **impaction colic** (*q.v.*), requiring continuous IV fluids and frequent administration of oral fluids and laxatives. Monitoring of any critical patient focuses on **frequent evaluation** of standard parameters such as those presented in Table 23.1.

This chapter focuses on guidelines for fluid and electrolyte replacement therapy, critical care protocols with emphasis on monitoring techniques and therapy, pharmacotherapeutics for critically ill patients, management of endotoxemia, and design principles for an intensive care facility. Resuscitation guidelines and principles of ventilatory and nutritional support are reviewed elsewhere, as are specific neonatal disease conditions (*q.v.*).

FLUID THERAPY

INTRODUCTION

Fluid therapy is an integral part of critical care, and is the foundation of hemodynamic support in the ICU. In the emergency setting, horses exhibit a variety of fluid, electrolyte and acid-base disorders. These arise due to a number of factors, including **anorexia** (inadequate intake), **excessive losses** (sequestration, third-space losses) and **hypoperfusion** associated with distributive or cardiogenic shock.

The primary goals of fluid therapy are to replace and correct these imbalances, to restore effective circulating volume and blood pressure, to provide the body's maintenance requirements for water and electrolytes, and to account for

Table 23.1 Physical parameters frequently evaluated in intensive care horses

Parameter	Abnormality	Interpretation
Breathing	Tachypnea	Pulmonary/pleural disease Pain, anxiety
	Dyspnea	Pulmonary/pleural disease
	Upper airway noise	Airway obstruction
Pulse quality	Bounding pulse	Hyperdynamic perfusion
	Weak, thready pulse	Poor peripheral perfusion
Capillary refill time	<1 s	Hyperdynamic state or peripheral vasodilatation
	>2 s	Poor peripheral perfusion, hypovolemia, dehydration
Heart rate	Tachycardia	Pain, anxiety, poor coronary diastolic filling
	Bradycardia	Bradyarrhythmia (AV block), impaired cardiac output
Mucous membrane color	White	Anemia, shock
	Blue	Cyanosis
	Yellow	Liver disease, fasting, hyperbilirubinemia, hemolysis
	Brick red	Hyperdynamic state, toxemia, peripheral vasodilatation
	Petechiation	Thrombocytopenia, disseminated intravascular coagulation
Attitude	Obtunded	CNS disease, hepatoencephalopathy, hypoglycemia
	Depressed	Pain, systemic infection, dehydration, CNS disease
	Maniacal	CNS disease, hepatoencephalopathy
Temperature	Fever	Bacterial or viral infection
Hypothermia	Shock, poor perfusion	
Gastrointestinal borborygmi	Reduced, absent	Ileus, impaction or other obstruction
	Increased	Enterocolitis
Digital pulses, coronary band integrity, foot temperature	Increased pulses, coronary band clefting, warm feet	Laminitis
Musculoskeletal pain	Non-weight bearing	Fracture, joint infection, laminitis

ongoing losses. Rational fluid therapy requires an understanding of the normal homeostatic mechanisms governing body water, electrolyte and acid-base balance, and the pathophysiologic processes that disrupt their homeostasis.

BODY WATER BALANCE

Total body water represents approximately 60–70% of body weight in adult horses and is comprised of the extracellular and intracellular spaces (Table 23.2). The extracellular compartment includes the intravascular (plasma), interstitial and transcellular fluid (gastrointestinal tract water and lymph). The distribution of water between plasma and interstitial fluid is maintained by differences in colloidal osmotic and hydrostatic pressure, and also depends on the integrity of the endothelium.

Table 23.2 Fluid compartments in adult horses

	Proportion of body weight (%)	Approximate volume (450 kg horse) (L)
Total body water	60–70	270–315
Intracellular fluid	35–45	180–203
Extracellular fluid	20–25	90–100
Intravascular fluid	7–8	30–36

Water balance is the difference between input and output. This is determined by the intake of water and fluid contained in food, and by the generation of water due to protein, fat and carbohydrate metabolism, versus water loss through urine and feces, respiratory tract and skin. The **normal water intake** for a 450 kg adult horse is approximately **20–30 L/day**, although this can vary depending on the water content of the diet, ambient temperature and activity level. The largest component of water loss is through the urine.

Dehydration is defined as a reduction in total body water. In the critical care setting, this usually refers to losses in the interstitial fluid compartment. Dehydration occurs with **water deprivation**, either through lack of access to water or through the inability to swallow. It also follows **excessive fluid loss**, most commonly from the gastrointestinal tract, but also sweating or urinary losses. As opposed to hydration status, circulating volume refers to the intravascular fluid compartment. In dehydration, circulating volume may be decreased, but if the onset of dehydration is insidious, it may be maintained despite a reduction in total body water. The effective circulating volume is also reduced when fluid is sequestered in abnormal quantities within one part of the body (third-space accumulation), in **hemorrhage** and in **hypovolemic shock**.

ASSESSMENT OF HYDRATION STATUS AND EFFECTIVE CIRCULATING VOLUME

Clinical examination

Clinical examination is the first, and most important, means of assessment of fluid disorders. The parameters used to evaluate both total body water (**hydration status**) and effective circulating volume are listed in Box 23.1. Clinical evaluation can be used to provide a rough estimate of the fluid deficit (Box 23.1). However, these are only guidelines and replacement fluid therapy is best evaluated by **serial monitoring** of the clinical response. Body weight can be used to determine ongoing fluid losses, however in many clinical situations the initial weight is unknown so it is of little value at the initial evaluation. Fluid deficits will lead to a **decrease in urine** production, and so measurement of urine production in relation to water intake is useful to monitor fluid therapy.

Clinical markers of **hydration status** (interstitial volume) include skin turgor, mucous membrane texture and corneal quality (tear film). Intravascular volume is reflected in capillary refill time, heart rate, pulse quality, mentation, mucous membrane color, extremity temperature, jugular fill and urine production.

Box 23.1 Guidelines for clinical assessment of hydration status and effective circulating volume

Clinical parameters

- Total body water
  - Skin turgor
  - Sunken eyes
  - Mucous membranes
- Effective circulating volume
  - Capillary refill time
  - Pulse quality
  - Heart rate
  - Jugular venous filling time
  - Temperature of the extremities

Interpretation

- Mild fluid deficit (estimated 5–7% of body weight)
  - Slightly decreased skin turgor
  - Dry mucous membranes
  - Prolonged jugular venous filling time
- Moderate fluid deficit (estimated 8–10% of body weight)
  - Decreased skin turgor
  - Dry mucous membranes
  - Prolonged capillary refill time
  - Prolonged jugular venous filling time
- Severe fluid deficit (estimated 11–12% of body weight)
  - Decreased skin turgor
  - Sunken eyes
  - Pale, dry mucous membranes [a]
  - Prolonged capillary refill time
  - Weak pulse volume
  - Tachycardia
  - Prolonged jugular venous filling time
  - Cool extremities
  - Obtundation
  - Marked tachycardia

[a] *In endotoxic shock, mucous membranes are hyperemic and congested except in the early stages where they are also pale.*

MONITORING CIRCULATORY STATUS AND FLUID THERAPY

Packed cell volume and total plasma protein

Packed cell volume (PCV) and total plasma protein (TP) are invaluable for assessing fluid deficits and monitoring the response to fluid therapy. They are quickly performed, using a microhematometer and refractometer, respectively. Guidelines for their interpretation are given in Table 23.3. PCV and TP should always be interpreted **together**. Both rise with simple dehydration.

Table 23.3 Interpretation of packed cell volume and total plasma protein concentrations

	Reference interval	
Packed cell volume (PCV)	32–52% (0.32–0.52 L/L)	
Total plasma protein (TP)	5.9–8.4 g/dL (59–84 g/L)	
	Interpretation	
	PCV	TP
Dehydration	↑	↑
Splenic contraction	↑	N
Dehydration with protein loss	↑	N
Acute blood loss	↓	↓
Chronic blood loss	↓	N
Dehydration with anemia	N	↑

↑, *Increased;* ↓, *decreased; N, within the reference interval.*

Table 23.4 Reference intervals for serum urea nitrogen, creatinine and electrolyte concentrations in adult horses

Urea	10–24 mg/dL (3.6–8.6 mmol/L)
Creatinine	0.7–1.8 mg/dL (62–159 μmol/L)
Sodium	132–146 mEq/L (132–146 mmol/L)
Potassium	2.4–4.7 mEq/L (2.4–4.7 mmol/L)
Chloride	99–109 mEq/L (99–109 mmol/L)
Calcium	10.9–12.8 mEq/L (2.7–3.2 mmol/L)
Magnesium	1.3–2.5 mEq/L (0.53–1.02 mmol/L)
Total carbon dioxide	20–36 mEq/L (20–36 mmol/L)
Anion gap	7–15 mEq/L (7–15 mmol/L)

In horses there is a wide reference range for PCV. Splenic contraction, which occurs under the influence of epinephrine/adrenaline, in association with pain, excitement or other stresses, can increase the PCV markedly but generally does not influence TP. An increased PCV with a normal TP, a relative hypoproteinemia, is also seen in animals that are both dehydrated and hypoproteinemic, a common finding in horses with **acute enterocolitis** (*q.v.*).

Despite their usefulness, PCV and TP also have limitations. **Anemia** (*q.v.*) may mask dehydration as a PCV within the normal range. Similarly, a normal total protein concentration suggestive of **euhydration** can be misleading in a hypoproteinemic animal. At the opposite end of the spectrum, hyperproteinemia due to **hyperglobulinemia** (*q.v.*), rather than dehydration, can be misleading in a normally hydrated horse.

Serum urea and creatinine

Serum urea and creatinine concentrations (Table 23.4) are increased in prerenal, renal and post-renal dysfunctions (*q.v.*). Urea is produced in the liver as a result of breakdown of ammonia. In horses and other large animals, urea concentrations may be influenced greatly by dietary factors, and as a result **creatinine concentration** is considered to be a better guide to renal function.

Creatinine is produced at a relatively constant rate as a by-product of muscle metabolism (creatine phosphate). It is excreted by **glomerular filtration**. Decreases in renal blood flow caused by reduction in effective circulating volume produce an increase in serum creatinine concentrations, yielding **pre-renal azotemia** (*q.v.*). Restoration of circulating volume should produce a rapid response in serum creatinine in these horses, and if serum creatinine concentrations remain persistently increased after rehydration, the presence of primary renal dysfunction or post-renal causes should be evaluated further.

Urine specific gravity

Urine specific gravity is a measure of **urine concentration**, which is made by refractometry. The normal range in adult horses is 1.020–1.050, while foals have more dilute urine. Neonates commonly have **hyposthenuric urine**. In dehydration, urine output decreases and specific gravity increases. The presence of a urine specific gravity of <1.020 in a dehydrated horse suggests that the renal function is impaired and should be evaluated further.

Arterial blood pressure

In many clinical situations, the initial goal of fluid therapy is to increase perfusion pressure by restoration of the effective circulating volume. Measurement of arterial blood pressure provides one objective means of determining and monitoring the **response to fluid therapy**. It is mandatory in cases in which inotrope or pressor support, in the form of pharmacologic agents to increase cardiac output or alter vascular tone, is being considered.

Arterial pressure is measured either directly via a manometer attached to an **intra-arterial catheter**, or indirectly using **Doppler or oscillation techniques**. Direct methods are more accurate and have the advantage that the pulse contour can also be assessed, providing information on the inotropic state and the afterload. Indirect methods are non-invasive, and thus are more readily performed in conscious horses (Table 23.5).

In standing horses, catheters are maintained most easily over prolonged periods in the **transverse facial artery**, to measure direct arterial blood pressure. For indirect arterial blood pressure, cuffs are generally applied to the tail to measure from the **middle coccygeal artery**. The cuff bladder width to tail circumference ratio should be approximately 25% to obtain most accurate results, and measurements should be taken with the horse in the same position for comparison purposes. When using extremities, a ratio of 40–50% should be used.

Table 23.5 Normal blood pressure in adult horses

Direct arterial	
Mean	80–110 mmHg
Systolic	110–160 mmHg
Diastolic	70–90 mmHg
Indirect arterial	
Mean	82–110 mmHg
Systolic	100–135 mmHg
Diastolic	70–97 mmHg
Central venous	0–15 cmH_2O

While most indirect means of blood pressure measurement provide only systolic pressures, oscillometric techniques, such as the Dinamap Blood Pressure Monitor (Critikon, Tampa, FL, USA), provide systolic, diastolic and mean blood pressures. Correlation of the displayed pulse rate to the actual heart rate is one means of checking the accuracy of the indirect technique, as is averaging repeated measurements.

Blood lactate concentration

Venous or arterial blood lactate concentration can be utilized as a marker of **peripheral perfusion**. Blood or plasma lactate concentrations represent the balance between production (primarily from glycolysis) and clearance (hepatic, renal). During **reduced oxygen delivery** states glycolysis predominates and results in hyperlactatemia. Other causes of high blood lactate include **proinflammatory states**, catecholamine surges, thiamine deficiency and alkalosis. Patients with liver failure and lymphosarcoma may have reduced clearance of lactate, and fluids devoid of lactate should be used in these groups (e.g. Normosol R, Plasma-Lyte 148). **Lactate concentrations** are <2 mmol/L in healthy adult horses, while they can be as high as 4 mmol/L 1–2 h post partum in neonatal foals. By 24 h of age lactate concentrations should be <2 mmol/L in healthy foals. **Serial measurement** of lactate concentrations is most useful in assessing perfusion responses to fluid volume replacement.

Central venous pressure

Central venous pressure (CVP; see Table 23.5) is dependent on cardiac output and the venous return. It is the pressure within the **intrathoracic vena cava** and approximates right atrial pressure. It is influenced by blood volume, vascular tone, heart rate and ventricular contractility. CVP falls in association with hypovolemia and rises if there is an increase in circulating volume. Measurement of CVP is used to assess cardiac function and to monitor fluid therapy and, in particular, to avoid **overzealous fluid administration**. As such, it can be used as one end point to fluid therapy.

Hypotension (*q.v.*) can be treated with volume support until CVP approaches maximum. Exceeding normal CVP values has the potential to cause pulmonary and tissue edema. CVP is easy to measure, requiring only a simple water manometer, IV catheter and extension tubing. A procedure for the measurement of CVP is described in Box 23.2. It should be noted that the monitoring of trends in CVP over time is crucial, rather than focusing on one value. Pleural and pericardial diseases will also cause increases in CVP (*q.v.*).

Colloid osmotic pressure

Colloid osmotic pressure (COP), or **oncotic pressure**, is the osmotic force within the intravascular compartment exerted by albumin and other macromolecules, which counteract capillary and venule hydrostatic forces in determining net fluid flux across the endothelium. Plasma COP is primarily determined by albumin (65–80%) and is required to maintain proper circulating volume. Patients with hypoalbuminemia are therefore at risk for edema formation and relative hypovolemia, both of which lead to **reduced tissue oxygen delivery**.

Box 23.2 Procedure for the measurement of central venous pressure

1. Advance a saline-filled IV catheter into the right atrium via the jugular vein (adult horses: 46 cm [18 in] or 61 cm [24 in] cm catheter; foals: 20–30 cm [12 in] catheter)
2. Attach a saline-filled extension tube to the IV catheter (patient line)
3. Attach a water manometer to the extension tube via a three-way stopcock
4. Attach a saline-filled syringe to the remaining inlet of the three-way stopcock
5. Suspend the water manometer so that the baseline (0 cm) is at the level of the right atrium, using the point of the shoulder as a landmark
6. Ensure that the horse's head is in a normal position
7. Close the water manometer and flush the patient line with saline
8. Close the patient line and flush the water manometer with saline
9. Turn the three-way stopcock so that the patient line is open to the water manometer
10. The fluid column in the water manometer will fall to the level of the central venous pressure

Although total protein and albumin concentrations provide indirect information about COP, and are crucial in monitoring albumin dynamics, they are not as well correlated with oncotic pressure in the critically ill animal as compared to healthy horses. In ill patients, direct measurement of COP using a **colloid osmometer** (Wescor 4420 colloid osmometer, Wescor, Logan, UT, USA) is important. Additionally, total protein concentrations do not measure the oncotic contribution of synthetic colloids such as hetastarch or Hextend. **Direct measurement** of COP in horses receiving synthetic colloids is the only means of monitoring the oncotic effects of these products. **Normal oncotic pressure** in adult horses is 20–30 mmHg, and in neonatal foals is 15–23 mmHg.

ELECTROLYTE BALANCE

Sodium

Sodium is the most abundant cation in the **extracellular** fluid (ECF; see Table 23.4). Sodium is ingested with feed and water intake, and is lost in urine, feces and sweat. It can be regarded as the "skeleton" of the ECF, as it is the principal determinant of the ECF osmolarity, and consequently its volume. Osmolarity can be measured directly with an osmometer, or alternatively calculated using the following formula:

$$\text{ECF osmolarity} = (\text{Na} \times 2) + \frac{\text{glucose}}{18} + \frac{\text{BUN}}{2.8}$$

where sodium is in mEq/L and glucose and BUN are in mg/dL.

The excretion of sodium via the kidney is controlled by the renin–angiotensin–aldosterone system (*q.v.*). **Hyponatremia** (*q.v.*) occurs if there is a

reduced intake of sodium, however deficits due to excessive losses are more common. These arise if sodium loss from the gastrointestinal or urinary tract is in excess of water loss, and thus hyponatremia indicates a **relative water excess**. Box 23.3 lists clinical conditions associated with hyponatremia.

Hypernatremia (*q.v.*) arises when water is lost in excess of electrolytes (see Box 23.3). Both hyponatremia and hypernatremia should be treated with caution; rapid correction of hyponatremia can result in demyelination and central pontine myelinolysis, while cerebral edema can result from overzealous treatment of hypernatremia. Plasma sodium concentrations should be **altered slowly**, not exceeding 0.5 mEq/h. Hyponatremia can be corrected using sodium-containing fluids such as 0.9% sodium chloride, lactated Ringer's solution, Plasma-Lyte 148, or Normosol R. Varying formulations of hypertonic saline can also be used depending on the rate of rise. Hypernatremia can be treated with the provision of **free water**, as with maintenance fluids. These include Plasma-Lyte 56 or Normosol-M, but 5% dextrose in water can also be used.

Potassium

Potassium is the primary **intracellular** cation. Potassium has a central role in the maintenance of cell membrane electrical potentials, and is important in muscle contraction. The normal intracellular potassium concentration is 145–150 mEq/L, whereas its extracellular concentration is 2.4–4.7 mEq/L. It is present in gastrointestinal secretions, sweat and urine. Its distribution between the intra- and extracellular compartments is influenced by the **acid-base status**; potassium leaves the cell in exchange for hydrogen ions so that in the presence of acidosis serum potassium concentrations increase.

In anorexic horses, potassium can quickly be depleted and diarrhea also frequently results in **hypokalemia** (see Box 23.3). Severe hypokalemia can be accompanied by muscle weakness and ileus. Management of hypokalemia should include supplementation of fluids with potassium chloride or potassium phosphate. The rate of supplementation should not exceed 0.5 mEq/kg/h. Empirical supplementation of fluids with 10–40 mEq/L of KCl is the usual range utilized to treat or prevent hypokalemia. As hypomagnesemia (*q.v.*) can be associated with refractory hypokalemia, magnesium concentrations should be monitored in these patients.

The causes of **hyperkalemia** are also listed in Box 23.3. Hyperkalemia must be regarded as an **emergency** as cardiac arrhythmias (*q.v.*) frequently occur as a result of the electrical instability of the myocardial cell membrane if serum potassium concentrations rise. Electrocardiographic changes associated with hyperkalemia include spiked T waves, prolonged PR interval, disappearance of P waves, prolongation of the QRS complex, shortening of QT or ST intervals and ventricular dysrhythmias (*q.v.*). Management of hyperkalemia includes the use of potassium-free fluids, dextrose, insulin and sodium bicarbonate. Dextrose can be added as a 5% solution. Insulin should be utilized only when plasma glucose concentrations can be monitored frequently and may be given as **regular insulin** (0.01–0.1 U/kg/h).

Sodium bicarbonate should be directed by **blood gas analysis**, but safe amounts can be administered at a dose of 0.5–1 mEq/kg over 30–60 min assuming the patient is not hypoventilating. **Calcium supplementation** can

Box 23.3 Conditions associated with electrolyte and metabolic imbalances in horses

Hyponatremia
- Esophageal obstruction
- Enterocolitis
- Intestinal obstruction
- Polyuric renal failure
- Urinary tract disruption
- Inappropriate antidiuretic hormone secretion

Hypernatremia
- Enterocolitis
- Excessive sweating
- Water deprivation

Hypokalemia
- Enterocolitis
- Intestinal obstruction
- Anorexia
- Renal tubular acidosis
- Polyuric renal failure
- Diuretic administration
- Bicarbonate administration
- Insulin administration

Hyperkalemia
- Muscle necrosis
- Urinary tract disruption
- Anuric renal failure
- Hyperkalemic periodic paralysis in Quarter-horses
- (in vitro hemolysis)

Hypocalcemia
- Stress
- Lactation and transit tetany
- Synchronous diaphragmatic flutter
- Acute renal failure
- Cantharidin toxicity

Hypercalcemia
- Chronic renal failure
- Hypercalcemia of malignancy
- Vitamin D toxicosis

Metabolic acidosis
- Enterocolitis
- Intestinal obstruction
- Renal tubular acidosis
- Lactic acidosis (shock, grain overload)

Box 23.3 continues on page 1267

Box 23.3 Conditions associated with electrolyte and metabolic imbalances in horses [continued]

Metabolic alkalosis
- Esophageal obstruction
- Nasogastric reflux
- Exertional rhabdomyolysis
- Excessive sweating
- Hyperalimentation
- Diuretic administration

be used to antagonize the membrane effects of potassium, but will not lower potassium concentrations directly. Enhancement of potassium clearance can be accomplished with **exchange resin enemas** (polystyrene sulfonate or Kayexalate) and the use of loop or other potassium-excreting diuretics.

Chloride

Chloride is present in high concentrations in the ECF (see Table 23.4). At most sites within the body, chloride tends to follow sodium passively by diffusion within the cell membrane, so that the regulation of chloride concentration in the ECF is **directly related to the sodium concentration**. In the ECF, chloride concentrations are inversely related to bicarbonate concentrations. Chloride is a strong anion, contributing to **strong ion difference (SID)**.

With increases in chloride concentrations, the SID will decrease, resulting in an acidosis [SID = (Na + K) − (Cl + lactate)]. This is the reason that physiologic saline (0.9% NaCl) tends to be mildly acidifying. The chloride content of saline is relatively greater than sodium relative to normal serum concentrations. Chloride is present without sodium in gastric secretions, and there is a specialized transport system for chloride in the loop of Henle. Chloride is excreted in the urine in quantities dependent on the body's need for bicarbonate.

In horses, chloride depletion occurs if there is loss of chloride-rich fluid from the proximal gastrointestinal tract, thus **hypochloremia** may be associated with esophageal obstruction (*q.v.*) or with nasogastric reflux due to ileus or proximal gastrointestinal obstruction (*q.v.*). Hypochloremia is usually accompanied by **metabolic alkalosis** (see Box 23.3) but may be seen in states of **metabolic acidosis** during attempts at metabolic compensation through enhanced excretion of urinary chloride.

Primary hyperchloremia due to excessive salt intake is uncommon, but may accompany renal dysfunction and dehydration due to water loss only. Hyperchloremia accompanies **renal tubular acidosis**.

Calcium

Calcium is an abundant divalent cation throughout the body. Absorption of calcium is via the gastrointestinal tract. It has an integral role in multiple biological processes, including nervous, skeletal, smooth muscle and myocardial

function, and blood clotting. It is excreted by the kidney, and bone represents a large calcium reservoir. Calcium homeostasis is regulated by the hormones **parathormone** and **calcitonin** (*q.v.*).

Hypocalcemia associated with **lactation** may produce signs of tetany, particularly in mares exposed to an additional stressor such as transport (see Box 23.3). Mild hypocalcemia is frequently observed with abdominal crises, and it may contribute to **postoperative ileus** (*q.v.*) and weakness in some of these horses.

Calcium supplementation should be performed **slowly** and diluted in fluids. Supplementation with 0.5–1 mEq/kg of **calcium gluconate** is indicated in horses with hypocalcemia or prolonged anorexia (250–500 mL of 23% calcium gluconate, diluted in fluids). Calcium-containing fluids should not be administered through the same lines as blood products or sodium bicarbonate, due to precipitation problems.

Hypercalcemia (see Box 23.3) is usually due to chronic renal failure (*q.v.*), a biochemical abnormality unique to the horse. Paraneoplastic syndromes (pseudohyperparathyroidism) and vitamin D excess are uncommon causes of hypercalcemia. Hypercalcemia is more difficult to treat, but as a minimum, calcium intake should be reduced by feeding a diet low in calcium; **alfalfa should be avoided**.

Monitoring of calcium in the ICU should include daily measurement of total calcium concentration, while ionized calcium concentrations should be checked more often in the patient receiving fluid therapy. Approximately 50% of calcium is bound to plasma proteins, while an additional 5–10% is chelated to plasma anions like phosphate. The remainder is free, ionized calcium, which is the physiologically active form.

Ionized hypocalcemia is the clinically significant form of hypocalcemia, while hypoalbuminemia causes a decrease in the amount of calcium in the protein-bound fraction and is not as physiologically important. Alkalosis causes a shift in calcium fractions and decreased ionized calcium concentration. This should be considered in patients being treated with sodium bicarbonate and in those with respiratory alkalosis. Patients receiving large volumes of blood products should also be monitored for ionized hypocalcemia because of calcium binding by citrate. Magnesium depletion is another risk factor for development of hypocalcemia in the ICU, by inhibiting parathyroid hormone secretion and target tissue responsiveness.

ASSESSMENT OF ELECTROLYTE DISORDERS

The assessment of electrolyte disorders must be based on laboratory evaluation of serum concentrations of electrolytes. Specific electrolyte disorders cannot be predicted simply from the clinical presentation or problem. Serum concentrations of sodium are accurate in assessing sodium deficits or relative excesses, as sodium is an extracellular ion. In contrast, measurement of serum potassium concentration does not reflect the whole body content of potassium, as this is primarily an intracellular ion. Acid-base status further complicates the interpretation of serum potassium concentrations. A decrease in pH of 0.1 units causes an increase in serum potassium concentration of 0.6 mEq/L. Thus, **acidosis can mask potassium depletion** by increasing the

concentration of potassium in the ECF. This is seen commonly with bicarbonate and potassium losses associated with enterocolitis (*q.v.*).

Estimates of sodium and potassium deficits for the purposes of replacement therapy are made by considering the difference between the measured and desired serum concentrations, the horse's body weight and the distribution of the ion within the body, as follows:

Sodium deficit (mEq) =
(sodium concentration desired − sodium concentration observed)
× body weight (kg) × 0.6 (total body water)

Potassium deficit (mEq) =
(potassium concentration desired − potassium concentration observed)
× body weight (kg) × 0.3 (ICF, intracellular fluid)

However, repeated **laboratory evaluations** are undoubtedly the most rational means by which to assess the response to replacement of electrolytes. Because potassium is primarily an intracellular ion, serum concentrations are poor indicators of whole body potassium balance. Urinary fractional excretion of potassium may improve understanding of body potassium stores. Fractional excretion is calculated as follows:

$$FE_k = \frac{S_{cr}}{U_{cr}} \times \frac{S_k}{U_k}$$

where S_{cr} is serum creatinine concentration, U_{cr} is urine creatinine, U_k is urine concentration of potassium, and S_k is serum concentration of potassium.

ACID–BASE BALANCE

The **blood pH** is dependent on the respiratory system and the function of a variety of buffering systems. The **carbonic acid/bicarbonate buffer system** is of most interest to the clinician, since it is amenable to clinical intervention. Hydrogen ions, carbon dioxide, water and bicarbonate are produced constantly by cellular metabolism. Carbon dioxide is transported in blood as dissolved or free carbon dioxide; in association with protein and hemoglobin; and as bicarbonate. In the lungs, bicarbonate dissociates to carbon dioxide and water, and carbon dioxide is exhaled. The regulation of serum bicarbonate concentration is achieved in large part by the kidneys.

Acid–base disorders may be classified as respiratory or metabolic in origin (see Box 23.3), and mixed acid-base disorders are common. Failure of ventilation results in the inability to remove carbon dioxide (**respiratory acidosis**), while hyperventilation decreases carbon dioxide and causes **respiratory alkalosis**. It is important to appreciate that acid-base disorders of respiratory origin cannot be alleviated by fluid therapy and require modification of respiratory function.

Metabolic acidosis can be the result of excessive production of organic acids (titration) or of loss of bicarbonate (secretion). The titration form of metabolic acidosis occurs when there is an increase in acid anions and bicarbonate

is required for buffering. In the horse, **lactic acidosis** (*q.v.*) occurs commonly. It is usually associated with hypovolemic, cardiogenic or endotoxic shock (*q.v.*) and inadequate tissue perfusion. The secretion form of metabolic acidosis occurs when bicarbonate ions are actively lost from the body (see Box 23.3). In some conditions, both secretion and titration of bicarbonate will occur.

Mixed metabolic acidosis and alkalosis may be present in horses with gastrointestinal disease (*q.v.*). This occurs, for example, when fluid is sequestered in the proximal gastrointestinal tract leading to chloride and hydrogen ion loss and metabolic alkalosis, with a concurrent reduction in effective circulating volume, producing shock, poor tissue perfusion and lactic acidosis.

Assessment of acid–base balance

An **arterial blood gas analysis** is required for full evaluation of both the respiratory and metabolic components of acid–base balance. Normal values for arterial and venous blood gas analysis are given in Table 23.6. Interpretation of the respiratory component is based on the partial pressure of carbon dioxide in arterial blood (Table 23.7). Metabolic disorders are manifested by alterations in bicarbonate concentrations and the base deficit. Both arterial and

Table 23.6 Reference intervals for blood gas analysis in horses

	Arterial	Venous
pH	7.347–7.475	7.345–7.433
PO_2 (torr or mmHg)	80–112	37–56
PCO_2 (torr or mmHg)	36–46	38–48
HCO_3^- (mEq/L or mmol/L)	22–29	22–29
Base excess (mEq/L or mmol/L)	−1.7 to +3.9	−2.7 to +4.1

Table 23.7 Interpretation of blood gas analysis and acid–base status

	pH	PCO2	$[HCO_3^-]$	Anion gap[a]
Respiratory acidosis	↓	↑	N	N
Respiratory alkalosis	↑	↓	N	N
Metabolic acidosis				
Secretion	↓	N	↓	N
Titration	↓	N	↓	↑
Metabolic alkalosis	↑	N	↑	N
Mixed metabolic acidosis and alkalosis	N	N	N	↑

↑, Increased; ↓, decreased; N, normal.

[a] *Anion gap = ([sodium] + [potassium]) − ([bicarbonate] + [chloride]).*

NB: In acid-base disorders, compensation may result in the following changes:

Respiratory acidosis: acute: $[HCO_3^-]$ increases 1 mEq/L for every 10 mmHg increase in PCO_2;
chronic: $[HCO_3^-]$ increases 3.5 mEq/L for every 10 mmHg increase in PCO_2.

Metabolic acidosis: PCO_2 decreases 1.2 mmHg for every 1 mEq/L decrease in $[HCO_3^-]$.

Metabolic alkalosis: PCO_2 increases 0.6–1 mmHg for every 1 mEq/L increase in $[HCO_3^-]$.

Respiratory alkalosis: acute: $[HCO_3^-]$ decreases 2 mEq/L for every 10 mmHg decrease in PCO_2;
chronic: $[HCO_3^-]$ decreases 5 mEq/L for every 10 mmHg decrease in PCO_2.

venous blood gas analysis are equally suitable for assessment of the metabolic component of acid–base disorders (see Table 23.6).

Respiratory and metabolic components of acid–base balance are interdependent so that a respiratory disorder may lead to compensation and concurrent alterations in bicarbonate concentrations. Equally, a metabolic disorder may induce changes in respiration pattern and alteration in the PCO_2.

The anion gap (the difference between cations and measured anions) is used to distinguish titration and secretion forms of metabolic acidosis (see Table 23.7). The **anion gap** is a reflection of those ions that are not measured, organic acids, phosphates, sulfate and protein. **Lactic acidosis** increases the anion gap, whereas the anion gap is unchanged when the primary problem is loss of bicarbonate. In that situation, chloride concentrations increase as bicarbonate concentrations fall to maintain electrical equilibrium. An increase in the anion gap with a normal pH and bicarbonate are the hallmarks of **mixed metabolic acidosis and alkalosis** (see Table 23.6). Without assessment of the anion gap, this abnormality might otherwise go unnoticed as alterations in both pH and bicarbonate are counteracted by the conflicting processes.

Blood samples for blood gas analysis are collected in **heparinized syringes**, and tightly capped prior to analysis to prevent air contamination. Ideally, the sample should be processed as quickly as possible, but samples may be stored on ice for up to 4 h if necessary. **Total carbon dioxide (TCO_2) concentration** can be used as an alternative to measurement of bicarbonate concentration for the assessment of metabolic acid-base disorders. Total carbon dioxide is slightly less accurate, but is usually adequate for clinical purposes. Various pieces of equipment are available for rapid "in practice" total carbon dioxide assays and this test is included in chemistry panels on many autoanalyzers. Base deficit can be estimated using the total carbon dioxide as well. Subtracting the TCO_2 from the median normal bicarbonate (24 mmol/L) will provide an estimate of the base deficit.

PRINCIPLES OF FLUID THERAPY

In most clinical situations, the plan for fluid therapy includes three components: replacement of existing deficits; supplying of maintenance requirements; and matching ongoing losses.

Over-hydration, the administration of fluid in excess of the body's requirements, is occasionally indicated. Colonic impactions (*q.v.*) represent clinical conditions that are treated with over-hydration. The selection of type of fluid and the rate of administration are dependent on the clinical problem and the specific deficits. The clinical and laboratory assessments described above are used to estimate deficits and evaluate ongoing losses.

In horses, fluids are administered either by oral or IV routes. In most clinical conditions in which replacement of fluid deficits or restoration of effective circulating volume is required, the IV route is mandatory because of the volumes required, and because many gastrointestinal diseases preclude oral administration. However, the **oral route should be used whenever possible**. It has the advantages that it is more physiological, it is considerably less expensive and the risk of iatrogenic or nosocomial infections is negligible.

REPLACEMENT THERAPY

Cardiovascular collapse

Replacement of fluid and effective circulating volume is the first priority in horses presenting with signs of cardiovascular collapse. IV administration is required to provide sufficient volumes. **Crystalloid solutions** are most widely used for replacement therapy. Effective circulating replacement can be achieved using crystalloid or colloidal solutions.

Crystalloids

The ideal crystalloid solution for **volume replacement** has a composition similar to that of plasma. These include lactated Ringer's (Hartman's) solution or similar balanced polyionic solutions such as Plasma-Lyte (Baxter Health Care Corp., Deerfield, IL, USA [available in 5 L bags]), Multisol-R (Normosol-R, CEVA) and Isolec (IVEX Ltd, Larne, Northern Ireland, UK [available in 5 L bags]) (Table 23.8). **Lactated Ringer's solution (LRS)** contains calcium, whereas Plasma-Lyte and Normosol contain magnesium.

Since blood products should not be administered through the same lines as calcium-containing fluids, the latter fluids should be used during blood or plasma transfusions. Another difference between LRS and Plasma-Lyte/Normosol is the type of alkalinizing agent present. LRS contains lactate and Plasma-Lyte/Normosol products contain acetate and gluconate. Lactate is cleared primarily by the liver, acetate is cleared primarily by muscle, and gluconate is metabolized by most cells.

Colloids

Colloid solutions contain glycerin, glucose polymers, or dextrans of high molecular weight. They are effective because they remain in the intravascular compartment longer than crystalloid solutions, assuming normal vascular integrity. **Anaphylactic or anaphylactoid reactions** (*q.v.*) have been associated with the use of dextrans in horses, and **hetastarch** appears to be safer.

Plasma is a suitable alternative for rapid replacement of circulating volume (see Table 23.8). However, in the volumes required it is often prohibitively expensive to be used for colloid support alone. Under these circumstances, plasma should be used in combination with synthetic colloids such as hetastarch.

The **rate of administration** of replacement fluid depends on the severity of the clinical signs and the ongoing losses. There is no one correct way to replace volume; one half of the deficit may be given in the first 2–6 h, with the remainder being given over the following 6–12 h. However, in adult horses with cardiovascular collapse, fluids may be administered safely at rates of **up to 30 L/h** if necessary to restore perfusion. Such boluses are often required in horses with **hypovolemic shock** (*q.v.*). The **clinical response** is often the best guide to rate of fluid administration.

Fluid overload produces **pulmonary edema**, thus the respiratory rate and effort and the quality of the lung sounds should be evaluated frequently

Table 23.8 Composition and indications for use of intravenous fluids

	pH	Tonicity	Na (mEq/L)	K (mEq/L)	Ca (mEq/L)	Mg (mEq/L)	Cl (mEq/L)
Lactated Ringer's (Hartmann's)	6.2–6.7	Iso	130	4	3	–	109
Plasma-Lyte R (Baxter)	5.5	Iso	140	10	5	3	103
Plasma-Lyte 148	5.5	Iso	140	5	0	3	98
Plasma-Lyte 56	5.5	Hypo	40	13	0	3	40
Multisol R/ Normosol R (CEVA)	6.4	Iso	140	5	0	3	98
Normosol M	–	Hypo	40	13	0	3	40
2.5% dextrose in 0.45% saline	4.5	Iso	77	–	–	–	77
5% dextrose	5.0	Iso	–	–	–	–	–
Normal saline	5–5.7	Iso	154	–	–	–	154
7% saline	–	Hyper	1200	–	–	–	1200
Plasma	7.0	Iso	142	5	5	3	103
5% sodium bicarbonate	7.8	Hyper	595	–	–	–	–
Isotonic sodium bicarbonate	–	Iso	150	–	–	–	–

	Buffer (mEq/L)	Calories/L	Indications
Lactated Ringer's (Hartmann's)	Lactate, 29	9	Volume replacement maintenance [a]
Plasma-Lyte R (Baxter)	Acetate, 47 Gluconate, 8	11	Volume replacement maintenance [a]
Plasma-Lyte 148	Acetate, 27 Gluconate, 23	18	Volume replacement
Plasma-Lyte 56	Acetate, 16	–	Maintenance
Multisol R/ Normosol R (CEVA)	Acetate, 27 Gluconate, 23	18	Volume replacement
Normosol M	Acetate, 16	–	Maintenance
2.5% dextrose in 0.45% saline	–	85	Maintenance
5% dextrose	–	170	Provision of water for maintenance
Normal saline	–	9	Sodium or chloride replacement Acidification [b]
7% saline	–	–	Expansion of circulating volume [c]
Plasma	Bicarbonate, 27	3	Expansion of circulating volume, hypoproteinemia
5% sodium bicarbonate	Bicarbonate	–	Replacement [d] of bicarbonate in metabolic acidosis due to bicarbonate secretion
Isotonic sodium bicarbonate	Bicarbonate, 150	–	Replacement [d,e] of bicarbonate in metabolic acidosis due to bicarbonate secretion

Iso, isotonic; Hyper, hypertonic.

[a] *These solutions are not designed for maintenance as their sodium concentration is excessive. However, they are commonly used for this purpose, largely for convenience, and are safe provided renal function is normal. Consideration should be given to simultaneous administration of 5% dextrose if they are to be used for maintenance purposes for extensive periods.*

[b] *Normal saline should not be used for volume replacement, but only to correct specific sodium or chloride deficits, and as an acidifying solution.*

[c] *Hypertonic saline is contraindicated in renal failure and must always be followed with isotonic solutions. Seven per cent sodium chloride is made by dissolving 175 g sodium chloride in 2.5 L of water.*

[d] *Serum potassium concentration must be monitored carefully.*

[e] *Isotonic bicarbonate is made by adding 250 mL of 5% sodium bicarbonate (150 mEq Na: 150 mEq HCO_3^-) to 750 mL of sterile water.*

during the rapid IV administration of large volumes. CVP is the most objective guide to the rate of fluid administration, but examination of the height of the **jugular pulse** also gives a crude estimation of rising CVP. CVP can be easily measured in both horses and foals, through the use of central lines and a water manometer as described in Box 23.2. Optimization of the CVP can be used as a fluid administration end-point goal. Once near maximum CVP (10 cmH_2O in a neonate; 12–15 cmH_2O in an adult) is achieved using fluid loading, rates of administration should be decreased to avoid risks of edema formation.

Hypertonic saline (7%) is a valuable alternative for the **emergency resuscitation** of horses with hemorrhagic, hypovolemic or endotoxic shock (see Table 23.8). Administration of hypertonic solutions increases the effective circulating volume, cardiac output and blood pressure. The precise mechanisms by which it is effective are still unclear. A number of processes may be involved, including a vagally mediated reflex, redistribution of blood from peripheral to central vascular beds, increasing cardiac contractility, and relocation of fluid from the interstitium and ICF to the intravascular space.

Urine output is increased following administration of hypertonic solutions and this leads to a decrease in total body water. For that reason, it is imperative that hypertonic solutions are followed with isotonic solutions to maintain total body water. Hypertonic saline is administered at 4 mL/kg and is given as quickly as possible (in approximately 10 min). It is **contraindicated** in horses with **renal failure**. Some authors have expressed reservations about its use in hemorrhagic shock, as increasing the blood pressure may promote further bleeding. It should not be used in horses with uncontrolled bleeding.

Hyperosmolarity is another consideration. Because hypertonic solutions borrow water from the interstitium and intracellular spaces, they should not be utilized in maximally dehydrated horses. In these cases, concurrent or prior administration of isotonic crystalloid should be performed.

METABOLIC ACIDOSIS

The approach to the correction of **metabolic acidosis** depends on the underlying cause. Acidosis due to depletion of bicarbonate by buffering acid anions in lactic acidosis (titration) is best addressed by the correction of the underlying cause. Hypoperfusion should be improved by volume replacement with a **balanced polyionic solution**. These solutions contain bicarbonate precursors such as lactate, acetate or gluconate. For horses with fluid-refractory hypotension, inotrope and vasopressor therapy should be considered. **Hypoxemia** or reduced oxygen carrying capacity should be addressed through oxygen supplementation or blood transfusions, respectively.

In horses with **enterocolitis** (*q.v.*) that are actively losing bicarbonate or sodium ions (secretion), administration of sodium bicarbonate may be warranted. **Hyperchloremic metabolic acidosis** may also benefit from sodium bicarbonate administration. Bicarbonate should only be supplemented when the serum base deficit is >6–8 mEq/L. The bicarbonate deficit may be estimated as follows:

$$\text{Bicarbonate estimate (mEq)} = 0.3 \times \text{body weight (kg)} \times \text{base deficit (mEq/L)}$$

or, if total carbon dioxide (TCO_2) is measured, as on a serum biochemistry profile:

Bicarbonate deficit (mEq) =
0.3 × body weight (kg) × (total carbon dioxide desired − total carbon dioxide measured)

It is often suggested that one half of the calculated deficit be given over 1 h, the blood gas analysis then repeated, and the remainder of the deficit replaced over the next 6 h. However, in horses with **diarrhea**, considerable quantities of sodium bicarbonate may be required simply to meet **ongoing losses**, and more than the initial calculated deficit may be needed. Repeated blood gas or total carbon dioxide measurements are the most reliable guides to the administration of bicarbonate.

Sodium bicarbonate administration may have a number of adverse effects. It can constitute an **excessive sodium load**. Potentially, a **paradoxical central nervous acidosis** may develop because carbon dioxide is formed following bicarbonate administration, and this diffuses through the blood–brain barrier, decreasing pH in the cerebrospinal fluid, while bicarbonate cannot pass the blood–brain barrier to buffer the carbon dioxide. Intracellular acidosis may also be potentiated through the rapid administration of sodium bicarbonate for similar reasons. Bicarbonate should not be administered to horses with impaired ventilation as carbon dioxide excretion is limited, and bicarbonate administration can potentiate carbon dioxide production.

Bicarbonate administration may induce **hypokalemia** as potassium ions enter the cells in exchange for hydrogen ions. Potassium concentrations should be monitored and potassium chloride (20 mEq/L) should be added to bicarbonate solutions to avoid this. Sodium bicarbonate can also produce decreases in plasma ionized calcium.

Sodium bicarbonate is available as 5% and 8.4% solutions, both of which are hypertonic and should be **diluted** before use. An isotonic solution of bicarbonate can be made by dilution with sterile water to a concentration of 150 mEq/L of sodium and of bicarbonate (1.3% sodium bicarbonate) (see Table 23.8). Bicarbonate should not be added to calcium-containing solutions as **precipitates** are formed.

METABOLIC ALKALOSIS

Metabolic alkalosis is uncommon in horses. It is seen as a result of loss of hydrogen and chloride ions in **nasogastric reflux** (*q.v.*), often accompanied by hypochloremia and hypokalemia. Horses with **heavy sweating**, such as those in **endurance rides**, can also develop alkalosis. Therapy is aimed at replacement of chloride, and promotion of excretion of bicarbonate via the kidney by restoration of body water. Normal saline, supplemented with potassium, is the fluid of choice for the treatment of metabolic alkalosis (see Table 23.8). Circulating volume deficits should be addressed. Supplementation with magnesium can also aid in treating refractory alkaloses.

Sodium

Hyponatremia rarely requires specific therapy, however **normal saline** can be used to increase serum concentrations of sodium. Hyponatremia should

be corrected slowly to prevent rapid dehydration of the central nervous system (CNS) thereby leading to central pontine dysmyelinolysis and demyelination (*q.v.*).

Hypernatremia indicates a water deficit. Replacement of water can be achieved using **5% dextrose**, as at this concentration dextrose is metabolized to carbon dioxide and water. Once glucose is metabolized, 5% dextrose is essentially free water. Alternatively, an infusion of 0.45% saline in 2.5% dextrose may be used for delivery of lower rates of free water.

Extreme caution should be exercised in the treatment of hypernatremia as **cerebral edema** (*q.v.*) may develop if the plasma osmolarity is reduced too rapidly. A safe rule of thumb is that both hyponatremia and hypernatremia should be corrected slowly, without exceeding 0.5 mEq/h.

Potassium

IV replacement of potassium deficits is difficult to achieve as **cardiac arrhythmias** can develop when excessive quantities of potassium are administered. No more than 0.5 mEq/kg/h should be given IV in horses with normal renal function, with lower amounts for those with **kidney disease**. Oral replacement of potassium is much safer, and larger quantities (up to 60 g at a time) can be administered. Potassium supplementation should be performed with extreme caution in horses with **hyperkalemic periodic paralysis (HYPP)** (*q.v.*) and those with acute anuria or oliguria.

Hyperkalemia is regarded as a medical emergency because of the risk of cardiac arrhythmias or dysrhythmias (*q.v.*), including diminished P wave amplitude, loss of P waves, spiked or tented T waves, increasing duration of the QRS complex and a variety of ventricular dysrhythmias.

The concentration of potassium in the ECF can be reduced by promoting cellular uptake by the administration of sodium bicarbonate, or insulin (0.1–0.5 units/kg), or enhancement of the secretion of insulin by dextrose infusion (4–6 mL/kg of 5% dextrose). Potassium-wasting **diuretics, such as furosemide or carbon anhydrase inhibitors**, may be used to remove potassium from the body. Calcium has been recommended for its cardioprotective effects in hyperkalemia because it raises threshold potential (0.2–0.4 mL/kg of a 23% calcium gluconate solution, administered very slowly and diluted, i.e. over no less than 20 min and preferably longer).

Calcium

Replacement of calcium in horses requires **extreme caution** in order to avoid development of **bradycardia** or dysrhythmias (*q.v.*). Calcium gluconate solutions designed for the treatment of hypocalcemia in ruminants can be administered to horses. However, they must be given considerably **more slowly** in horses than in ruminant species. Unless calcium is being administered for its life-saving cardioprotective effects, e.g. in HYPP, it is wise to supplement calcium slowly over a period of 12–24 h.

Accurate estimation of calcium deficits is impossible, and calcium is given to effect, ideally based on serum ionized calcium concentrations. Calcium supplementation should be performed diluted in fluids, and it should not be administered along with sodium bicarbonate or blood/plasma products. Average-sized

and adult horses require 10 g of calcium per day (20 g orally), which can be supplied through 1 mEq/kg/day calcium as 23% calcium gluconate.

MAINTENANCE FLUID THERAPY

The maintenance requirements may be divided into those required by normal body losses, and additional losses that are incurred as a result of the animal's clinical problem (ongoing losses). It is estimated that **maintenance requirement** for fluid in adult horses is 40 mL/kg/day or more, thus a 500 kg horse needs at least 20 L/day. Based on water intake studies, a rate of 2–3 mL/kg/h is a reasonable maintenance rate to be utilized in most horses. Diarrhea or nasogastric reflux can considerably increase this figure.

In horses with **nasogastric reflux** (*q.v.*) it is easy and helpful to quantitate fluid losses, however with diarrhea this is generally difficult. Regardless, clinical parameters, biochemical markers such as lactate, and the **PCV and TP** should be serially evaluated to determine the adequacy of fluid administration. If **over-hydration** (*q.v.*) is a concern (e.g. in horses with renal failure) CVP should be measured and fluid administration tailored to ensure that CVP remains below 15 cmH_2O. Serial monitoring of CVP is more important than single measurements in order to follow trends.

IV maintenance

Fluids **specifically designed** for IV maintenance therapy are isotonic to hypotonic. To avoid an excessive sodium load, these solutions generally contain dextrose and water in addition to saline, e.g. 2.5% dextrose in 0.45% saline (see Table 23.8) or free water, e.g. Plasma-Lyte 56 or Normosol M (osmolarity 110 mOsm/L).

Some free water is needed for hydration of the intracellular fluid compartment. However, balanced polyionic replacement fluids such as lactated Ringer's (LRS) or equivalent balanced polyionic solutions can be, and frequently are, used for short-term maintenance (see Table 23.8). Although these solutions contain more sodium than is necessary, the excess sodium load can readily be excreted if renal function is normal. In addition, replacement fluids such as LRS can be utilized as maintenance fluids for horses that are allowed access to oral water. True "maintenance fluids" will be necessary for long-term fluid management of horses not allowed oral water, and for those with **renal failure**.

The horse has a high requirement for potassium (approximately 3000 mEq/day for a 450 kg horse). It is therefore standard practice to add 20 mEq of potassium chloride per liter of prepared balanced polyionic solutions. However, this will provide only approximately 1250 mEq of potassium per day, and further supplementation may be required in some cases. Potassium should be administered IV at rates of 0.3–0.5 mEq/kg/h or less.

Ideally, maintenance fluids should be administered as a **constant infusion**. Automated digital fluid pumps can accurately deliver fluids as a constant rate infusion (CRI). However, if necessary, the daily requirement can be divided into 4–6 doses and administered as boluses. This is an inefficient method, as some fluid is lost by urination following rapid boluses. In addition, CVP may

increase after boluses, which may promote edema in hypo-oncotic horses, horses with increased vascular permeability, or those with high venous pressures (e.g. cardiac failure).

Oral maintenance

The **oral route** should always be used for fluid administration whenever possible. In addition to a financial advantage, oral fluid therapy is more physiological and carries little risk of over-hydration. Potassium, which can be dangerous when administered in large doses IV, can be administered orally in larger quantities. Horses unwilling or unable to drink and those with mild dehydration associated with chronic diarrhea or other fluid losses may be managed very successfully with fluids given by **nasogastric tube**. Some horses will drink electrolyte solutions voluntarily, but **fresh water** should also be offered.

The horse has a small stomach relative to its size (12 L capacity). In horses with normal gastrointestinal function, **up to 7 L isotonic solution** can be administered safely by nasogastric tube and this can be repeated within 1 h if necessary. Fluids should not be administered by nasogastric tube to recumbent horses. The presence of nasogastric reflux should be evaluated carefully prior to administration of fluids by nasogastric tube.

For repeated administration, indwelling nasogastric tubes are fairly well tolerated for a short time but may cause **pharyngitis** (*q.v.*). Equally, repeated stomach tubing can be traumatic, and even the quietest horse will become frustrated by repeated tubing. If fluids are to be administered for more than a few days, an indwelling soft and small diameter nasogastric or esophageal tube should be considered. Complications associated with esophagostomies and esophageal tubes include **cellulitis** and **stricture formation**. A number of commercially available soft and small diameter feeding tubes allow for longer duration maintenance of nasogastric tubes, with fewer side effects.

Oral fluid therapy requires adequate gastrointestinal absorption to be successful. In **bacterial enterocolitis**, such as salmonellosis (*q.v.*), diarrhea is secretory in origin and fluid absorptive function should not be impaired to a great extent. However, in **viral diarrhea**, villus atrophy can reduce the absorptive capacity and limit the effectiveness of oral fluid therapy. Many commercially available oral hydration solutions contain glucose or glucose and glycine. These are included to promote water absorption through the coupled transport of sodium and glucose. A potential disadvantage is that they can induce **bacterial fermentation** of glucose in the large colon if it is not absorbed in the small intestine.

OVER-HYDRATION

The main indication for over-hydration as a therapeutic goal in horses is the treatment of pelvic flexure, cecal or small colon **impactions** (*q.v.*). The goal of over-hydration is to hydrate the gastrointestinal contents as part of the extracellular fluid compartment, to increase the plasma hydrostatic pressure, and to reduce plasma oncotic pressure, thereby allowing the secretion of fluid into the intestinal lumen. It has been proposed that, in the presence of an

impaction, the interstitial pressure in the surrounding gut wall may be increased, enhancing fluid secretion into the intestine. However, this remains speculative. Over-hydration is performed using a combination of oral and IV fluid administration. Rates of twice the daily maintenance fluid requirement have been suggested for increasing gastrointestinal water content.

TECHNICAL CONSIDERATIONS IN FLUID THERAPY

IV catheterization

The **jugular vein** is most commonly used for venous access in horses. It is large, has high flow and is easily accessible, making jugular catheters easiest to maintain. The lateral thoracic and cephalic veins can be used as alternatives. The most common complication of IV catheterization is **thrombophlebitis** (*q.v.*). Others include septic phlebitis, local cellulitis, and dislodgement of injection ports with subsequent hemorrhage. Attempts should be made to minimize complications by ensuring **sterile insertion** techniques and a rigorous catheter care protocol.

The composition of the catheter influences thrombogenicity: polyethylene catheters are most thrombogenic, and they should be removed within a maximum of 72 h after insertion. Teflon (tetrafluoroethylene) is intermediate in reactivity. Siliconized rubber and polyurethane (Mila International, Florence, KY, USA and Arrow International, Reading, PA, USA) catheters are least thrombogenic and can be left in place for extensive periods.

The maximum rate of fluid delivery through IV administration sets is influenced by both the bore and the length of the catheter, an important consideration in replacement therapy in adult horses. Size 14 G catheters are most popular for routine use in adult horses. Size 10 or 12 G catheters can be used to provide larger volumes of fluid quickly. The diameter and length of IV administration tubing also affect rates of delivery. Fluid pumps and pressure bags can be utilized to hasten fluid delivery.

Fluid delivery systems

The ideal fluid delivery system is sterile and resistant to contamination, allows the horse to move around freely without obstructing flow, and can achieve a wide range and accuracy in flow rates. In most cases, sufficient volumes of fluid can be delivered by **gravity flow** using a large bore, disposable coiled administration set, e.g. the Large Animal Stat IV Set (Win International Ltd., Kennett Square, PA, USA), particularly if a 10 G catheter or two catheters are used for initial replacement therapy. However, in some instances when extremely large volumes of fluid are necessary, **pressurized fluid pumps** may be advantageous. Homemade fluid delivery systems can be manufactured using large (20 L) carboys and coiled tubing. However, their major disadvantages are difficulty in the maintenance of sterility and limited ranges in flow rate.

In veterinary medicine, guidelines for use of IV administration sets and equipment have been extrapolated from human medicine. Ideally, administration sets should be changed on a daily basis. Particular care should be

employed when solutions containing dextrose are used. Handling of the administration set should be minimized, and injection ports swabbed with alcohol before use and changed daily.

Formulation, handling and storage of IV fluids

The **maintenance of sterility** is the overriding priority in the handling of IV fluids. A sterile technique, and ideally a flow hood, should be used during the insertion of additives to fluids for IV use. Commercially prepared solutions are undoubtedly the most convenient. Sterility of the product is assured and appropriate quality control of pH and osmolarity can be expected.

The manufacturer's instructions for storage of fluids should be carefully adhered to. Homemade fluids are considerably less expensive (estimated at half price), and in horses, where the volumes required are often extremely large, this may be an important factor. However, if homemade fluids are to be used, careful consideration should be given to the ability to maintain sterility and to ensure consistent composition. Such homemade fluids are associated with thrombophlebitis and endotoxemia in horses, and are not ideally suited for use in the ICU.

INOTROPES AND VASOPRESSORS

Indications for use of inotropes and pressors include **fluid-refractory hypotensive states**. Before administration of inopressors, fluid balance must be optimized. Preload and stroke volume should be maximized without compromising CVP. Once maximum fluid loading has occurred, inotropes should be utilized to treat persistent hypotension.

Inotropes act primarily by increasing cardiac output through enhancement of stroke volume. It is safest to start with inotropes, because use of vasopressors increases cardiac afterload and can therefore decrease cardiac output. **β_1-Agonists** are the mainstay of inotrope therapy. **Dobutamine** and **β-dose dopamine** are most commonly employed. Suggested doses of dobutamine include 1–10 μg/kg/min as a constant rate infusion.

Vasopressors should be utilized only after cardiac output has been maximized through the administration of fluid boluses and inotrope infusions. The most commonly utilized pressor is **norepinephrine/noradrenaline**, because of its primarily **α_1-agonist** activity. If norepinephrine/noradrenaline is utilized, it should be used with **low dose dobutamine** (1–5 μg/kg/min) in order to preserve splanchnic circulation. Suggested dosages for norepinephrine/noradrenaline infusions include 0.01–0.1 μg/kg/min diluted in 5% dextrose in water, whereas individual animals may require higher doses.

Vasopressin is a newer pressor receiving attention in human and veterinary critical care. Vasopressin acts on V1 receptors present on the vasculature smooth muscle. Animals treated with pressors should be monitored for paradoxically reduced perfusion, because pressors can increase afterload and peripheral resistance excessively. Increases in blood lactate concentrations, reductions in mixed venous oxygen tension, or decreasing urine output warrant reconsideration of pressor therapy.

Horses being treated with inotropes and vasopressors should be monitored for dysrhythmias and tachycardia (*q.v.*) with serial or continuous **electrocardiography**.

PHARMACOTHERAPY OF THE CRITICALLY ILL NEONATE AND HORSE (Table 23.9)

INTRODUCTION

For the foal, any number of conditions that present pre partum, at birth or develop shortly post partum may necessitate hospitalization and intensive care. (See also Chapter 14, page 765.) Once in intensive care, the **immunologically immature** foal is at risk from serious focal infection (pneumonia, septic arthritis or osteomyelitis) (*q.v.*) and septicemia, particularly if access to the mother's **colostrum** has been limited or curtailed. The incidence of infection among critically ill equine neonates is not known, but may be as high as 40% with an additional 30% unconfirmed but suspected cases. Over 70% of critically ill premature foals may be infected, often in utero.

Diagnosis of infection in neonates is quite problematic. Physical signs can be vague and non-specific. **Sepsis** often develops and is well established before any clinical signs are observed. For this reason, any newborn foal that appears weak, depressed or lethargic, or exhibits behavioral changes or decreased suckling should be presumed to be septicemic and treated accordingly. Since the course of infection in newborns is quite rapid, therapy should not await the results of blood cultures, but **must be instituted at once**. While **blood cultures** are indicated in all critically ill foals, results are sometimes misleading. A false negative rate that has been estimated at 25% or higher should not be relied upon for defining sepsis.

Infections in neonatal and young foals are predominantly **Gram negative**. When streptococci or staphylococci are cultured, Gram-negative species are also usually present in **mixed infections**. One retrospective study reported 108 positive cultures in 27% of a total of 251 foals admitted to an ICU over a 6 yr period. Among these foals, Gram-negative organisms accounted for 76% of total organisms cultured, of which 42.5% were *Escherichia coli*, 9% were *Klebsiella pneumoniae*, 7% were *Actinobacillus equuli*; the rest of the foals showed multiple other organisms as the infectious agents.

Another retrospective study of septicemic foals ⩽8 days old reported that Gram-negative organisms were cultured from 100% of 72 foals. *E. coli* was isolated from over 50% of septicemic and pneumonic neonates and 30% of foals with septic arthritis. *Actinobacillus* spp. (36%) and *Klebsiella pneumoniae* (24%) were the second and third most common isolates. Entirely Gram-positive pathogens—most frequently β-hemolytic streptococci—were isolated in 12 of 46 foals with septic arthritis (*q.v.*). Among septicemic and pneumonic foals, **Gram-positive bacteria** occurred only in **mixed infections** alongside Gram-negative organisms.

The selection of an antimicrobial and a dosing regimen is complicated by the **physiologic immaturity** of the newborn foal, in which the absorption, distribution, metabolism and elimination of drugs differ markedly from the

Table 23.9 Pharmaceutical preparations for the critically ill equine patient

Agent	Route of administration	Spectrum of activity
Antimicrobial agents		
Aminoglycosides		
Amikacin	IV, IM	Gram-negative aerobic bacilli
Tobramycin	IV, IM	Gram-negative aerobic bacilli
Gentamicin	IV, IM	Gram-negative aerobic bacilli
Kanamycin	IV, IM	Gram-negative aerobic bacilli
Cephalosporins		
Cefazolin	IV, IM	Penicillinase-producing *Staphylococcus*, streptococci, *Escherichia coli, Klebsiella* and *Proteus mirabilis*
Cefoperazone	IV, IM	Expanded Gram-negative aerobes, anaerobes
Ceftiofur	IV, IM	Expanded Gram-negative aerobes, anaerobes
Moxalactam	IV, IM	Expanded Gram-negative aerobes, anaerobes
Penicillins		
Aqueous benzylpenicillin	IV	Streptococci, non-penicillinase-producing staphylococci, *Pasteurella*
Procaine benzylpenicillin	IM	Streptococci, non-penicillinase-producing staphylococci
Benzathine benzylpenicillin	IM	Streptococci
Oxacillin	IV, IM	Penicillinase-producing staphylococci
Ampicillin	IV, IM	Greater activity against Gram-negative bacilli
Ticarcillin	IV, IM	Anti-pseudomonal activity
Ticarcillin—clavulanic acid	IV, IM	Broad Gram-negative activity—aerobes and anaerobes
Tetracyclines		
Oxytetracycline	IV	Broad-spectrum antimicrobial activity
Sulfonamides		
Trimethoprim—sulfamethoxazole	IV	Gram-positive and Gram-negative aerobes
Macrolides		
Erythromycin lactobionate	IV	Gram-positive cocci
Miscellaneous antibiotic agents		
Vancomycin	IV	Methicillin-resistant staphylococci, group D streptococci, enterococcus
Metronidazole	IV PO	*Bacteroides fragilis* plus other Gram-positive and Gram-negative anaerobes
Chloramphenicol	IV	Gram-negative aerobes and anaerobes

Agent	Dosage	Comments
Aminoglycosides		
Amikacin	21–25 mg/kg q 24 h	Potential nephrotoxicity/ototoxicity
Tobramycin	3–7 mg/kg/day	Potential nephrotoxicity/ototoxicity
Gentamicin	6.6 mg/kg q 24 h	Potential nephrotoxicity/ototoxicity
Kanamycin	5 mg/kg q 8 h	Potential nephrotoxicity/ototoxicity
Cephalosporins		
Cefazolin	12–22 mg/kg q 6–8 h	Synergistic with aminoglycoside
Cefoperazone	No dosage reported for horses	Expensive
Ceftiofur	2.2 mg/kg q 12–24 h Up to 10 mg/kg q 6–12 h	Third generation, use cefotaxime susceptibility disk in neonates
Moxalactam	50 mg/kg q 6–12 h	Expensive

Table 23.9 (*Continued*)

Agent	Dosage	Comments
Penicillins		
Aqueous benzylpenicillin	22 000 IU/kg q 6 h	$Na^+ K^+$ salt form available
Procaine benzylpenicillin	22 000 IU/kg q 12 h	Synergistic with aminoglycosides
Benzathine benzylpenicillin	40 000 IU/kg q 2–3 day	Repository form
Oxacillin	16–50 mg/kg q 8–12 h	Synergistic with aminoglycosides
Ampicillin	22–100 mg/kg q 6–8 h	Inactivated by β-lactamases
Ticarcillin	50–100 mg/kg q 6 h	Synergistic with aminoglycosides
Ticarcillin—clavulanic acid	50–100 mg/kg q 6 h	Clavulanic acid inhibitor of β-lactamases
Tetracyclines		
Oxytetracycline	4.4–5 mg/kg q 12–24 h	Gastrointestinal irritation
Sulfonamides		
Trimethoprim—sulfamethoxazole	15–30 mg/kg q 12 h	Gastrointestinal irritation
Macrolides		
Erythromycin lactobionate	15–20 mg/kg q 6–8 h	May be given in combination with rifampicin
Miscellaneous antibiotic agents		
Vancomycin	5–7 mg/kg q 8 h	Potential nephrotoxicity
Metronidazole	7.5 mg/kg q 6 h	IV preparation expensive in ready-to-use-form
	15 mg/kg q 8 h	Active when given orally, relatively inexpensive
Chloramphenicol	50 mg/kg q 8 h	Blood dyscrasias in humans

Agent	Route of administration	Dosage
Gastrointestinal drugs		
Metoclopramide	IV, PO	0.1–0.2 mg/kg q 12 h
Loperamide	PO	8.0 mg/40–70 kg
Bismuth subsalicylate	PO	0.5–1.0 mg/kg
Ranitidine	IV	1.5–2 mg/kg q 8 h
	PO	6.6 mg/kg q 8–12 h
Cimetidine	IV	6.6 mg/kg q 6 h
	PO	6.6–20 mg/kg q 6–8 h
Sucralfate	PO	20–40 mg/kg q 6 h
Prostaglandin E_2 analogues	PO	2–5 μg/kg q 8–12 h
Anticonvulsants		
Diazepam	IV	5–10 mg/45 kg
Phenobarbital	IV	3–5 mg/kg diluted in 30 mL saline
Phenytoin	IV	5–10 mg/kg first 12 h
	IM	1–5 mg/kg q 2–4 h
	PO	1–5 mg/kg q 2–4 h
		1–5 mg/kg q 6–12 h
Pentobarbital	IV	2–4 mg/kg to effect
Anti-inflammatories/analgesics		
Xylazine	IV	0.1–0.5 mg/kg
	IM	0.25–1.0 mg/kg
Butorphanol	IV	0.01–0.04 mg/kg
	IM	0.02–0.08 mg/kg
Detomidine	IV	10–40 μg/kg
	IM	Start at 1–5 μg/kg initially
Dimethyl sulfoxide (DMSO)	IV	1.0 g/kg diluted to 10–20% saline 5% dextrose
Phenylbutazone	IV	Up to 2 mg/kg q 12 h
Flunixin meglumine	IV	0.25 mg/kg q 8–12 h

(*Continued*)

Table 23.9 (*Continued*)

Agent	Uses
Gastrointestinal drugs	
Metoclopramide	Promotes gastric emptying
Loperamide	Slows gastrointestinal motility
Bismuth subsalicylate	Intestinal protectant
Ranitidine	H_2 antagonist
Cimetidine	H_2 antagonist
Sucralfate	Gastric protectant
Prostaglandin E_2 analogues	Increases gastric mucosal blood flow, bicarbonate secretion, gastric mucous viscosity
Anticonvulsants	
Diazepam	Stops recurring and refractory seizures
Phenobarbital	Stops recurring seizures if diazepam ineffective
Phenytoin	Controls seizures if phenobarbital ineffective
Pentobarbital	Controls seizures as a direct result of anesthetic effects
Anti-inflammatories/analgesics	
Xylazine	Potent sedative-hypnotic drug
Butorphanol	Narcotic agonist-antagonist
Detomidine	Very potent sedative-hypnotic drug
Dimethyl sulfoxide (DMSO)	Diuretic, anti-inflammatory effects in CNS
Phenylbutazone	NSAID
Flunixin meglumine	Anti-endotoxic effect

adult horse. Moreover, there are significant physiologic differences between the premature foal, the full-term newborn, and the 1-wk-old neonate (*q.v.*), all of which will respond differently in terms of pharmacokinetics and pharmacodynamics. The pharmacokinetics of antimicrobials and other drugs have been little studied in the foal. Many of the available guidelines and dosages rest on surmise, extrapolation and clinical experience rather than hard data.

PHYSIOLOGIC AND PHARMACOKINETIC DIFFERENCES IN THE NEWBORN

Drug elimination is slower in the newborn (*q.v.*). Both the hepatic metabolic pathways and the renal excretion mechanisms are immature at birth. Non-polar drugs, such as chloramphenicol, theophylline, phenobarbital and phenytoin, must be metabolized in the liver prior to excretion. They can, therefore, be presumed to have a **longer half-life** in the newborn. Studies in other species have demonstrated that the liver's enzyme systems and smooth endoplasmic reticulum achieve mature functioning around the third to fourth week of life. Some reported determinations of non-polar drug half-lives suggest that these drug-metabolizing mechanisms may develop somewhat more rapidly in the foal.

The more water-soluble polar drugs (e.g. penicillins, cephalosporins and aminoglycosides) do not require hepatic metabolism, but are eliminated by renal excretion. The excretory mechanisms of glomerular filtration and tubular secretion appear to mature rapidly over the first month, based on studies

of non-polar drug half-lives. The mean elimination half-life for amikacin has been determined to be 3 h in 2–11-day-old foals, compared with 2.3 h in the adult. Glomerular filtration may develop more rapidly than tubular secretion. In general, then, a longer half-life can be anticipated for many drugs, particularly the non-polar agents, and, thus, **less frequent dosing** is advisable in the newborn. Dosing rates and intervals should be determined by **therapeutic drug monitoring**.

Total body water in the foal may equal 75% of total body weight, compared with 60–70% in the adult animal. Extracellular fluid volume in the 2-day-old foal is approximately 39% of total body weight, decreasing to 36% by 2 weeks. In contrast, the full-grown horse has an extracellular fluid volume of 22% of total body weight.

The **greater fluid compartment** in the foal would suggest that increased doses are required to reach the desired bactericidal concentration. However, some oral drugs are expected to have higher blood concentrations in the newborn compared with the adult receiving the same mg/kg oral dose. The ability of the foal to absorb antibodies, which are macromolecules, from the mother's colostrum suggests that the intestinal epithelium may be **more permeable** to drugs, and drugs that are normally poorly absorbed from the gastrointestinal tract, such as the aminoglycosides, may be better absorbed in the newborn. However, the high calcium content of the milk diet of the suckling foal may reduce or retard absorption of orally administered drugs that form calcium chelate complexes, such as the tetracyclines.

Other differences in gastrointestinal function and maturity can be presumed to have an impact on the rate and extent of gastrointestinal drug absorption. At birth, the pH of the stomach and upper intestine is relatively high, decreasing with milk intake and the development of pepsin activity over the first few weeks. During the same time period, venous blood flow, gastrointestinal surface area and mucosal enzyme activity all increase and the intestinal microflora establish their presence. Gastric emptying time, ingesta and intestinal transit time all differ substantially from the adult horse. The overall impact of these rapidly changing variables is not known.

Drug binding to plasma albumin directly affects drug distribution since only the free, unbound fraction will penetrate target tissues. The relative hypoalbuminemia observed in many species at birth is much less marked in the foal, however, and so this factor is thought to require little dosage adjustment.

The "blood—brain barrier" is more permeable in the newborn for about the first 7–10 days, a potential advantage in treating conditions such as **meningitis** (*q.v.*), but also a complicating factor when selecting the proper dosage for a CNS depressant such as xylazine and the barbiturates. The latter agents may also achieve somewhat higher plasma concentrations in the young foal, because the lower body fat proportion of the neonate (2–3% compared with 5% in the adult) limits the sequestration of lipid-soluble drugs, including barbiturates.

It is relatively straightforward to enumerate the physiologic differences of the neonate, and quite another matter to apply them to working out an appropriate drug regimen. Because developmental pharmacokinetics in the foal have been little studied, the following section will draw on clinical experience and set out basic principles to provide guidelines for administering antimicrobial agents in the equine neonate.

Antimicrobials

Because of the rapid progress and severe consequences of infection and the high susceptibility of the neonate, all at-risk foals should be started on antimicrobials early. Foals with **pre partum** risk factors, such as **placentitis** (*q.v.*) or premature placental separation, should be treated with antimicrobials **shortly after birth**. **Intra partum** considerations include dystocia and asphyxia (*q.v.*), while **post partum** risk factors for sepsis include failure of passive transfer, contaminated birthing environment or concurrent disease (meconium impaction, enteritis, uroabdomen) (*q.v.*).

Broad-spectrum combinations of antimicrobials that provide good coverage of the common Gram-negative organisms are optimal. **Bactericidal** agents are preferred to bacteriostatic drugs because of the neonate's relatively immature humoral and cell-mediated immune responses. Antibiotics that do not require extensive hepatic metabolism prior to excretion (e.g. penicillins, aminoglycosides and cephalosporins) are preferred in the management of premature and newborn foals. A combination of an aminoglycoside (gentamicin or amikacin) with a penicillin or cephalosporin provides broad, relatively safe coverage pending culture results. If use of an aminoglycoside is contraindicated by the presence of renal disease, a third generation cephalosporin, including ceftiofur, will provide Gram-negative coverage.

β-Lactam antimicrobials

The penicillins are bactericidal agents that act by interfering with cell wall formation. They are generally more effective against Gram-positive organisms than Gram-negative bacteria, which have a more complex cell wall. **Benzylpenicillin,** the most commonly employed antimicrobial in the horse, is particularly effective against **β-hemolytic streptococci**, the most commonly isolated bacteria in sepsis in the adult, although not in the neonate. Most **corynebacteria**, with the exception of *Rhodococcus equi*, are quite susceptible to benzylpenicillin. A high percentage of anaerobes are also susceptible to penicillin (up to 80–90% of isolates). Very high doses of benzylpenicillin may put the newborn at risk for **central nervous system toxicity** and **platelet- associated hemorrhaging**, although these are rare. The recommended dose is 25 000–50 000 IU/kg IV q 6 h or q 8 h for sodium or potassium benzylpenicillin, or q 12 h for procaine benzylpenicillin.

The broad-spectrum penicillins, such as ampicillin and amoxicillin, were developed to provide coverage against a range of Gram-negative species. Over time, however, most Gram-negative enterics, such as *Escherichia coli* and *Klebsiella* spp., have become **resistant** to these agents. Thus, these compounds should not be used as single therapy for broad-spectrum effect against unidentified pathogens in the foal. Suggested dosage for amoxicillin, which is more rapidly bactericidal than ampicillin, is 22 mg/kg IM q 6 h.

The extended spectrum penicillins, which include ticarcillin and carbenicillin, have increased activity against Gram-negative organisms, including many isolates of *E. coli*. Resistance is still a problem, particularly in the treatment of *Pseudomonas* infections. These agents are best used in combination with another antimicrobial, such as an aminoglycoside. The suggested dose regimen for carbenicillin is 100 mg/kg IV q 6 h or q 8 h, and for ticarcillin

50 mg/kg IV q 6 h or q 8 h, extrapolated from pharmacokinetic studies in adult horses.

Third generation cephalosporins, such as cefotaxime or ceftazidime (20–50 mg/kg, IV q 6 h), and higher class penicillin drugs, such as imipenem (15 mg/kg IV q 6 h), can be utilized in foals with isolates that are resistant to ceftiofur or aminoglycosides, or in foals with compromised renal function. However, these drugs should be used judiciously in order to minimize microbial selection pressure. Recently, a fourth generation cephalosporin, cefepime, has been studied in healthy neonatal foals. The suggested dose is 11 mg/kg IV q 8 h. This drug should also be reserved for use in refractory cases.

Aminoglycosides

This group of bactericidal agents includes streptomycin, kanamycin, gentamicin, tobramycin, netilmicin and amikacin. The aminoglycosides are primarily active against aerobic, Gram-negative bacteria; some of the aminoglycosides are also active against staphylococci. **Potential nephrotoxicity** and **ototoxicity** are the major limitations in using aminoglycosides. It has been suggested that foals are more susceptible than adult horses to the nephrotoxic effects of the aminoglycosides, particularly gentamicin, because of their slower rate of elimination, but there is little evidence to support or refute this supposition.

Streptomycin has been so widely used that many microorganisms are now quite resistant to it. Kanamycin, which has been previously active against most Gram-negative enteric organisms except *Pseudomonas aeruginosa*, has become less effective due to plasmid-mediated resistance among Enterobacteriaceae in many veterinary settings.

Gentamicin, tobramycin, netilmicin and amikacin are active against *Proteus*, *Klebsiella*, *Enterobacter*, *Serratia*, *Salmonella* and *Shigella* species, *E. coli*, and *Pseudomonas aeruginosa*. However, resistance to gentamicin and tobramycin has occurred in many areas and therapy should be guided by antimicrobial susceptibility testing once available.

Optimal peak and trough levels in the foal may be attained with 6.6 mg/kg **gentamicin** IV or IM q 24 h or with 21–25 mg/kg **amikacin** IV or IM q 24 h. However, because of the high degree of **interindividual variability** in the pharmacokinetic disposition of aminoglycosides in neonatal foals, therapeutic drug monitoring should be performed on all foals in the ICU. Peak plasma concentrations for aminoglycosides should be 10 times the minimum inhibitory concentration (MIC) of the offending microorganism. The MIC of common equine pathogens for amikacin is 4–8 μg/kg, and therefore peak concentrations should be at least 40 μg/kg. Trough concentrations should be <2 and <1 μg/kg for amikacin and gentamicin, respectively.

Cephalosporins

The cephalosporins, being β-lactam drugs, are similar to the penicillins both functionally and structurally. These bactericidal agents are classified into three generations according to their in vitro spectrum of activity. Cefalotin, cefapirin, cefazolin, cefadroxil and cefalexin are all first generation cephalosporins and are active against most aerobic Gram-positive cocci, many anaerobic cocci and bacilli, and some aerobic Gram-negative bacteria. Some Gram-negative

bacteria are resistant, but the relative safety of the cephalosporins makes them commonly used agents in human neonates with septicemia and meningitis caused by Enterobacteriaceae.

Second generation cephalosporins include cefamandole, cefoxitin, cefuroxime, cefonicid and cefaclor. These agents retain the Gram-positive and anaerobic activity of the first generation agents and are more effective against specific Gram-negative bacteria. The latter, nonetheless, frequently exhibit resistance.

The **third generation agents** are moxalactam, cefotaxime, cefoperazone, ceftizoxime, ceftriaxone, ceftazidime and ceftiofur. These cephalosporins penetrate the "blood–brain barrier" well in humans and are largely reserved for the treatment of meningitis (*q.v.*). They are expensive, and resistance to them can develop.

A suggested regimen for **sodium cefazolin** is 11 mg/kg IM or IV q 6 h. Cefalotin can be administered IM or IV in doses of 18 mg/kg q 6 h. Dosage recommendations for the other cephalosporins are based on data in humans and other species and so require careful monitoring and adjustment. The suggested dosage for ceftizoxime and ceftazidime is 20–50 mg/kg IV q 6–8 h. The recommended dosing protocol for ceftriaxone is 20–50 mg/kg IV q 12 h.

Other antimicrobials

Combinations of trimethoprim and sulfonamides (the potentiated sulfonamides) are believed to be bactericidal against a broad spectrum of Gram-positive and Gram-negative organisms, although resistance is developing among Enterobacteriaceae in response to their widespread use in the horse. Theoretically, the oxidative effects of the sulfonamide on the newborn's erythrocytes may lead to hemolysis and methemoglobinemia. In the adult horse, this combination has rarely been associated with neutropenia, acute enteritis and transient ataxia. Sulfonamides bind competitively with albumin, resulting in higher serum concentrations of other administered drugs and endogenous substances such as bilirubin. The elimination of trimethoprim is delayed in the newborn due to the immaturity of the hepatic metabolic pathways in the first weeks of life. The recommended dosage in the neonate, based on data obtained from adult horses, is 15–25 mg/kg IV or PO q 12 h, depending on the problem being treated.

Chloramphenicol is a broad-spectrum bacteriostatic agent that acts by inhibiting ribosomal protein synthesis. Toxic bone marrow depression and bone marrow aplasia have occurred rarely in humans, and the neonates of some species are more susceptible to **toxicity** due to a deficiency of the enzymes required for its metabolism. This does not appear to be the case in the foal, however, and the pharmacokinetics of chloramphenicol in the older foal are similar to those of the adult horse. Elimination is delayed in 1–3-day-old foals. Chloramphenicol can **potentiate** hexobarbital, pentobarbital, aminopyrine, dicumarol (dicoumarol) and phenytoin in impeding their biotransformation. The recommended dosage has been reliably set at 50 mg/kg IV q 4 h for chloramphenicol succinate, and 40–50 mg/kg q 6–8 h for oral chloramphenicol base or chloramphenicol palmitate.

Other antimicrobials commonly used in the horse, such as erythromycin, oxytetracycline and rifampicin, have specific indications in the neonate. **Erythromycin** is administered at 10–15 mg/kg IV or 20–25 mg/kg PO q 4–6 h for peracute and **acute respiratory infections**, such as *Rhodococcus equi* (*q.v.*) in foals 3 weeks and older. Rifampicin is dosed at 5.0 mg/kg PO q 12 h.

Anticonvulsants

Foals may exhibit **seizures** (*q.v.*) associated with septicemia and bacterial meningitis, electrolyte imbalances, asphyxial injury or hypoglycemia. Seizures are caused by aberrant electrical activity in the brain. Phenothiazines, such as acepromazine, may decrease the seizure threshold and induce seizures in foals. They should not be used as anticonvulsants at any time. Neonatal foals appear to have a **low seizure threshold**, believed to be due to cortical immaturity.

The signs of seizures are often subtle and difficult to recognize but include oral and buccal movements, referred to as "**chewing-gum fits**", jaw chomping, drooling, facial grimacing and twitching. Other clinical signs include repetitive eye blinking and rapid eye movements, tachypnea and apneustic breathing, as well as paddling or tonic posturing of a limb. Differentiation of the subtle signs of seizure activity from the foal in deep sleep (REM) may be achieved by the response to noxious stimuli and easy arousal in the normal foal. Additionally, there is a marked difference in **pupillary light response** in the normal and abnormal foal. Current or continuous seizure activity may cause **brain injury**, resulting from increased cerebral metabolic needs, altered cerebral blood flow, respiratory depression with hypoxia, secondary metabolic derangements and increased intracranial pressure.

Therapy for generalized seizures is focused on controlling the seizure using appropriate anticonvulsant therapy.

Diazepam has a rapid effect, but may require several doses to stop recurring and refractory seizures. The duration of action is short, and the IV form should not be used for maintenance purposes, as it may cause respiratory depression. Suggested doses include 5–10 mg/45 kg administered by slow IV administration or the drug can be used as needed. Diazepam in prolonged contact with plastic (e.g. a syringe) is inactivated, therefore **the drug should not be stored in plastic syringes**. **Midazolam** is a newer benzodiazepine that can be utilized for anticonvulsant therapy. It has a very rapid onset of action that may be advantageous in treating seizures. Doses suggested for horses include 0.011–0.044 mg/kg IV.

Phenobarbital is used if several doses of diazepam do not control the convulsions. An IV loading dose of 3–5 mg/kg IV diluted in 30 mL of saline is administered over a 25–30 min period. Higher loading doses may be needed for neonates, although premature foals may have prolonged elimination half-lives. Therapeutic drug monitoring is therefore crucial in this signalment. Once the convulsions are controlled, a maintenance dose of 5–9 mg/kg IV (diluted and infused over 25–30 min) or PO q 8–12 h can be given. Peak and trough blood levels of the drug should be monitored to titrate the dose to the minimum effective dose to control seizures. Adequate levels appear to range

from 10 to 30 μg/mL. The dose of phenobarbital should be tapered over 7–10 days before discontinuation, to prevent precipitation of seizures.

Bromide (sodium or potassium) is another drug available for controlling convulsions. Suggested oral doses include 44 mg/kg q 24 h for sodium bromide and 50 mg/kg q 24 h for potassium bromide in adult horses. Bromide is renally excreted. Because of its long half-life (5.2 days), bromide should not be utilized to treat active seizures in the acute stages. Bromide administration has few complications and the drug is considered an **effective anticonvulsant** for long-term management of horses with seizure disorders.

Phenytoin is an alternative drug to control seizures, if others are ineffective. A loading dose of 5–10 mg/kg IV is used, followed by a maintenance dose of 1–5 mg/kg q 2–4 h IM or PO. Thereafter (≥12 h), a q 8–12 h schedule may be used with a dose of 2.83–16.43 mg/kg. The major side effect is **prolonged depression** in the foal.

Sodium pentobarbital is an inexpensive drug and has profound depressant effects on respiration with repeated doses. Its ability to control seizures is a direct result of its anesthetic effects, rather than it being a true anticonvulsant. Doses of 2–4 mg/kg IV to effect are used.

MANAGEMENT OF ENDOTOXEMIA AND SYSTEMIC INFLAMMATORY RESPONSE SYNDROME

INTRODUCTION

Acute toxic enteritis, strangulating obstruction of the intestine and overwhelming Gram-negative infections such as those seen with acute pleuropneumonia (*q.v.*) are associated with a high degree of morbidity and mortality. Many times, the complications associated with these diseases, such as hypovolemia and dehydration, coagulopathies, ileus, intra-abdominal adhesions and laminitis (*q.v.*), can be traced back to an endotoxic insult.

PATHOPHYSIOLOGY

The outer membrane of Gram-negative bacteria is composed of a lipid bilayer, of which the characteristic component is **lipopolysaccharide (LPS)** or **endotoxin**. LPS is a major factor in the pathogenicity of these bacteria, a receptor site for bacteriophages, and a permeation barrier for the intact bacterium. The LPS molecule is composed of three portions: (1) phospholipid A; (2) a core oligosaccharide; and (3) an "O-specific antigenic" polysaccharide side chain.

Lipid A is the most well conserved portion of the LPS molecule and has the same basic structure for all Gram-negative bacteria. Most importantly, it is the portion of the molecule primarily responsible for the pathophysiologic effects of endotoxin in mammals. The core is the next most well preserved, with only six different varieties identified. In contrast, the O side chains are a very diverse group, of which the structure and composition are different for each bacterial species.

Bacteria do not actively excrete endotoxin; rather, it is released during bacteriolysis and the **rapid growth phase of bacterial multiplication**. The largest

source of **equine endotoxin** is contained within the gastrointestinal tract lumen and is a result of the normal turnover of enteric bacteria. In health, the mucosal layer acts as an efficient barrier to the transmural movement of endotoxin. However, damage from ischemia, inflammation or parasites can result in mucosal compromise, alteration of intestinal motility and a decrease in intraluminal pH. This may result in loss of mucosal integrity, with subsequent **leakage** of endotoxin into the portal circulation and peritoneal cavity.

If endotoxin escapes neutralization by the hepatic reticuloendothelial system or by antibodies in the systemic circulation, it can initiate a variety of hemodynamic, hematologic and metabolic disturbances. Endotoxin is a potent stimulator of a **systemic inflammatory response syndrome (SIRS)**. SIRS (*q.v.*) is a clinical state of exuberant inflammatory and/or anti-inflammatory responses to a number of septic and non-septic triggers. It is defined clinically by the presence of two or more of the following: tachycardia, tachypnea or hyperventilation, hyperthermia or hypothermia, and leukocytosis or leukopenia.

The underlying features of endotoxemia are **inadequate perfusion** of vital tissues and **multisystemic organ dysfunction** and failure. Early on, vasodilation yields red mucous membranes with rapid capillary refill time. Next, vasoconstriction results in pale mucous membranes with prolonged capillary refill. With time, pooling of blood in the capillaries and increased permeability result in dark, muddy membranes with prolonged capillary refill. Hypoxemia, and decreases in arterial pressure and cardiac output accompany increases in heart and respiratory rates. Ileus, abdominal pain and/or diarrhea may occur as a result of blood pooling in the mesenteric vasculature.

One of the most **sensitive indicators** of endotoxemia is the rapid margination of neutrophils and release of immature cells causing leukopenia with a left shift. Dehydration and hypovolemia with loss of intravascular volume and splenic contraction (increased sympathetic tone) lead to **hemoconcentration**. Intravascular platelet aggregation and endothelial adhesion result in thrombocytopenia while coagulopathies such as disseminated intravascular coagulation (DIC) occur secondary to release of tissue factor and other procoagulants.

Metabolic alterations include **hyperglycemia** (increased glycogenolysis, sympathoadrenal activation), soon followed by **hypoglycemia** (glycogen depletion and inhibition of gluconeogenesis). Pyrexia occurs as a result of direct stimulation of the thermoregulatory center and release of pyrogens, such as interleukins 1 and 6 and tumor necrosis factor (TNF-α). Free radical release occurs subsequent to tissue ischemia. Circulatory failure, free radicals, edema formation, damage from inflammatory mediators, and coagulopathies result in tissue and subsequent organ dysfunction and failure. Mitochondrial dysfunction is another sequel to SIRS and the secondary derangements that follow.

ANTIBIOTICS AND HYPERIMMUNE PLASMA

Endotoxin plays a significant role in the morbidity and mortality of many Gram-negative bacterial diseases and is often the reason for failure despite the use of appropriate broad-spectrum antibiotics. Even when endotoxin is present in undetectable amounts, the position of the LPS molecule on the bacterial surface allows for activation of many biological mediators of SIRS and circulatory

or distributive shock. The clinical features of **Gram-negative sepsis** (bacteremia with subsequent SIRS) are identical to the effects of IV administered endotoxin. Therefore, **antimicrobials cannot be expected to reverse the clinical signs attributed to circulating endotoxin**. This does not preclude the use of antibiotics in the treatment of Gram-negative infections, since it is often difficult to differentiate between bacteremia and endotoxemia. Rather, they should be used judiciously and directed at the invading Gram-negative organisms involved.

Blood, transtracheal aspirations and pleural or peritoneal fluids should be sampled for **culture** when appropriate. Perioperative antimicrobials in the management of patients with strangulating intestinal lesions should be broad spectrum in coverage, used only as long as necessary, and used with caution to minimize the risks of potential side effects (e.g. nephrotoxicity, drug-induced diarrhea).

Recently, **passive immunotherapy** directed against the common structural and immunogenic properties of the LPS molecule has shown promising results. Mortality was substantially reduced in human patients with Gram-negative bacteremia when treated with human antiserum to the common core structures of LPS. Clinical trials have been performed comparing the use of hyperimmune plasma with control plasma in horses suffering from a variety of gastrointestinal crises and demonstrating signs of endotoxic shock. In one study, horses receiving hyperimmune plasma experienced reduced mortality rate, improved clinical score and shorter recovery times. It is recommended that horses suffering from endotoxemia that weigh ⩾250 kg receive 2 L **hyperimmune plasma**.

Occasionally, individuals that do not respond may require additional plasma. Other advantages of plasma transfusions include the presence of immunoglobulins, clotting factors, antithrombin, activated protein C, fibronectin, albumin and other proteins.

In other studies, administration of hyperimmune plasma failed to alter the course of experimentally induced endotoxemia in horses. A variety of causes for these divergent results have been proposed. For example, LPS in clinical situations exists in various forms. During an infection, bacteria rapidly multiply; if they come in contact with core antibody during early cell wall synthesis, before side chain attachment is complete, the antibody could easily bind to the naked core. Host defense mechanisms and antimicrobial agents can also alter the structure of the LPS molecule and enhance antibody binding.

FLUNIXIN MEGLUMINE

Endotoxin interacts with a variety of inflammatory cells and **induces the synthesis** and/or secretion of numerous humoral mediators. Mediators produced as a result of the arachidonic acid cascade have been the focus of recent endotoxin research in horses. Arachidonic acid is incorporated in the phospholipids of all plasma membranes of mammals. Once liberated during endotoxin-induced cell activation, it is further metabolized by two major enzyme systems—the cyclo-oxygenase and lipoxygenase cascades.

Prostaglandin (PG) reductase results in the formation of the stable prostaglandins PGE_2 (a vasodilator) and $PGF_{2\alpha}$ (a vasoconstrictor). Thromboxane (TX) synthetase activity, which is found primarily in platelets and mononuclear cells, produces TXA_2, a potent vasoconstrictor and promoter of platelet

aggregation. Prostacyclin synthetase, contained in endothelial cells, produces prostacyclin PGI_2, a potent vasodilator and inhibitor of platelet aggregation. In health, this system keeps a "**check and balance**" on vasoactivity and maintains homeostasis.

During endotoxemia, **endothelial damage** initially allows TX activity to prevail, resulting in widespread vasoconstriction, platelet aggregation, microthrombosis and tissue ischemia. The beneficial effects of non-steroidal anti-inflammatory drugs such as **flunixin meglumine**, a cyclo-oxygenase inhibitor, support the role of these mediators in equine endotoxemia.

The role of the products of the lipoxygenase pathway during equine endotoxemia has not been clearly elucidated. In other species, these mediators produce vasoconstriction and bronchoconstriction, elicit plasma exudation and are involved in microthrombi formation and leukocyte chemotaxis.

It has been demonstrated that NSAIDs, most specifically flunixin meglumine, are not only useful as analgesics but are potent mediators of the arachidonic acid cascade during equine endotoxemia. Because of the popular use of NSAIDs and their potential for gastrointestinal and renal toxicity (*q.v.*), investigations of minimal dosages required to manipulate the arachidonic cascade were undertaken. Horses experimentally challenged with endotoxin were treated with doses of 1.1, 0.25 and 0.1 mg/kg flunixin IV. Clinical parameters, although altered by flunixin, remained useful for evaluating the horses' status during the endotoxemia challenge. Horses receiving the 0.25 mg/kg dose showed milder signs of colic and regained their appetite and drank water earlier than those receiving 0.1 mg/kg. Endotoxin-induced lactic acidosis was reduced comparably in the groups receiving 1.1 and 0.25 mg/kg flunixin. The reduction in lactic acidosis may be attributed to inhibition of TXA_2, a potent vasoconstrictor, thus allowing better tissue perfusion. Data from this study suggest that flunixin meglumine, in doses $\leqslant$1.0 mg/kg, follows relatively linear pharmacokinetics, even in the face of endotoxin challenge. It should be expected that 0.25 mg/kg flunixin q 8 h would reduce eicosanoid generation in response to endotoxin challenge.

The potential toxic side effects associated with the use of NSAIDs in the hypovolemic patient necessitate that **flunixin meglumine be used with caution when treating horses with colic**. In health, prostaglandins help protect the gastrointestinal mucosal barrier by enhancing mucosal microcirculatory blood flow, improving re-epithelialization and restitution following mucosal injury, promoting mucus and bicarbonate release at the mucosal surface, and moderating acid secretion. Interference with their production can lead to intestinal ulceration. Prostaglandin precursors shunted down the alternate lipoxygenase pathway may form other biologically active eicosanoids. Prostaglandins are also important mediators of renal blood flow during hypovolemia. Disruption of that balance can lead to **renal tubular damage**.

Flunixin meglumine at the manufacturer's recommended dose of 1.1 mg/kg can be used judiciously in cases that are not hypovolemic, and such horses should be monitored for signs of deterioration in condition. **Repeated doses are not recommended without thorough patient re-evaluation**. Alternatively, 0.25 mg/kg can be used in order to minimize side effects of NSAID use and still provide for reductions in eicosanoid production.

POLYMYXIN B

Polymyxin B is a cationic polypeptide antimicrobial drug that binds to circulating endotoxin (lipid A portion) and thereby prevents its binding to cellular receptors. This agent has shown promise in horses experimentally, but it needs further evaluation clinically. Side effects of polymyxin B include neurologic signs and nephrotoxicity. Renal function should be evaluated serially in horses receiving polymyxin B. Doses range from 1000 to 6000 IU/kg q 12 h, and each dose of polymyxin B should be diluted in 1 L saline and infused over 30–60 min.

LOW MOLECULAR WEIGHT HEPARIN

Horses experiencing endotoxemia and SIRS are at risk for development of **coagulopathies** and subsequent **thromboses** (*q.v.*). **Heparin** is indicated to minimize the complications of **intravascular coagulation**. Low molecular weight heparin has constant anticoagulant properties, greater bioavailability and longer half-life than unfractionated heparin. Low molecular weight heparin (LMWH), such as **dalteparin** or enoxaparin, has been recently studied in both experimental horses and clinical cases.

A randomized double-blind clinical trial compared unfractionated heparin (UFH) with LMWH in horses with colic. The authors concluded that LMWH has markedly fewer side effects than UFH in horses. Packed cell volume decreased in horses treated with UFH, but did not change significantly in horses administered LMWH. The activated partial thromboplastin time (APTT) and thrombin time (TT) were prolonged in horses administered UFH, but not in those treated with LMWH. Horses receiving LMWH had fewer injection site skin reactions than those receiving UFH. In addition, horses given UFH had significantly more subclinical jugular vein changes or partial thromboses than those treated with LMWH. Suggested dosages for dalteparin in horses include 50 IU/kg q 24 h SC.

IV FLUID THERAPY

Correction of the cardiac collapse and decreased peripheral perfusion associated with endotoxemia requires aggressive IV fluid management. **Prognosis** is often directly related to the rapidity with which homeostasis is re-established.

IV fluid therapy starts with an evaluation of the patient's circulating volume status and hydration, electrolyte and acid-base status. Mucous membrane color and refill, skin turgor, PCV and TP concentration are useful in determining the degree of hypovolemia and dehydration (Tables 23.10 and 23.11).

Markers of volume status include capillary refill time (CRT), heart rate, extremity temperature, jugular refill time, mentation, mucous membrane color and pulse quality. Blood or plasma lactate concentration, urine output and specific gravity, acid-base status (anion gap, base excess) and mixed venous oxygen tension are biochemical and hematologic markers of circulating volume status. **Hydration** can be assessed by using skin turgor, mucous membrane texture and corneal quality. Once the degree of hypovolemia and dehydration has been

Table 23.10 Clinical signs of dehydration and estimated fluid lost in a 400 kg horse

%	Signs	Fluid loss (L)
0–5	Not detectable	0–24
5	Delay in return of skin to normal position, sunken eyes, slightly prolonged capillary refill time (CRT), dry mucous membranes	24
8–10	Tented skin stands in place, prolonged CRT, may see signs of shock (increased heart rate, weak pulse, delayed jugular filling [flat veins])	32–40
12–15	Shock, decompensation, may be moribund, death imminent	48–60

Table 23.11 Evaluation of packed cell volume (PCV) and total plasma protein (TPP)

PCV (%)	TPP (g/dL)	Possible interpretation
↑	↑	Dehydration
↑	N or ↓	Splenic contraction Erythrocytosis Hypoproteinemia with dehydration
N	↑	Hyperproteinemia Anemia with dehydration
↓	↑	Anemia with dehydration Anemia with pre-existing hyperproteinemia
↓	N	Non-blood loss anemia, normal hydration
N	N	Normal hydration Dehydration, after secondary compartment shift Dehydration, with pre-existing anemia and hypoproteinemia Acute hemorrhage
↓	↓	Blood loss anemia Over-hydration

↑, *Increase;* ↓, *decrease; N, normal.*

established, the volume needed to replace the patient's fluid deficit can be calculated:

$$\% \text{ dehydration} \times \text{body weight (kg)} = \text{fluid deficit (L)}$$

The **calculated fluid deficit** can be given quite rapidly to an adult horse (10–20 L isotonic fluids/h) with frequent reassessment. The response to therapy should be monitored closely, especially in patients that may be **hypoproteinemic** or experiencing **capillary leak syndrome** and leaking plasma proteins into interstitial spaces. Improved mucous membrane color and refill, decreased skin tenting (increased turgor), decreased heart rate, urination, and warming of cool extremities indicate a response to therapy. Serial PCV and TP evaluations should be obtained and the rate of fluid administration adjusted accordingly. If the total protein approaches 4.0 g/dL, the patient should be monitored closely for signs of pulmonary and upper airway edema that can result in acute respiratory distress and death.

Fluid administration is best achieved using a 14 gauge or larger catheter aseptically placed in the jugular vein. Size 10 gauge catheters are especially

useful for rapid fluid administration. A variety of types are available, but "over the wire" models with minimally thrombogenic material such as polyurethane have proved most useful. The catheter should be **securely sutured** to the skin to minimize its movement and the tension on the administration set. "Superglue" sparingly used at the venepuncture site is also helpful. Fluid administration is most commonly achieved with gravity flow using 5 L bags of commercial, sterile IV fluids. Mechanical pumps that can increase flow rates are available.

When available, **arterial blood gas analyses** provide the most accurate determination of acid-base status. Most equine patients suffering from endotoxemia experience some degree of **metabolic acidosis** (*q.v.*). Because the acidosis is primarily a result of decreased tissue perfusion and impaired lactate metabolism, rapid restoration of circulating blood volume in most cases of mild to moderate endotoxemia will produce dramatic improvements without buffer supplementation. Many commercial fluid preparations contain bicarbonate precursors such as acetate or lactate that also help to counter the effects of metabolic acidosis. **Sodium bicarbonate** is often chosen as a supplemental buffer because of its practicality, availability and compatibility when mixed with other fluids. However, it is **not compatible** with fluids containing large volumes of calcium. If sodium bicarbonate supplementation is necessary, the amount required can be estimated by:

$$\text{base excess (mEq/L)} \times \text{body weight (kg)} \times 0.3 = \text{base deficit}$$

Sodium bicarbonate administration is necessary when the base deficit is 10 mEq or greater and only after organic acidoses (lactate) are corrected by addressing perfusion with volume replacement and inotropes and pressors (*q.v.*). Over-administration of bicarbonate can cause hypernatremia and hyperosmolality as well as paradoxical intracellular acidosis and should be avoided. One gram of sodium bicarbonate provides 12 mEq of bicarbonate and 12 mEq of sodium. An isotonic solution can be obtained by mixing 50 g (600 mEq) of sodium bicarbonate in 4 L sterile water. Bicarbonate can also be administered safely with other isotonic fluids if the combined tonicity remains near normal (i.e. $<2 \times$ isotonic).

Alternatively, small amounts (1–2 L) of 5% sodium bicarbonate can be administered concurrently with large volumes of isotonic replacement fluids. Specific guidelines for fluid and electrolyte replacement are presented in the section on fluid therapy (*q.v.*).

Hypertonic saline

Based on their relative safety and beneficial effect, **isotonic replacement solutions** have been considered the fluid of choice for volume resuscitation of adult horses in hypovolemic shock for many years. However, there are certain disadvantages. In many instances, it is often necessary to administer **large volumes** (20–60 L) of isotonic fluids to achieve a desirable effect. Under field conditions, these volumes may not be readily available for many practitioners. In addition, maximum benefit is achieved from continuous rather than

bolus administration, which is time consuming for the practitioner and may not be safely undertaken by an unsupervised owner or trainer.

The time required to administer such large volumes of fluids safely can delay referral and pre-anesthetic time by hours. This time can mean the difference between success and failure for many critically ill patients, especially those suffering from **strangulating intestinal obstructions** (*q.v.*). If large volumes of isotonic fluids are administered too rapidly, complications (e.g. pulmonary edema, hypoproteinemia, anemia, phlebitis) can occur. Large volumes of sterile preparations are also expensive.

Hypertonic saline has been studied in a variety of endotoxemia models and shows promise as an inexpensive and rapid resuscitative fluid with administration of small volumes. In horses previously challenged with endotoxin, administration of **hypertonic saline** was associated with increased cardiac output, increased heart rate, and decreased pulmonary artery pressure. Plasma volume increased, as indicated by decreased PCV and TP concentrations, to a greater extent than can be explained by the small volume of fluid administered. Other benefits include improved arterial pressure and reductions in pulmonary and peripheral vascular resistance. Hypertonic saline also attenuated the effects of endotoxin on PCV, lactate production and arterial blood temperature and resulted in the development of less concentrated urine, natruresis, chloruresis and kaluresis.

The mechanism of action of hypertonic saline is believed to be due to increased plasma osmolality resulting in increased plasma volume expansion. A reflex arc involving the pulmonary osmoreceptors, efferent and afferent pathways and vagus nerve has been described, but its importance is not well known.

Little information is available on the use of hypertonic saline in clinical cases of equine endotoxemia. Although no clinical trials have been published, small volumes (4–6 mL/kg) of approximately 7% hypertonic saline have been used in patients needing rapid circulatory restoration or as part of pre-anesthetic stabilization. It should be administered over approximately 15 min and followed by 15–20 L (or greater amounts as needed) of isotonic fluids within 1–2 h. Serial re-evaluation of the patient's clinical parameters including lactate concentration, PCV and TP should be undertaken.

Until further studies on its mechanism of action and clinical application are completed, hypertonic saline is contraindicated in horses with **hyperosmotic states** (salt intoxication, water deprivation, heat prostration, certain renal diseases), exhaustion and electrolyte depletion, and hyperkalemic periodic paralysis. In addition, horses with maximal interstitial dehydration should be administered isotonic crystalloid prior or concurrent to hypertonic saline, in order to allow for fluid shifting from the interstitium to the plasma compartment and to prevent significant hyperosmolarity.

PATIENT CARE PROTOCOLS FOR THE CRITICALLY ILL HORSE

INTRODUCTION

In recent years, large animal adult intensive care has made numerous advances. A better understanding of disease processes, expansion of the field

of veterinary emergency and critical care into equine medicine, improved medical and surgical techniques, and a commitment on the part of veterinarians and owners regarding the care of critically ill horses have been important to this progress. This section focuses on patient care protocols in the critically ill **adult** equine patient.

INITIAL PATIENT EVALUATION

Equine clinicians commonly encounter emergencies. In most instances, the presenting complaint will guide initial therapeutic and diagnostic efforts. In life-threatening situations, the "**ABC**" **of acute care** (***A*irway, *B*leeding, *C*ardiovascular**) is attended to concurrently. First a patent airway is established and cardiopulmonary cerebral resuscitation performed as needed. Bleeding should be controlled by application of pressure and lacerated vessels ligated. Heart rate and rhythm, pulse character and peripheral perfusion must be assessed.

The physical examination and diagnosis of a critically ill adult equine patient must sometimes be performed simultaneously with life-saving treatment. Once the patient is stabilized, a more thorough physical examination can be performed to assess the degree of injury or illness with attention refocused on the primary problem. The examination should include evaluation of abnormalities in **attitude or mentation** (pain, anxiety, depression), **body conformation** (distended abdomen, obvious lameness/fracture) and evidence of **nasal discharge** (regurgitant food, blood, purulent exudate). **Colic** is the most common form of pain. However, encephalopathies, botulism, exertional rhabdomyolysis, hyperkalemic periodic paralysis and severe lameness (*q.v.*) can be confused with colic. Depression can result from a variety of disorders including neurologic, renal, hepatic and cardiac failure, enteritis and respiratory disease.

Abdominal distension with abdominal pain is usually due to large colon obstruction, but less commonly can be due to severe colitis or extensive small intestine distension (*q.v.*). Abdominal distension without pain can be due to ascites, peritonitis and pregnancy. **Regurgitant food** or gastric reflux at the nares may indicate dysphagia or excessive gastric fluid accumulation requiring immediate nasogastric decompression (*q.v.*). **Epistaxis** may signify a variety of respiratory disorders including guttural pouch mycosis, coagulopathies, ethmoid hematoma or pulmonary hemorrhage (*q.v.*).

Once the initial examination is completed and the patient is out of immediate, life-threatening danger, a thorough history can be obtained, problem list and rule outs considered, a diagnosis made and appropriate medical and/or surgical therapy initiated.

ACUTE RESPIRATORY DISTRESS

Etiology

Respiratory distress exists when the effort to breathe, as assessed by respiratory rate or effort, rhythm and auscultation, is disproportionate to the level of ventilation actually achieved. In most cases, a lesion of the upper and/or lower airways is the problem. In some cases, other underlying systemic

diseases such as cardiac and renal failure should be considered. Major categories of **differential diagnoses** for acute respiratory distress syndrome in horses include the following:

1. Upper airway obstruction, e.g. laryngeal paralysis (*q.v.*). Clinical hallmarks include stertor or stridor.
2. Lower airway obstruction, e.g. recurrent airway obstruction (*q.v.*). Clinical hallmarks include expiratory wheezing on auscultation and double expiratory efforts.
3. Parenchymal disease, e.g. pneumonia (*q.v.*).
4. Pulmonary vascular disease, e.g. pulmonary thromboembolism or infarctive pneumonia (*q.v.*).
5. Pleural disorders, e.g. pneumothorax and pleural effusion (*q.v.*).
6. Chest wall or diaphragm disorders, e.g. botulism or trauma (*q.v.*).
7. Abdominal distension, e.g. ascites or colonic torsion (*q.v.*).
8. "Look alike" disorders. These are non-respiratory origin causes of tachypnea or increased effort. Examples include hyperthermia, anxiety, hypotension, anemia and neurologic disease (*q.v.*).

Clinical signs

Evaluation begins with a history of the duration and progression of clinical signs as related to the respiratory tract. Concurrent or recent systemic illness should be investigated. Any history of recent trauma, such as a collision, fall or administration of oral medications with a balling gun, may be important to the diagnosis.

Physical examination includes rectal temperature, pulse and respiratory rate. Anxiety associated with respiration, flared nostrils, expiratory grunting, increased intercostal or abdominal effort and the presence of a "**heave line**" characterize respiratory distress. Upper airway obstruction may be associated with respiratory stridor, asymmetry of airflow from the nostrils, halitosis, abnormal sinus resonance and the presence of unilateral nasal discharge.

Thoracic auscultation at rest and with a **rebreathing bag** helps identify lung parenchymal disease. Mucous membrane color is assessed for cyanosis, hemorrhage, congestion and injection. If pleural fluid, pneumothorax, lung consolidation or a space-occupying mass is suspected, thoracic percussion should be performed. Serial arterial blood gas analysis and pulse oximetry help to monitor progression of disease and response to therapy.

A **thorough physical examination** helps localize the problem to the upper or lower airway. If an upper airway lesion is suspected, endoscopic examination should be performed immediately to evaluate the nasal passages, nasal septum, ethmoid turbinates, pharynx, larynx, guttural pouches and trachea. Radiography allows further evaluation of the upper airways. Abnormalities include increased soft tissue density, bony lysis or proliferation, fluid lines and distortion of the normal architecture of the head or larynx.

Abnormalities of the lungs, pleura and pericardium that can be demonstrated with radiographs and ultrasonography include obstructive space-occupying masses such as tumors, abscesses or hematoma, and diffuse disease such as lung consolidation, pleural effusion, hemothorax or pneumothorax (*q.v.*) resulting in reduced lung capacity.

The clinical signs and therapeutic approaches for common problems resulting in respiratory distress are described in Table 23.12.

Treatment

A **tracheotomy** should be performed in cases of obvious or potentially life-threatening upper airway obstruction. Although the procedure is usually performed at the junction of the proximal and middle thirds of the neck, it is important that the tracheotomy is distal to the upper airway obstruction.

Once the site is determined and aseptically prepared, local anesthetic is infiltrated into the skin and underlying cutaneous muscle in a linear fashion. The horse's head is then stabilized, the skin tensed, and a 6–8 cm longitudinal incision is made through the skin and cutaneous colli muscle, exposing the paired sternothyroid muscles. These deeper muscles are then separated along their median raphe with a scalpel or scissors to expose the trachea. The tracheotomy is performed by **transverse incision of the annular ligament** between two centrally located cartilaginous rings. The incision should be just slightly wider than the tracheotomy tube for ease of placement and be limited to one third of the tracheal circumference to maintain tracheal stability and minimize complications of wound healing. The tube is secured in place and, if the site of obstruction has been bypassed, air should flow easily through the tube and the horse's respiration return toward normal. It is important to confirm or have strong suspicion of an upper airway obstruction before performing a tracheotomy. Critically ill horses suffering from lower airway obstruction or endotoxemia can have very little airflow at the nares, mimicking an upper airway obstruction. In these cases a tracheotomy will not help.

Thoracocentesis should be performed if the horse is in respiratory distress due to accumulation of effusion, blood or air within the pleural space. The preferred site is the **sixth or seventh intercostal space** just dorsal to the costal–chondral junction for fluid accumulation, but the caudodorsal region for pneumothorax. Ultrasonography should be utilized to select an appropriate site whenever possible. Free blood within the pleural space should not be tapped unless it is the source of hypoventilation or respiratory distress. Any fluid obtained should be submitted for cytologic examination and microbiologic culture (aerobic and anaerobic culture and antimicrobial susceptibility testing). Repeated thoracocentesis or placement of a chest drain may be warranted if fluid or air reaccumulates rapidly.

If blood loss is severe, IV fluid therapy and replacement with whole blood may be necessary. In the case of **hemothorax**, the cause of the hemorrhage should be treated if possible. For example, **fractured ribs** (*q.v.*) are common in foals and should be stabilized. Cases of uncomplicated trauma usually respond quite well, although secondary infection and pleural pneumonia may affect the outcome. Broad-spectrum antimicrobial therapy is indicated in cases of **bacterial pleuropneumonia** (*q.v.*).

Intranasal oxygen insufflation or mechanical ventilation may be needed in severe cases of pulmonary edema, regardless of the underlying etiology. IV fluids, if required, should be administered cautiously in order to avoid potentiation of edema. **Diuretics** such as furosemide may be helpful, although the effects of furosemide on pulmonary hemodynamics in the presence of

Table 23.12 Characteristics and treatment of acute respiratory distress

Disease	Clinical signs	Other diagnostics
Upper airway obstruction, e.g. laryngeal paralysis, arytenoid chondrosis, tracheal stenosis, foreign body, neoplasia, abscessation	Anxiety with increased respiratory effort, decreased or absent airflow at nares; no or limited thoracic airflow auscultated: cyanotic mucous membranes	Obstruction observed endoscopically and/or radiographically
Pulmonary disease, pleuropneumonia	Fever, anorexia, depression, cough, weight loss, respiratory distress, pleural pain; airflow auscultated dorsally, minimal to none ventrally; pleural friction rubs	Thoracic percussion—dull resonance ventrally; ultrasound—hypoechoic and anechoic fluid in pleural space, increased density ventrally with horizontal fluid line. Leukocytosis, hyperfibrinogenemia
Hemothorax (may occur in conjunction with pneumothorax)	History of trauma, signs of coagulopathy, erosion of vessel by abscessation, neoplasia; lung sounds are normal dorsally, muffled ventrally; heart sounds may radiate widely; may be unilateral or bilateral	Thoracic percussion—normal dorsally, dull ventrally; radiographs—increased density ventrally, normal lung dorsally; ultrasound—blood in pleural space
Pneumothorax	History of trauma or disease with airway or parenchymal erosion, i.e. neoplasia or abscessation, difficult to auscultate air sounds especially dorsally	Thoracic percussion—abnormal resonance dorsally; radiographs—evidence of air in pleural space or mediastinum; ultrasound
Pulmonary edema	Often a life-threatening complication of other disease (renal failure, cardiac failure, sepsis, DIC, hypoxic acidosis) or over-zealous fluid administration. Auscultation—shallow rapid respirations with crackles, ± clear or frothy fluid at nares	Radiographs—peribronchial and perivascular cuffing, increased prominence of vessels, hazy reticular pattern

Disease	Treatment
Upper airway obstruction, e.g. laryngeal paralysis, arytenoid chondrosis, tracheal stenosis, foreign body, neoplasia, abscessation	Relief of obstruction Tracheotomy distal to the site of obstruction
Pulmonary disease, pleuropneumonia	Thoracocentesis for culture and sensitivity and cytologic examination, to remove large volumes of fluid; may repeat or leave indwelling catheter in place Antibiotics
Hemothorax (may occur in conjunction with pneumothorax)	Thoracocentesis to remove blood May need to repeat if reaccumulates Broad-spectrum antibiotics. Treat the source of hemorrhage if possible, e.g. fractured ribs
Pneumothorax	Thoracocentesis to remove air. Repeat as necessary or indwelling catheter. Treat source
Pulmonary edema	Treat underlying disease. Intranasal/tracheal oxygen; decrease rate or stop IV fluids. Diuretics—furosemide (1–2 mg/kg IV), NSAID (flunixin meglumine 0.1 mg/kg), corticosteroids (50–100 mg adult horse)

DIC, disseminated intravascular coagulation.

pulmonary edema have not been studied. Plasma products may help to increase oncotic pressure, but these should also be administered cautiously since colloids increase vascular pressure. In addition, colloids may extravasate into pulmonary edema fluid in capillary leak states such as acute respiratory distress syndromes.

NSAIDs, antihistamines and corticosteroids may also be useful in treating some forms of pulmonary edema, particularly those caused by inflammatory or allergic states.

EXERTIONAL RHABDOMYOLYSIS

Exertional rhabdomyolysis (*q.v.*), otherwise referred to as azoturia, Monday morning disease, tying up and paralytic myoglobinuria, can be a severe, life-threatening condition. It is of particular importance in draft breeds, but can occur in light breeds as well.

Etiology

Classically, the disease has been described in draft horses following Sunday's day of rest, hence the name Monday morning disease. In the light breeds, exertional rhabdomyolysis often occurs in fit horses in **rigorous training** programs that are rested for a period of time while being maintained on the same **high concentrate diet** required while in work. The disease occurs once the horse returns to work, even after light exercise. Sudden increases in exercise level may also be associated with sporadic forms of the disease. Exertional myopathies may also be observed in horses that are **inadequately fit** for competition and over-exerted. Disease pathogenesis is poorly defined. A variety of factors that result in metabolic alterations of the muscle, mitochondrial function and electrolyte and fluid balance are involved.

Two specific heritable syndromes have been recently described: **polysaccharide storage myopathy (PSSM)** and **recurrent exertional rhabdomyolysis (RER)**. PSSM mostly affects **Quarter-horses** and Quarter-horse crosses (Appaloosas, Paints). It is a glycogen storage disorder with accumulation of glycogen and abnormal polysaccharide with enhanced insulin sensitivity. Another similar syndrome occurs in draft breeds. RER primarily affects **Thoroughbreds**. It is due to a defect in intracellular calcium regulation, with subsequent muscle hypercontraction and necrosis. Nervous animals are most commonly affected, with young race fillies being over-represented.

Clinical signs

Clinical signs are variable. During **acute episodes** of rhabdomyolysis, horses walk with a stiff, stilted gait and may have muscle fasciculations. Severe cramping results in reluctance or inability to move. In extreme cases, animals are recumbent and unable to rise. Typically, muscles of the back and hindlimbs are tight and painful to palpation. These horses are often anxious, sweat profusely and have elevated vital signs. Exacerbation of the condition may occur during attempts to move the affected horse. Myoglobinuria occurs in severely affected animals.

Creatinine phosphokinase (CPK) and aspartate aminotransferase (AST) levels rise markedly with rhabdomyolysis. CPK levels increase rapidly, peaking at 4–6 h after muscle damage has occurred and returning to normal levels in 36–72 h. Levels of AST rise more slowly, peaking at 24–48 h and declining by 2–3 wk after the insult. The **degree of elevation** often reflects the extent of myonecrosis. Therefore, serial evaluation of both enzymes to monitor the progression of the disease and rate of recovery is suggested.

Treatment

Treatment of the severely affected horse involves **preventing further muscle damage**, correcting metabolic abnormalities and dehydration, and providing analgesia in animals that are in extreme pain and reluctant to move. In severe cases, even walking back to the barn is contraindicated. In those cases, transport to a stall should be arranged. In mild cases with minimal muscle damage, hand-walking has proven to be beneficial. Experienced clinical judgment is necessary to ascertain which cases benefit from additional exercise.

In cases with **severe dehydration** or hypovolemia and electrolyte imbalances a balanced polyionic electrolyte solution should be administered IV or through a nasogastric tube. Many **endurance horses** suffering from this disease will be alkalotic with hypochloremia and hypocalcemia, and therefore bicarbonate therapy should be avoided. **Myoglobin can be nephrotoxic**, especially in the dehydrated animal. Myoglobin possesses vasoactive properties that in the dehydrated horse may encourage the development of **renal ischemia** (*q.v.*) and tubule damage, and its presence warrants IV fluid diuresis. Serial monitoring of the PCV, TP, serum electrolytes and creatinine should be performed.

NSAIDs, such as phenylbutazone or flunixin meglumine, help relieve muscle pain and spasm. Acepromazine reduces anxiety and improves peripheral blood flow through α-adrenergic blockade. In extremely anxious horses, small doses of xylazine, butorphanol or detomidine may be indicated.

Good nursing care is essential. A warm, comfortably bedded stall in an environment that encourages the horse to rest is important. The horse should not be forced to stand if it wishes to remain recumbent. However, **prolonged recumbency** in one position can be detrimental, and frequent repositioning may be necessary. If the patient remains recumbent for a long period, a **padded helmet** helps protect the head and eyes, and **ocular lubricant** and antibiotic ointments help prevent corneal ulcers.

Intermittent slinging of recumbent horses for short periods is beneficial in some cases. The distal limbs should be bandaged to prevent self-trauma. Massage and warm blankets may also encourage muscle relaxation and blood flow. A variety of hand-held electric, pulsating massagers or therapeutic ultrasound units are commercially available. Using light pressure, the massager is directed in a circular motion over the large muscle groups for 10–15 min 2–4 times daily. Severely affected horses with painful muscles may object to this technique.

Prevention of rhabdomyolysis episodes in horses with RER or PSSM includes **dietary and exercise management**. These horses should be fed diets low in simple carbohydrates, meaning no grain for horses with PSSM and less

than 2–2.5 kg per day for horses with RER. Additional calories should be provided in the form of fat. Exercise management includes regular exercise and turnout rather than stall confinement.

ACUTE RENAL FAILURE

Etiology

Nephrotoxicity and ischemia are the most common causes of acute renal failure (ARF) (*q.v.*), which is associated with **acute tubular necrosis**. Clinical signs and progression of the disease are dependent upon the severity of the insult and therapeutic aggressiveness.

Box 23.4 includes a list of common causes of acute renal failure in the horse.

Clinical signs

The clinical signs of ARF are similar regardless of the etiology and are often overshadowed by signs of the primary disease. **Azotemia** (*q.v.*), as indicated by increases in creatinine and BUN, can be caused by pre-renal, primary renal or post-renal problems. Initially, oliguria will be present; only rarely will anuria occur in the adult horse. Pre-renal azotemia, due to hypovolemia, is associated with decreased urine production and highly concentrated urine. Renal azotemia results in isosthenuria despite dehydration.

If oliguria and isosthenuria persist after rehydration, tubular damage has occurred, signifying renal disease. Following this acute oliguric phase, diuresis accompanied by polydipsia and polyuria can persist for many weeks while tubular cell regeneration occurs.

In ARF, the **left kidney** may be swollen and painful to palpation per rectum. In severe cases, the right kidney may also be palpated. Ultrasonographic evaluation can reveal renal enlargement and changes in parenchymal architecture due to inflammation, hemorrhage, edema or infiltrative disease.

Box 23.4 Common causes of acute renal failure in the horse

Nephrotoxicities
- Aminoglycosides
- NSAIDs
- Vitamin D
- Mercury

Hemodynamic causes
- Hemorrhagic shock
- Endotoxic/septic shock
- Heart failure
- Coagulopathies

Immunologic causes
- Drug-induced interstitial nephritis
- Glomerulopathy

Ultrasound-guided **percutaneous renal biopsy** can confirm the diagnosis and aid in provision of a prognosis. Ischemia often damages tubular epithelial cells and basement membrane while toxicities may damage only the epithelial cells, leaving the basement membrane intact. **Urinalysis** (*q.v.*) is important in the differentiation of pre-renal and primary renal disease. Table 23.13 outlines common abnormalities of urinalysis and their causes.

Serum electrolyte concentrations vary depending on the degree of renal failure, water loss and concurrent disease processes. Severe tubular disease may cause total body sodium depletion but, because of accompanying water loss, plasma sodium concentration may remain normal. **Hyponatremia** may also occur with acute renal failure. **Hypernatremia** can occur with acute oliguria or anuria, but is most commonly associated with hypovolemia due to gastrointestinal obstruction or diarrhea. Increased sodium conservation by the kidney is counterbalanced by electrolyte loss into the gut lumen and feces. Chloride loss tends to follow sodium concentrations.

Because the kidney is the main site of potassium excretion, **hyperkalemia** may occur with acute oliguria or anuria. Unlike other species, the horse's major site of calcium regulation is the kidney. During chronic renal failure (*q.v.*), hypercalcemia and hypophosphatemia can occur, while hypocalcemia and hyperphosphatemia are often present with acute disease. Acid-base balance may also be disturbed if there is a failure to conserve bicarbonate and/or excrete hydrogen ions (renal tubular acidosis).

Treatment

Treatment of ARF is initially directed at **replacing fluid volume deficits** and **correcting electrolyte and acid-base abnormalities**. IV administration of a **balanced polyionic solution** is sufficient in most cases. During polyuria, additional sodium and chloride replacement may be necessary in order to match fluid input with output. However, excessive administration of sodium can result in sodium retention and edema formation. During oliguric renal failure, the volume of fluid administered and electrolyte balance should be monitored very carefully. Changes in daily body weight, PCV and central venous pressure (CVP) help assess plasma volume expansion.

Table 23.13 Common abnormalities of urinalysis and their causes

Abnormality	Cause
Small volume, highly concentrated urine	Hypovolemia, dehydration
High volume, dilute urine or isosthenuria	Polyuric phase of failure
Blood	Polydipsia or fluid administration
Hemoglobin	Intravascular hemolysis
Erythrocytes	Acute glomerular damage, hemorrhage into the urethra, bladder or ureters
Protein	Glomerular damage. Tubular failure to absorb
Glucose	Renal threshold exceeded, renal tubular damage and failure to absorb
Sediment	
Hyaline casts	Seen in a variety of systemic diseases; not necessarily indicative of renal disease
Granular and epithelial casts	Formed from diseased tubules

Attempts should be made to determine **daily fluid intake and urine output**. Urine collection in the male can be accomplished by strapping a urine collection device around the abdomen. In mares, an indwelling Foley catheter attached to a closed collection system can be used.

During oliguric renal failure, an IV solution of 20% mannitol (0.25–1 g/kg) and furosemide (1 mg/kg q 2 h) may help improve urine production. Failure to respond to **furosemide** may indicate severe tubular disease. Low doses of **dopamine** (1–5 μg/kg/min) can be used in conjunction with furosemide during oliguria or anuria in an attempt to improve renal blood flow through vasodilation. Recent evidence in human critical care suggests that low dose dopamine therapy may not be indicated in patients with oliguric/anuric renal failure despite successful urine production, due to an increase in oxygen consumption by the renal tubular epithelium. However, because hemodialysis is currently not readily available for adult horses, dopamine is still indicated for use in anuric/oliguric renal failure by promoting urine flow, thereby providing time for regeneration of the renal epithelium.

High doses of dopamine produce α-adrenergic vasoconstriction with possible systemic hypertension. Therefore, **blood pressure** must be monitored during the dopamine infusion. Hypotension should be treated aggressively in ARF patients with the use of crystalloids, colloids, and inotrope and pressor agents (*q.v.*).

Most cases of ARF in adult horses are **non-oliguric** and do not require mannitol, furosemide or dopamine. Plasma-Lyte 148, lactated Ringer's solution, Hartman's solution, sodium chloride (0.9%) or other **balanced polyionic solution** can be administered at 48–100 mL/kg/day until a significant decrease in serum creatinine is observed. It is not uncommon for creatinine to stay high without decreasing for up to 72 h of fluid therapy. IV fluid therapy should be continued at 10–20 mL/kg/day until the serum creatinine is normal. Once a steady state has been achieved, and the patient is eating and drinking adequately, IV fluids may be gradually discontinued over the next several days. Renal function should be re-evaluated after discontinuing therapy to assure against relapse of the condition.

Prognosis

Generally, ARF due to **toxicity** (except with heavy metals) has a reasonable prognosis and will respond to therapy unless persistent oliguria develops. **Hemodynamic causes** of renal failure have a more variable prognosis, but often respond to therapy if the underlying disease (such as colitis) can be corrected. If renal histopathology reveals an intact basement membrane, and appropriate therapy corrects the underlying cause, the prognosis is good. Patients with perirenal edema and marked renal enlargement have a poorer prognosis, as do horses with chronic disease.

ACUTE CRANIAL AND SPINAL CORD TRAUMA

Etiology

Acute trauma to the CNS (*q.v.*) is relatively common in the horse. Unfortunately, regardless of the location of the lesion, it can be one of the most debilitating

injuries. Falls at high speeds, collisions and penetrating wounds can result in fractures or **subluxation of the vertebral column** (*q.v.*). Falling over backwards with concussion to the poll is common in young horses and may result in **basilar fractures** of the basioccipital or basisphenoid bones. In most cases, the fracture or subluxation is not the primary problem; rather, the underlying neural damage results in the greatest morbidity and mortality.

With acute disruption of neural tissue the degree of clinical dysfunction is proportional to the degree of compression, traction or crushing involved. Progressive changes following the initial injury are common and are often due to vascular damage. **Ischemic injury** to the brain or spinal cord results in secondary injury, including release of free radicals, prostaglandins and other vasoactive compounds that in turn cause further inflammation. As neural tissue becomes more edematous within the confines of the cranium or vertebral canal, vascular occlusion and tissue compression increase. Hemorrhage causes further vascular compromise and exacerbates edema formation.

Clinical signs

Thorough physical examination to assess involvement of other organs and stabilization of life-threatening lesions are the first steps. Respiratory rate and character, hydration and volume status, and the presence of other fractures or severe injury should be addressed first. Hypoxemia, hypercapnia, and hypovolemia or hypotension can significantly worsen secondary injury and subsequent prognosis for recovery. These should be avoided or treated immediately when found on initial examination or clinicopathologic assessment.

An accurate description of how the injury occurred and the horse's condition at the time of injury are important for rapid localization of the CNS lesion(s) and for comparison with the present condition. **Neurologic examination** (*q.v.*) includes evaluation of the patient's mentation, ocular response and position, vestibular system, posture and motor function. Additional diagnostics that may be necessary include radiography and myelography. **Cerebrospinal fluid** is commonly xanthochromic with an increased protein, but can be normal. In cases of severe trauma, frank hemorrhage may be observed. Hemorrhage noted in the external ear canal can be due to cranial fractures. **Bilateral epistaxis** may be associated with basilar fractures of the cranial vault, although it may also be seen with guttural pouch or other bleeding.

Treatment

Treatment of acute, traumatic neurologic injuries is aimed at control and prevention of cerebral edema and/or hemorrhage. Supportive care to maintain hydration and prevent infection and self-trauma should be instituted early. Patients should be **routinely re-evaluated** during therapy to assess progress. Oxygen insufflation and ventilation may be required in patients with severe hypoventilation.

Many horses that are involuntarily recumbent can be quite violent and may require **sedation** to prevent self-inflicted trauma. Phenothiazine derivatives may lower the seizure threshold and should be **avoided** in horses with intracranial disease. Ketamine and xylazine are **contraindicated** in horses with cranial trauma because of their hypertensive effects, especially in cases

of known cerebral hemorrhage. Chloral hydrate (15–60 g IV, to effect) can be used in the adult horse for sedation and to control seizures. If this fails, IV anesthesia with **pentobarbital** is usually successful. **Diazepam** (0.1 mg/kg IV) may be administered four to five times at 3–4 min intervals to the recumbent patient for sedation and seizure control.

The patient should be monitored closely while sedated or anesthetized for changes in heart and respiratory rates and rhythms, and response to external stimuli. Indirect blood pressure measurements should be made to avoid hypotension and reduced perfusion.

When possible, **arterial blood gases** should be monitored, especially in patients with abnormal breathing patterns or rates. Increases in arterial CO_2 can cause cerebral vasodilation and encourage **intracranial hemorrhage**. If hypercapnia is present, increasing the minute ventilation will help decrease the CO_2. This is best accomplished in the ICU using a mechanical ventilator that can blend oxygen and compressed air and provide a large enough tidal volume to ventilate an adult horse. Although most clinical information on the ventilatory management of acute head trauma comes from small animals and humans, the principles can be applied to the care of large animals if the equipment is available. Current recommendations from human critical care include mild hyperventilation to normoventilation, with a goal of 32–40 mmHg for $PaCO_2$.

Corticosteroids have been recommended for the control of CNS pressure caused by edema of the spinal cord and are most beneficial when administered early in the course (within 8 h of spinal cord injury). The use of corticosteroids for head trauma is controversial in human medicine and may be contraindicated. Dexamethasone (0.1–0.2 mg/kg) can be administered q 12–24 h for 1–2 days to reduce edema formation and inflammation associated with spinal cord injuries.

Mannitol (0.25–2 g/kg IV) in a 20% solution generally works rapidly and can be useful in reducing cerebral edema. It is a hypertonic solution and should be used with caution in the presence of ongoing intracranial hemorrhage. If the hemorrhage is not under control, decreasing the edema may increase available space for hemorrhage. Over-hydration with supportive maintenance fluids should be avoided.

Hypertonic saline (1232 mmol Na/L) has recently been advocated in human critical care. Doses suggested include 2 mL/kg every 4 h for 5 infusions. The hyperosmolar infusions aid in reducing extravascular volume of the brain.

Dimethyl sulfoxide (DMSO) has been used to treat acute neurologic trauma. The recommended dose of 1 g/kg in no greater than a 20% solution is administered IV q 24 h for 3 days. The use of DMSO in CNS trauma remains controversial.

Antimicrobial therapy should be instituted in cases with suspected basilar skull fractures and blood in the nasal passage or ear canal. Antibiotics should be considered in recumbent patients who are more susceptible to respiratory infection. Trimethoprim–sulfadiazine (5 mg/kg of trimethoprim portion, IV or PO, b.i.d.) is a good choice although other broad-spectrum drugs should achieve adequate levels in the CNS with blood–brain barrier disruption. Tetanus prophylaxis is also important.

Good nursing care for the recumbent horse is essential. If possible, the patient should be attended by a trained assistant who can recognize changes in condition, help prevent self-trauma and manage the necessary support equipment. Patients that are able to sit sternally can be propped up using pads or bales of straw. **Ventilatory and circulatory problems will be minimized if the patient can maintain sternal rather than lateral recumbency**. In lateral recumbency, large foam mats or deep bedding should be used and repositioning performed q 2–6 h to help prevent compartmental syndrome and to maintain adequate respiratory function. Large mats, designed to pad the walls of the stall, help prevent self-trauma in violent patients. Sharp, hard or immobile objects such as buckets, feed tubs, salt lick holders, and hay racks should be removed or be padded. Helmets can be used to protect the head from self-trauma, and the head should be elevated by 10° in head trauma cases to minimize intracranial pressure.

A sling may help support patients that can bear some weight or are weak and cannot get up without assistance. It can also facilitate the repositioning of large patients. Those patients that tolerate the sling require **constant observation** to prevent self-trauma by entanglement or asphyxia. They should be allowed to lie down and rest intermittently. Some horses must be assisted to lie down.

Decubitus is a serious problem in the recumbent horse and usually develops over pressure points such as the tuber coxae, tuber ischii, point of the shoulder, zygomaticotemporal protuberance, lateral malleolus and greater trochanter. Prevention focuses on minimizing pressure over these points by applying **extra padding** or redistributing the pressure by **frequent patient repositioning**. Deep, dry bedding that is highly absorbent and provides good footing should be used. Non-abrasive thick mats are helpful. Wet skin should be towel dried. Grooming and massage can also stimulate circulation and encourage the development of healthy skin. If decubitus develops, infrared laser therapy can be employed once to twice daily for a period of time proportional to the size of the wound. The beam should be set at medium and used with constant motion over the wound to prevent blistering.

The eyes should be protected from **corneal abrasion** with an ophthalmic **lubricant** applied every 4–6 h. Products containing corticosteroids should be avoided. Ophthalmic antimicrobial products should be utilized if a corneal ulcer is present. Rubber helmets are available that not only protect the eye but the head as well. If the patient is unable to blink, care should be taken to assure the down eyelid is closed and that the bedding is non-abrasive or covered with soft padding. If a corneal ulcer is suspected, **fluorescein staining** (*q.v.*) should be performed and appropriate therapy instituted.

Prolonged recumbency and the associated lack of normal exercise, interruption in feeding schedule, and decreased water intake may result in the development of **colic**, most commonly from **impactions of the large intestine** (*q.v.*). Animals that can eat and drink should be offered fresh water frequently (q 2–4 h) and highly digestible feeds. In animals unable or unwilling to drink or eat, nasogastric intubation with water may be necessary unless IV fluids are provided. **Hypotension** must be avoided at all costs in horses with neurologic injury.

Table 23.14 Recipe for hyperalimentation diet

Maintenance electrolyte mixture (daily requirement for 450 kg horse)	
Sodium chloride (NaCl)	10 g
Sodium bicarbonate ($NaHCO_3$)	15 g
Potassium chloride (KCl)	75 g
Potassium phosphate (dibasic anhydrous) (K_2HPO_4)	60 g
Calcium chloride ($CaCl_2$ $2H_2O$)	45 g
Magnesium oxide (MgO)	24 g

Recommended tube feeding schedule (for 450 kg horse)	Day						
	1	2	3	4	5	6	7
Electrolyte mixture (g)	210	210	210	210	210	210	210
Water (L)	21	21	21	21	21	21	21
Dextrose (g)	300	400	500	600	700	800	900
Dehydrated cottage cheese (g)	300	450	600	750	900	900	900
ME (Megacalories/day)	2.4	3.8	4.4	5.4	6.4	6.8	7.2

The above allowances should be divided up and fed in three feeds daily. Alfalfa meal is added to make a slurry.

Hyperalimentation can be initiated using alfalfa meal gruel or other liquid diets administered by **nasogastric tube** (Table 23.14). Alternatively, a complete pelleted diet, such as Equine Senior (Purina) or other product, can be blended to a slurry and easily administered via nasogastric tube. Impactions (*q.v.*) can be treated with laxatives, mineral oil and IV fluids. Ileus (*q.v.*), not uncommon in the recumbent patient, precludes oral intake and necessitates IV fluid support when present. **Manual evacuation of the rectum** several times a day may be necessary since many recumbent patients are unable to exert sufficient abdominal pressure for defecation.

Recumbent patients that are reluctant or unable to urinate require continuous or intermittent **urethral catheterization**. Long-term catheterization is best accomplished by using an aseptic, closed system. Complications of catheterization include cystitis and ascending pyelonephritis. Antimicrobial therapy should be directed by urine culture and sensitivity.

LAMINITIS

Etiology

The development of laminitis (*q.v.*) is not clearly understood. Possible causes include carbohydrate overload, endotoxemia, sepsis, excessive unilateral weight bearing and administration of corticosteroids. Laminitis often occurs as a complication of serious systemic disease and frequently has a **fatal outcome**. Due to the numerous predisposing factors and systemic pathologic events associated with laminitis, therapy is often complicated and controversial.

Clinical signs

Acute laminitis may affect one or more feet. Usually both front feet are affected, and the horse will stand with the hind legs well under the body and

front legs extended with weight on the front heels. If all four feet are affected, the horse will stand with the legs tucked under the body to form a narrow base stance. In either case, the horse will often lie down for extended periods of time.

Classically, the laminitic horse is in pain and reluctant to move, with tachycardia, tachypnea and muscle trembling. The affected feet have increased warmth and digital pulses. **Pain** can be elicited from the sensitized sole, usually in the toe region, with or even without hoof testers. In severe cases, the coronary band becomes edematous with clefting, and may ooze serum and blood. **Penetration of the sole** after rotation and/or sinking of the third phalanx can also occur. Lateral radiographs of the foot help evaluate the degree of rotation and/or sinking of the third phalanx.

Treatment

The goals of therapy are outlined in Box 23.5.

Box 23.5 Goals of therapy in laminitis

1. **Treat the primary illness if one exists**
   Treatment will vary with the systemic disease associated with laminitis. However, a few principles should be kept in mind. Dehydrated animals require fluids to replace volume deficits. Broad-spectrum antimicrobials, flunixin meglumine (0.25 mg/kg IV q 8 h) and endotoxin antisera should be considered in suspected cases of septicemia and endotoxemia (*q.v.*). In cases of **grain overload** (*q.v.*), mineral oil administered by nasogastric tube may slow the absorption of endotoxin, and adsorbents such as activated charcoal or smectite (ditrioctahedral smectite: Bio-sponge, Platinum Performance, Buellton CA, USA) may reduce the extent of endotoxin absorption.

2. **Provide analgesia**
   NSAIDs, especially phenylbutazone, have been useful in the treatment of laminitis, and act by decreasing inflammation, edema and pain in the digit. Dosage of phenylbutazone is dependent upon the degree of discomfort and ranges widely, but is most commonly 2.2 mg/kg IV/PO q 12–24 h. A maximum of 4 mg/kg q 12 h should not be exceeded, and the dosage should be reduced within 4–5 days in order to minimize NSAID toxicity. To avoid drug toxicity (e.g. gastrointestinal ulceration, diarrhea, azotemia, renal papillary necrosis) the minimum dose that provides adequate analgesia should be used. Some clinicians consider that the degree of analgesia provided should not be complete, but rather **a balance** between providing some relief and not providing enough to encourage standing or increased ambulation with increasing risk of **damage to laminae**.

   Padded floors and deeply bedded stalls improve phalangeal support and digital comfort and provide protection for recumbent animals. Straw mixed with wood shavings, sand and peat moss are good choices, although if the patient is frequently recumbent, sand can be abrasive and contribute to

Box 23.5 continues on page 1312

Box 23.5 Goals of therapy in laminitis [continued]

decubitus. With increasing comfort, mild exercise encourages a return of normal digital circulation.

Local anesthesia with **digital nerve blocks** (*q.v.*) has been advocated in the early phase to relieve pain transiently, to promote digital vascular dilatation and to encourage weight bearing. However, this is controversial as it can promote increased **laminar damage** by encouraging ambulation and shearing.

Although **some exercise** may be warranted in the early phase to encourage normal circulation in the foot, too much exercise may increase the mechanical forces producing third phalanx rotation. Therefore, nerve blocks should be used judiciously. Slinging in a pool has been used successfully to provide pain relief and exercise with reduced weight bearing in some recumbent patients.

3. Promote normal circulation of the digit

Laminitis is thought to occur as a result of two interrelated mechanisms: a **vasoactive process** and a **coagulopathy**. More recent work indicates involvement of zinc metalloproteases. Although there is an overall increase in blood flow to the foot, ischemia develops from decreased capillary perfusion in the laminae due to bypass of blood through arteriovenous shunts regulated by vasoactive hormones and toxins. Pain and subsequent catecholamine release contribute to vasoconstriction by activation of α-adrenergic receptors within the dermal vasculature. Alterations in the intrinsic coagulation system have also been identified.

Acepromazine (0.04 mg/kg IV/IM 3–6 times a day) and phenoxybenzamine (2 mg/kg PO b.i.d.) have been used to **reduce vasoconstriction** by non-competitive α-adrenergic blockade. Hypotension can occur with these drugs and they should be used cautiously in hypovolemic patients. The **sedative effects** of acepromazine are also beneficial and may encourage the horse to lie down.

Heparin has been used to prevent coagulation within the microcirculation in the foot. Unfortunately its efficacy in the treatment of laminitis is unknown, and the use of unfractionated heparin is associated with erythrocyte agglutination. Unfractionated heparin has been used at a variety of dosages, most commonly 40–70 IU/kg SC or IV q 8–12 h. Low molecular weight heparin (dalteparin, 50 IU/kg SC q 24 h) is associated with fewer side effects in humans and horses, and may be more effective in preventing thrombosis, although further study is required. **Aspirin** (10–20 mg/kg PO every other day) is a potent inhibitor of platelet aggregation and thromboxane synthesis, and may help minimize coagulation within the microvasculature of the foot.

DMSO, an anti-inflammatory agent and free radical scavenger, has been used to prevent reperfusion injury of the laminae although its efficacy in the treatment of laminitis is unproven. The recommended DMSO dose is 1 g/kg IV diluted to a 10% or less solution daily for 3 days.

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Box 23.5 Goals of therapy in laminitis [continued]

Corticosteroids are **contraindicated** in treatment of laminitis because they enhance the vasoconstrictive effects of catecholamines and may contribute to the development of laminitis.

The use of hot and/or cold soaking of the foot remains controversial. Since the foot is ischemic, decreased temperatures may decrease the metabolic demands for oxygen. However, increasing the temperature may promote vasodilatation and increase capillary perfusion. **Icing of the feet** has recently been advocated.

4. Prevent further rotation/sinking of the third phalanx

Sand stalls provide good sole support, reduce the mechanical forces required to flex and extend the digit and allow the horse to stand in a comfortable position. Cushioning the sole with supportive material, such as foam, cast material, Orthoplast, soft rubber and silicon, has been advocated but care must be taken to distribute the weight **evenly** to avoid point pressure and sole necrosis. Support of the frog with pads or shoes is useful in some cases, but may complicate compression of the vasculature between the third phalanx and the sole and subject the horse to more pain.

In advanced cases, **hoof wall resection** may be necessary to remove necrotic debris and relieve the pressure from fluid accumulation between the third phalanx and hoof wall. Resection should only be considered when there is serous or purulent drainage from the coronary band or when the hoof wall is completely separated from the skin and gas lucencies are visualized radiographically between the hoof and the third phalanx.

Pain that is refractory to other shoeing techniques may be relieved with hoof wall resection. If complete separation is evident, the entire toe is usually resected and may extend to the coronary band—hoof wall junction. A power rotary burr is commonly used although hoof nippers, rasp and cast cutters can be substituted. The cuts are made to the level of the stratum medium, where a texture change should be felt. The affected wall can be gently peeled away from the laminae and necrotic debris removed. Care must be taken to avoid damaging the coronary band.

After hoof wall resection, the foot must be aseptically bandaged and cleansed daily until healthy horn covers the exposed wound. Healing proceeds by granulation. Once the corium covers the granulation tissue, new horn is produced, accompanied by growth from the coronary band. During the growth period strict attention to asepsis must be maintained and areas of infection adequately drained. Exercise should be limited to stall confinement. Depending on the amount resected, 6 mo to 1 yr should be allowed for hoof regrowth.

Prognosis

The prognosis for laminitis is always **guarded**, particularly if rotation or distal displacement of the third phalanx is evident. The prognosis is good for horses with mild laminitis that respond to anti-inflammatory/analgesics and rest almost immediately. If the duration is short and the symptoms mild,

lameness can be controlled with proper shoeing and low doses of analgesics. If the third phalanx is severely rotated or sunken with sole penetration, euthanasia is often recommended due to the poor prognosis and extensive care required for further treatment.

ACUTE ABDOMINAL CRISIS (COLIC)

Etiology

Despite significant advances in prevention and treatment, colic (*q.v.*) remains a relatively common problem associated with a high degree of morbidity and mortality. A wide variety of intestinal and non-intestinal causes can result in colic (Table 23.15), of which most respond to analgesic therapy alone. In more serious cases, early detection and referral for intensive therapy or surgical intervention can dramatically improve prognosis and outcome.

Physical examination and diagnosis

A thorough history with emphasis on the husbandry, previous episodes of illness, and duration and severity of present condition should be completed. General questions that should be asked are listed in Box 23.6.

The **physical examination** starts with observation of the horse's general appearance and attitude. Horses with abdominal pain that is unrelenting or minimally responsive to analgesics more often have a lesion requiring surgery. Horses that are depressed or only intermittently painful have a better chance of responding to medical therapy. Evidence of **sweating** and **self-inflicted trauma** is consistent with previous uncontrolled pain.

Temperature, pulse and respiration rate are evaluated on initial examination and should be assessed intermittently to evaluate the progression of the disease. The **temperature** is usually normal, although it may be elevated from overexertion in the violently painful horse or in cases of enteritis or colitis (*q.v.*).

Patients in hypovolemic or endotoxic shock (*q.v.*) may have subnormal temperatures. **Pulse** rate and character, **mucous membrane** color, moistness and capillary refill time, skin turgor and temperature of extremities should be assessed as markers of circulating volume and hydration status. Direct or indirect blood pressure should be measured when available. Tachycardia (pulse greater than 52 bpm), poor pulse pressure, cool extremities and dry mucous membranes with a prolonged capillary refill time reflect significant volume contraction and the need for IV fluid therapy.

Evaluation of the gastrointestinal tract includes auscultation and percussion of the abdomen, nasogastric decompression, rectal examination, abdominal radiography, abdominal ultrasonography and abdominocentesis. Although not inclusive, Table 23.16 includes a list of general findings when evaluating the intestinal tract of a colic patient.

Abdominocentesis should be performed in most cases of colic, particularly referral cases and those that are persistent or recurrent. Although the peritoneal fluid responds quite rapidly to inflammation of the peritoneum or intestine, the sample obtained may not accurately reflect the general health of the abdomen. Fluid can pool between layers of mesentery and it may take time for the fluid to mix at the sample site. **Intussusceptions and entrapment**

Table 23.15 General description of common colic etiologies and their treatment

Disease	Treatment
Large colon impaction	
Alert with intermittent mild to moderate pain Pain may be severe, but responsive to analgesics Heart rate—normal to mild elevation Mucous membranes—pink with mild to moderate dehydration Borborygmi—normal to slight decrease Cecal tympany—± Rectal exam—ingesta filled large colon; colon in normal orientation; ±cecal distension Peritoneal fluid—normal Gastric reflux—unusual, but possible if generalized ileus	**Aggressive medical therapy** with oral fluids and laxatives; IV fluids may be necessary; no feed until problem resolved; surgery may be necessary in refractive cases—enterotomy and evacuation of colon with postoperative supportive care
Large colon displacement/volvulus	
Pain—moderate to severe; often unresponsive to analgesics (volvulus) Heart rate—moderate to marked increase Mucous membranes can be toxic with prolonged capillary refill time; dehydration Borborygmi—decreased to absent Cecal tympany—common Rectal exam—gas-distended large colon with abnormally taut and oriented teniae Peritoneal fluid—normal to moderate increase in protein and white blood cells Reflux—unusual, but possible if generalized ileus	**Surgery**—correction of displacement or volvulus; enterotomy in selected cases; resection or colopexy in selected cases; postoperative supportive care (IV fluids, antibiotics, NSAIDs); some cases of left dorsal displacement may respond to phenylephrine administration
Small colon impaction	
Pain—moderate to severe, usually with marked abdominal distension (large colon and cecum) Heart rate—moderate increase Mucous membranes—mild toxicity and dehydration Borborygmi—normal to decreased Cecal tympany—common Rectal exam—loops of ingesta-filled small colon, usually do not have distinct fecal balls; cecum and large colon may be gas filled Peritoneal fluid—usually normal, but may have increased protein and/or white blood cells if bowel is necrotic	**Aggressive medical therapy**—oral and IV fluids, laxatives; may require cecal decompression; if unresponsive, surgery—relieve impaction with high enema, ± enterotomy; large colon may need to be evacuated as well; fecolith or enterolith may be present
Small intestinal strangulation	
Pain—moderate to severe, often unresponsive to analgesics Heart rate—marked increase that does not improve with gastric decompression Mucous membranes—often toxic and very dehydrated Borborygmi—near absent Rectal exam—distended loops of small intestine, usually gas filled and non-compressible, often painful to palpation Peritoneal fluid—serosanguineous with increased protein and white blood cells Reflux—large volume; may be only small amount if the obstruction is in the distal small intestine and early on in course of disease	**Immediate surgical intervention** once patient's cardiovascular system is stable; resection of diseased intestine and anastomosis; postoperative supportive care

(*Continued*)

Table 23.15 (*Continued*)

Disease	Treatment
Duodenitis/proximal jejunitis	
Pain—moderate which responds to gastric decompression of fluid Heart rate—increased when stomach full of fluid; improves once decompressed Mucous membranes—often toxic with marked dehydration; often pre-renal azotemia marked Borborygmi—decreased but present; generally more than with a small intestinal strangulation Rectal exam—fluid/gas-distended loops of small intestine, easily compressible, non-painful to palpation Reflux—large volume often blood tinged and fetid	**Supportive care**: IV fluids; nothing per os; frequent gastric decompression to prevent rupture; NSAIDs; ± antibiotic; attempt to prevent laminitis

This table is not inclusive and should serve only as a guide when making a diagnosis and establishing a treatment plan. Clinical signs of many of these diseases can overlap, making diagnosis more difficult.

Box 23.6 Basic questions regarding the history of a colic patient

Husbandry

- What kind of parasite control program is in place and when was the horse last wormed?
- What kind of diet is the horse on—type of hay, grain, pasture?
- Is the horse housed inside, outside or a combination of both? If inside, what type of bedding is used?
- What kind of exercise program is the horse on?
- Have there been any recent changes or injuries requiring rest?
- Has the horse recently been shipped a long distance or exposed to a new environment or different horses?
- Are any other horses on the farm sick, and if so, with what?

Previous illness

- What, if any, previous illness and/or bouts of colic has the horse had?
- How long ago?
- What was the therapy and how did the horse respond?

Present illness

- How long has the horse been in pain and to what degree?
- What are the temperature, pulse and respiratory rates and how have they progressed through the course of illness?
- Are gastrointestinal sounds present?
- Is the abdomen distended?
- Results of the rectal examination?
- Results of nasogastric intubation?
- What drugs have been administered? How much and when? What was the response to the medication?

Table 23.16 Abnormalities of the gastrointestinal tract in the colic patient

Procedure	Finding	Cause/comment
Abdominal auscultation	Borborygmi absent[a]	Ileus; strangulating lesion
	Normal	Medical colic; resolving colic; enteritis
	Hyperactive, fluidy	Enteritis
Percussion	Large tympanic region—right flank	Cecal distension secondary to large colon obstruction (volvulus, displacement, impaction)
	Tympanic region—left flank	Large colon tympany associated with displacement or volvulus
Nasogastric intubation[b]	Gastric fluid obtained after intubation or siphoning	Small intestinal obstruction—mechanical or functional
Rectal examination	Large amount of firm ingesta in large colon	Large colon impaction; enterolith—right dorsal or transverse colon
	Large colon distension—gas with abnormal orientation of teniae	Large colon volvulus or displacement
	Large colon distension—fluid	Colitis
	Small colon distended with heavy ingesta, often formed fecal balls	Small colon impaction; feco- or enterolith
	Cecal distension	
	Gas	Colonic obstruction
	Ingesta	Cecal impaction
	Small intestinal distension—gas, taut, ±pain on palpation	Strangulating obstruction
	Compressible, non—painful small intestinal distension	Ileus; duodenitis—proximal jejunitis
Abdominocentesis[c]	Increased protein	Initial response to inflammation
	Serosanguineous fluid	Diapedesis of RBC with progressive vascular leakage
	Increased WBC	Migration of cells into fluid in response to progressive intestinal vascular compromise
	Mixed population of bacteria and plant material[d]	Intestinal rupture

[a] *The presence of borborygmi does not necessarily correlate with motility.*

[b] *Nasogastric reflux usually indicates a small intestinal obstruction. Strangulating obstructions (e.g. volvulus, lipomas, epiploic foramen entrapment, internal or inguinal hernia, etc.) and mechanical obstructions (e.g. adhesion, intussusceptions, etc.) must be differentiated from functional obstructions (ileus); the former two require surgical intervention for correction. Impingement of a distended large colon on the small intestine can result in gastric reflux. pH should be evaluated along with color, content and odor.*

[c] *Normal peritoneal fluid will be clear yellow and contain less than 5000 white blood cells/μL and less than 2.0 g protein/dL.*

[d] *Peritoneal fluid with an intestinal rupture can be distinguished from intestinal contents by the presence of phagocytized bacteria within neutrophils. Intestinal contents will contain very few neutrophils.*

of intestine in the epiploic foramen are examples in which the exudate from severely compromised bowel may not be reflected in the fluid sample.

The risk of **intestinal laceration** is real, and extreme caution should be used when sampling largely distended abdomens, particularly when small intestinal distension is evident. **Fractious horses** pose not only a threat to the sampler, but to themselves as well, and should be properly restrained or sedated with short-acting α_2-agonists, such as xylazine, before the procedure.

Aside from cytologic evaluation, **biochemistry tests** can also assist in evaluating abdominal fluid. These include pH, glucose, LDH and lactate

Table 23.17 Clinicopathologic evaluation of the colic patient

Laboratory findings	Problem	Comments
Increased PCV and TP	Dehydration and shock	PCV is somewhat dependent upon splenic contraction; PCV >60% indicates a poor prognosis
Increasing PCV with decreasing TP	Ongoing dehydration with protein loss into the bowel or peritoneal cavity	Often secondary to intestinal compromise or severe enteritis/colitis
Increased creatinine	Volume contraction and pre-renal azotemia	Renal dysfunction may be present and caution should be used when administering NSAIDs and aminoglycosides
Electrolytes (sodium, potassium, chloride calcium)	Concentrations depend on nature of problem and duration of disorder	Hypokalemia and hypocalcemia may induce intestinal stasis and should be replaced if low
Acid–base balance		
Metabolic alkalosis	Sequestration of hydrogen and chloride ions in stomach	May be seen early on, but with progressive dehydration metabolic acidosis is usually observed
Metabolic acidosis	Occurs with progressive dehydration	Bicarbonate replacement is usually not necessary unless base deficit is greater than 10 mEq. Most imbalance is corrected with fluid replacement
Leukogram	Normal with most obstructive disorders	Leukopenia seen with endotoxemia or enteritis (e.g. salmonellosis)

concentrations. With **sepsis** the pH and glucose concentration decrease, while lactate and LDH increase. A gradient between serum and abdominal glucose concentrations >50 mg/dL is consistent with a septic process. A peritoneal pH <7.3, absolute glucose concentration <30 mg/dL, and peritoneal fibrinogen concentration >200 mg/dL are also indicative of **septic peritonitis** (*q.v.*). Aerobic and anaerobic culture and susceptibility testing should be performed if peritonitis is present. Clinicopathologic evaluation of the colic patient focuses on assessment of hydration, electrolyte imbalance and acid–base status. Table 23.17 lists some common abnormalities.

Treatment

Analgesia

Often the most immediate problem is control of **abdominal pain**. During small intestinal ileus or obstruction (*q.v.*), a great deal of the pain results from gastric distension. Decompression of the stomach by **nasogastric intubation** (*q.v.*) relieves pain and helps prevent gastric rupture. Even in cases with severe gastric distension with fluid and gas, the pressure in the stomach may not force the fluid/gas freely out of the tube, and suction or siphoning is required. To avoid trauma associated with repeated intubation the tube may be secured in place at the halter. However, **prolonged intubation** should be avoided to prevent pharyngitis and esophageal ulceration/trauma.

Cecal tympany (*q.v.*) due to obstruction of the large and/or small colon can be relieved by **cecal decompression**. The horse is sedated with a short-acting analgesic such as xylazine or butorphanol and the right flank is aseptically prepared between the last rib and tuber coxae at the level of the ventral aspect of the tuber coxae. Percussion of the abdomen with localization of pinging will aid in placement of the catheter. After a small bleb of local anesthetic is placed in the skin, a 14 G 13.4 cm over-the-needle catheter is placed through the abdominal wall into the cecum. Gas is allowed to escape freely or can be drawn off with suction. Once the gas is removed, the catheter can be flushed with an antimicrobial while it is being withdrawn to minimize contamination of the body wall.

Walking can increase motility and decrease pain, but is best used in conjunction with other therapy. **Excessive walking can exhaust the horse** and prevent ongoing treatment with other therapeutics.

Prostaglandins and thromboxane play a role in the development of pain associated with gastrointestinal distension and ischemia. NSAIDs limit the production of these mediators via the arachidonic acid cascade and have been useful as analgesics in the treatment of equine colic. **Flunixin meglumine** is most commonly used for its analgesic and anti-endotoxin properties. However, it should be used judiciously to prevent **masking** of clinical signs of diseases requiring surgical intervention. Failure to relieve abdominal pain with flunixin meglumine suggests a more serious disease requiring surgery. Phenylbutazone and dipyrone are also used as analgesics but in general are less effective than flunixin meglumine in treating colic. Because of the potential toxic side effects, NSAIDs should be used cautiously in the **hypovolemic patient** that may already be experiencing gastrointestinal and renal hypoperfusion.

Xylazine and detomidine are the most commonly used α_2-agonists in the treatment of colic. They are potent analgesics and sedatives and are very effective at relieving colic pain. If repeated doses are required to control pain, serious abdominal disease should be suspected and prompt referral for surgical evaluation is indicated. Because the duration of effect from xylazine is shorter than that of detomidine, it is less likely to **mask signs of a strangulating obstruction** for an extended period of time. Xylazine and detomidine will cause bradycardia, transient vasoconstriction and increased urine production, and their use may adversely affect horses with hypovolemic shock. In addition, intestinal motility can be decreased, which may not be desirable in the treatment of impaction colic. Because of its longer duration of effect, **detomidine should not be used in cases that are surgical candidates**.

Butorphanol is a very effective analgesic with minimal side effects. It is a partial opioid agonist and antagonist that causes some reduction in intestinal motility, but has minimal cardiovascular effects except at higher doses. Although morphine is a potent analgesic, its use for treatment of colic remains limited because of its **excitatory effects** and tendency to reduce intestinal motility. Pentazocine and pethidine have less predictable analgesic effects than other opioids.

Common analgesics and their dosages are listed in Table 23.18. The degree of pain, specific diagnosis and the veterinarian's clinical experience will all determine the ideal analgesic drug regimen. Once the diagnosis of a surgical problem has been made, more potent analgesics can be used to control pain

Table 23.18 Analgesics for abdominal pain

Analgesic	Dosage	Effectiveness
Flunixin meglumine	0.25–1.1 mg/kg IV or IM	Excellent
Phenylbutazone	2.2–4.4 mg/kg IV	Fair
Dipyrone	10 mg/kg IV or IM	Fair
Xylazine	0.2–1.1 mg/kg IV or IM	Good
Detomidine	10–40 μg/kg IV	Excellent
Butorphanol	0.02–0.08 mg/kg IV	Good
Pentazocine	0.3–0.6 mg/kg IV	Fair
Pethidine	1.1–2.2 mg/kg IV or IM	Fair

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during the preoperative preparation, provided the patient has adequate cardiovascular status.

Fluid therapy

Severely dehydrated horses, especially those requiring surgical intervention, require **rapid volume replacement** with a **balanced polyionic IV solution**. It is not unusual for a colic case to require 40–60 L of IV fluid for preoperative stabilization. Even marginal dehydration and hypovolemia, in combination with the cardiovascular depressant effects of the anesthetic agents and endotoxemia, and compromised venous return due to abdominal distension, can severely complicate the anesthetic procedure and outcome. **Colloids**, particularly in the form of plasma products, have several advantages for use in colic patients. Synthetic colloids, such as hetastarch, are best administered postoperatively in surgical cases due to potential concerns over coagulation disorders.

Rapid fluid administration may be achieved after aseptic insertion of a size 9 French introducer catheter in the jugular vein (Deilets-Hoffman Introducer Set, Cook Critical Care, Bloomington, IN, USA). Four 5 L bags of commercially prepared sterile fluids can be administered at one time by gravity flow with a large bore coiled administration set and hanger system (Stat IV 1000 International WIN Inc., Kennett Square, PA, USA). In some cases of severe dehydration, hypertonic saline may be indicated.

If dehydration is not severe and gastrointestinal function is not impaired, oral fluids can be used for rehydration and continued maintenance therapy. Oral fluids are contraindicated in the presence of gastrointestinal reflux and small intestinal disease. **Enteral fluid therapy** is particularly effective in the treatment of large colon impactions (*q.v.*) due to its ability to **stimulate gastric motility** and to penetrate the impaction. Six to eight liters of fluid can be administered safely to an adult horse, 3–4 times daily or more often. Fluid composition varies and is dictated by the disease being treated and the clinician's personal preference. Water alone, or with an electrolyte solution, may be used. Some commercially available products contain glucose and/or glycine to promote sodium and water reabsorption.

Stimulation of motility

Increasing the water content of the ingesta often improves intestinal motility, decreases transit time and encourages resolution of the impaction. **Lubrication**

Table 23.19 Common cathartic drugs used for treatment of equine abdominal diseases

Name	Action
Bulk cathartics (fiber)	
Bran Psyllium Methylcellulose	Cause retention of water via hydrophilic action; increased bulk and water transit speeds
Saline cathartics	
Magnesium sulfate Sodium sulfate	Cause osmotic retention of intestinal water with possible stimulation of the small intestine and decreased transit time
Surfactants	
Dioctyl sodium sulfosuccinate Dioctyl calcium sulfosuccinate	Increase penetration of ingesta with water and cause reduction of net absorption of water
Emollient	
Mineral oil	Lubricates and softens ingesta

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of the tract eases transport. Table 23.19 lists **common cathartics and hydrophilic substances** and their mechanism of action.

Mineral oil has been used for years as an intestinal lubricant for impaction colic. Commonly, 2–4 L of mineral oil is administered to a 450 kg horse. If intestinal transit is normal, oil-covered feces should be passed within 12–24 h. Mineral oil is not good at penetration of firmly impacted material such as sand and can be passed around the impaction. Its use is contraindicated in horses with gastrointestinal reflux and those requiring abdominal surgery, especially if an enterotomy or anastomosis is anticipated, because the serosal surface of the intestine may become contaminated with oil.

Parasympathomimetics can be used judiciously to increase intestinal motility. **Neostigmine** (1–2 mg SC q 30–60 min to effect in an average sized horse) is an anticholinesterase that increases progressive motility of the large intestine with minimal effect on small intestinal activity. It has been helpful in treating large colon impactions (*q.v.*) that are soft and easily indented but are not moving. Stimulating motility with a firm impaction could initiate pain and predispose to bowel rupture, and should therefore be used with caution. Neostigmine is contraindicated in cases of strangulation, obstruction or large colon displacement (*q.v.*) and should be used only after aggressive oral and IV fluid therapy has proven unsuccessful. **Metoclopramide** has been shown in other species to coordinate gastric emptying and improve small intestinal activity. However, in the horse, the dose–response curve has been varied and extrapyramidal neurologic side effects have been observed. Its mechanism of action is not clear, but probably involves direct cholinergic stimulation and dopamine antagonism. **Erythromycin** has been used as a prokinetic drug in humans with reasonable success and has been used in horses with unresponsive ileus (*q.v.*).

Calcium may also help stimulate intestinal motility, especially if hypocalcemia is present. IV administration of 500 mL 23% calcium gluconate solution diluted to 5–10% is relatively safe, but it should be done slowly while monitoring heart rhythm and rate.

Nutrition

Horses with colic of undetermined origin should be held off feed until the primary problem is corrected. Horses with large colon or cecal impactions (*q.v.*) may be allowed oral fluids but should not be fed until the impaction is passed. Gastrointestinal reflux indicates small intestinal ileus (*q.v.*) and addition of food or water will only add to the gastric distension and discomfort. Postoperative nutritional management is dependent upon the primary problem, what was done to correct it, and gastrointestinal function.

Enteral support should be started as soon as gastrointestinal function resumes. **High quality**, **highly digestible feeds** should be fed in small quantities. Examples include complete pelleted feeds, fresh grass and alfalfa leaves. Hand-walking and grazing small amounts of grass is a safe way to begin. Small quantities of high quality alfalfa hay and bran mashes can be used as well. If function exists but the horse refuses to eat, enteral support can be achieved by administering a hyperalimentation diet via stomach tube.

Parenteral nutrition (total or partial) may be necessary in critically ill patients with prolonged gastrointestinal dysfunction, increased metabolic needs (e.g. sepsis, peritonitis, pleuritis) or those that are unable to eat or need to be force fed (oropharyngeal surgery, pharyngeal trauma).

Prognosis and referral

Horses with progressive, non-responsive abdominal pain, cardiovascular deterioration (dehydration, tachycardia, poor perfusion), distended small intestine or significant volumes of gastric reflux (*q.v.*) should be referred to a surgical facility for further evaluation. Because simple medical colics usually resolve in 2–4 h, referral should also be considered in patients whose pain persists beyond this time interval. The **travel time** to a referral center should also be considered.

Early surgical intervention in cases with strangulation obstruction improves prognosis. Overall, the current survival rate with surgery exceeds 50% and is highly variable with the underlying problem. Individuals with a systolic blood pressure <100 mmHg, weak pulses, heart rate >80 bpm, PCV >60% and evidence of a coagulopathy should be given a guarded to poor prognosis.

DESIGN OF AN INTENSIVE CARE UNIT

INTRODUCTION

The design of a large-animal ICU should not be left to hospital administrators, architects and engineers, but requires the input of all the veterinary medicine specialists who will be caring for critically ill patients in the unit. A **planning team** should be formed at the outset that includes administrators, veterinarians and architects who will be able to communicate easily and exchange information vital to basic design decisions. The veterinary members of the

planning team must educate the architects about necessary instrumentation and patient management practices that will affect unit design. The architect, in turn, will need to provide the ICU veterinarians with relevant information about building materials and architectural and engineering issues involved in ICU design and construction.

An essential part of the design process is planning for the future. The veterinarian members of the planning team must make intelligent predictions about the ways in which ICU medicine will change over the next decade, both in technology and in the kinds of conditions treated and their treatment. Trends in human medicine often are useful harbingers of new developments in veterinary medicine.

LOCATION

The placement of the ICU relative to other departments is a necessary consideration, except where existing space limitations have forced selection of a particular site. Traditionally, of course, the ICU is located near surgery and medicine services. Intensive care is being provided for diverse medical conditions, not just surgical sequelae, and there may be equally valid reasons for locating the ICU adjacent to the emergency room or near vital support services, particularly given the difficulties of transporting bulky equipment and/or immobilized or unconscious animals.

CAPACITY

The greatest difficulty in planning an ICU is in calculating the optimal capacity, given the fluctuations in ICU patient population. A unit that is always near capacity may be too small, or the criteria for admission may be too broad. However, a unit with overall low occupancy will have an unnecessarily high operating cost per animal.

The most important factors involved in determining the appropriate capacity for the unit are the admission and discharge criteria (in particular, the presence or absence of a step-down unit) and the total patient capacity of the hospital. A criterion suggested for human hospitals calculates the optimal ICU capacity as 15% of adult medical beds or 20% of adult surgical beds.

PHYSICAL DESIGN

After the location and capacity of the ICU have been decided, the planning team can move on to considering the physical design of the facility. The physical plan should balance considerations of convenience and efficiency of operation for the nursing staff with the goal of **minimizing stress** to the animals. Thus, noise and harsh lighting should be avoided, along with excessive traffic of attendants, trolleys and equipment.

The overall dimensions of the ICU can be calculated as a ratio of total unit square meterage (footage) per patient area. In human hospitals, this ratio ranges from approximately 137 to 182 m^2 (450–600 ft^2) per bed and has been increasing steadily as ICUs treat more gravely ill patients with a greater array of medical technology. In determining the total area for ICUs treating human

patients, this calculation is sometimes made by factoring the total bed space by 2.5–3.0.

The **stall dimensions** in the ICU should vary to accommodate the mix of cases that will be admitted to the unit. The standard 3 × 3 m (ca. 10 × 10 ft) or 3.0 × 3.6 m (ca. 10 × 12 ft) stall is acceptable for most patients; however, if the ICU is to be fully utilized, it should have flexibility in the design and stall configuration to allow for different size and species patients, plus monitoring equipment (Figure 23.1). Mare and foal pairs require larger stalls, as do larger breeds of horses.

The design and location of electrical and gas outlets in the stalls is another important consideration. Gas and electric outlets can be suspended from the ceiling on a recoil mechanical system, reducing problems of patient interference during delivery of care or, typically, these devices can be built into the head wall, with the essential concern being the simultaneous access to the patient and damage to the lines if they are on the stall floor. The overhead arrangement seems ideal. Whether the gas or electrical outlets are in the ceiling or in a wall chase, they should be of high quality materials, waterproof, and grounded, to reduce the hazard to the patient and withstand frequent cleaning. Generally, **oxygen** and **suction** are minimum requirements in each stall; the addition of compressed air is useful for the blending of gases in respiratory therapy. This combination of gases should meet all the needs in the ICU. Furthermore, oxygen delivery in each stall should be of sufficiently high flow rates to operate several ventilators simultaneously in the unit.

Facilities for **feeding** and **waste removal** are equally as important as the stall dimensions. The goals are to minimize traffic in the unit, ease cleaning and maintenance, improve labor efficiency and provide minimal risk to the critically ill patient within the unit. Several ideas that have proven useful in the Connelly Intensive Care Unit/Graham French Neonatal Section of New Bolton Center include manure removal using a chute for dumping and a holding

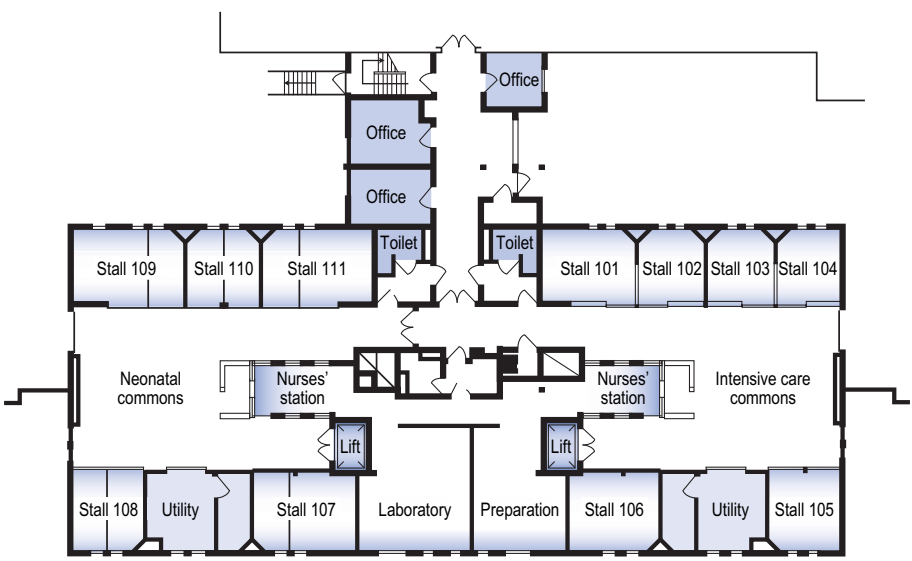

Figure 23.1 Main level plan of the intensive care/neonatal unit at New Bolton Center.

container on a lower level to minimize handling and rapid and easy disposal. This system limits the steps in handling equipment and the need for more than a single individual to work in the unit. The chute and utility room should be easily disinfected and maintained; this will limit nosocomial infections.

The **equipment needs** in the ICU will depend on the level of care provided for the critically ill patient. This may range from basic cardiovascular and respiratory monitoring to total parenteral nutrition and kidney dialysis. The equipment should be portable and permit upgrading to meet the changing technological developments and training of the ICU personnel. As a minimum, blood pressure monitors (direct and indirect), ECG, fluid infusion pumps and respiratory monitoring (expired gases, pulse oximetry) should be readily available. Other equipment considerations include portable radiographic and ultrasound units. The equipment should be stored in a clean, climate-controlled environment. This will prolong the life of equipment and minimize malfunction when used.

A central nursing station (see Figure 23.1) is an ideal arrangement for maintenance and storage of equipment, and ICU personnel use. The nursing station allows for centralizing supplies, pharmaceutical preparation and patient monitoring. Additionally, the nursing station serves as a staging area for equipment, a basic clinical laboratory and pharmaceutical preparation. The nursing station should be maintained as the cleanest part of the ICU. The design of the station should envision flexibility, labor efficiency, and ease of flow for people in the unit. A sterile hood in the nursing station is important in preparing hyperalimentation fluids and other admixtures.

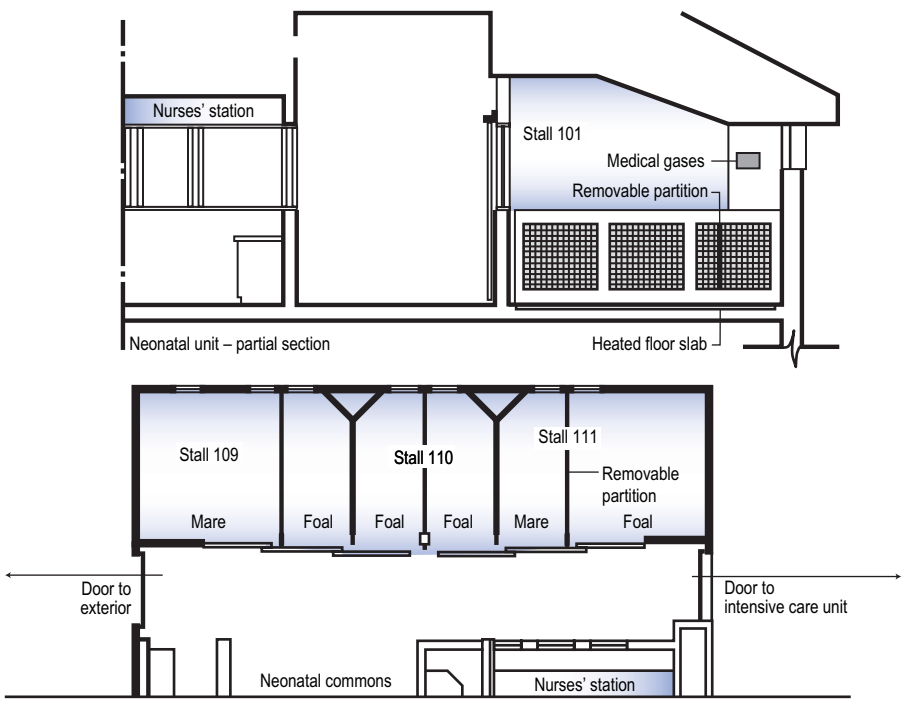

Figure 23.2 Partial plan of the neonatal unit at New Bolton Center.

Sinks used in the ICU should be strategically placed to stress cleanliness and encourage frequent hand washings. They should be designed to be operated with foot pedals or knee controls to minimize hand contact. Additional design considerations in the unit are concerned with the high risk of cross-infection in an open ICU, thus the justification for solid partitions. Studies on the relationship between ICU and nosocomial infections have been inconclusive to date. However, it seems prudent to physically separate the neonate from the adult patients, because of concerns with increased risk of septicemia in the younger animals. The mare/foal stalls should allow controlled separation of dam and neonate in such a way as to prevent the mare from interfering with care of the foal, while still allowing her to see, smell and touch the foal to foster normal bonding (Figure 23.2).

Rapid advances in veterinary medicine, combined with the limits imposed by budgetary constraints and available space in a given institution, will probably conspire to create a situation with some design limitations and some requirements that are not adequately foreseen or accommodated. Nonetheless, careful and creative planning will result in a well-designed facility that will respond well to the present and future developments in critical care medicine for large animals.

Abbreviations list

5-LO	5-lipoxygenase
α	alpha
AAEP	American Association of Equine Practitioners
ABC (of acute care)	*A*irway *B*leeding *C*ardiovascular
ACD	acid citrate dextrose solution
ACE	angiotensin-converting enzyme
ACP	acepromazine
ACTH	adrenocorticotropic hormone
ADF	acid detergent fiber
ADG	average daily gain
ADH	antidiuretic hormone
ADP	adenosine diphosphate
AELRU	Australian Equine Laminitis Research Unit
AF	amniotic fluid
AF	atrial fibrillation
AFP	alpha-fetoprotein
AFV	amniotic fluid volume
AHS	African horse sickness
AHSV	African horse sickness virus
AI	artificial insemination
AID	anemia of inflammatory disease
AIHA	autoimmune hemolytic anemia
ALP	alkaline phosphatase
AMP	adenosine monophosphate
ANS	autonomic nervous system
AP	antiplasmin
APC	activated protein C
APTT	activated partial thromboplastin time
ARF	acute renal failure
AST	aspartate aminotransferase
AT	antithrombin
ATN	acute tubular necrosis
ATP	adenosine triphosphate
AUC	area under the curve
AUIC	area under the inhibitory curve
AV	atrioventricular
AVP	arginine vasopressin
AVT	atrioventricular tachycardia
β	beta
BAL	bronchoalveolar lavage
BALF	bronchoalveolar lavage fluid
BBB	blood–brain barrier
BCG	bacillus Calmette–Guérin
β-END	β-endorphin
BEVA	British Equine Veterinary Association
b.i.d.	bis in die (twice a day)
BMC	bone mineral content
BMD	bone mineral density
BP	blood pressure
bpm	beats per minute
BPP	biophysical profile
BSP	sulfobromophthalein (clearance test)
BUN	blood urea nitrogen
BW	body weight
ca.	circa (about)
Ca	Calcium
CAH	chronic active hepatitis
CAT	computed axial tomography
CBC	complete blood count
CD	cluster of differentiation
CEM	contagious equine metritis
CF	complement fixation; crude fiber
CFT	complement fixation test
CFU	colony-forming units

CID	combined immune deficiency
CIN	chronic interstitial nephritis
CINOD	cyclooxygenase inhibiting nitric oxide donor
CK	creatinine kinase
Cl	chloride
Cl_B	systemic clearance
CLIP	corticotropin-like intermediate lobe peptide
cm	centimeter(s)
C_{max}	peak plasma concentration
CN	cranial nerve
CNA	colistin–nalidixic acid
CNS	central nervous system
CO	cardiac output
CO_2	carbon dioxide
COP	colloid osmotic pressure
COPD	chronic obstructive pulmonary disease
COX	cyclo-oxygenase
CP	creatine phosphate
CP	crude protein
CPAP	continuous positive airway pressure
CPE	cytopathic effect
CPK	creatine phosphokinase
CPR	cardiopulmonary resuscitation
CRF	chronic renal failure
CRI	constant rate infusion
CRT	capillary refill time
CS	condition score
CSF	cerebrospinal fluid
CT	computed tomography
CTL	cytotoxic T cells
CVID	common variable immunodeficiency
CVM	cervical vertebral malformation
CVP	central venous pressure
CVS	cardiovascular system
δ	delta
Da	Dalton(s)
DCAB	dietary cation–anion balance
DCP	digestible crude protein
DDAVP	1-deamino-8-D-arginine-vasopressin
DDFT	deep digital flexor tendon
DE	digestible energy
Defra	Department of Environment, Food and Rural Affairs
DFA	Directigen Flu A (test)
DHA	dihydroepiandrosterone
DI	diabetes insipidus
DIC	disseminated intravascular coagulation
DIP	distal interphalangeal (joint)
DJD	degenerative joint disease
dL	deciliter(s)
DLE	discoid lupus erythematosus
DM	dry matter
DMSO	dimethyl sulfoxide
DNA-PK	DNA-dependent protein kinase
DOD	developmental orthopedic disease
DST	dexamethasone suppression test
DYP	dyschondroplasia
EAV	equine arteritis virus
ECD	equine Cushing's disease
ECF	extracellular fluid
eCG	equine chorionic gonadotropin
ECG	electrocardiogram/electrocardiography
EDDI	ethylenediamine dihydroiodide
EDM	equine degenerative myeloencephalopathy
EDSS	Equine Digital Support System
EDTA	ethylenediaminetetraacetic acid
EE	Eastern encephalitis
EEDS	eosinophilic exfoliative dermatitis and stomatitis
EEV	eastern encephalitis virus; equine encephalosis virus
EFD	early fetal death
EFP	equine fetal protein
EHSLC	European Horserace Scientific Liaison Committee
EHV	equine herpesvirus
EIA	equine infectious anemia
EIPH	exercise-induced pulmonary hemorrhage
ELISA	enzyme-linked immunosorbent assay
EMG	electromyography
EMND	equine motor neuron disease
EPC	effective plasma concentration
EPF	early pregnancy failure
EPG	eggs per gram
EPH	equine purpura hemorrhagica
EPM	equine protozoal myeloencephalitis
EPSM	equine polysaccharide storage myopathy
ERAV	equine rhinitis A virus
ERBV	equine rhinitis B virus
ERDC	equine respiratory disease complex
ERS	equine rhabdomyolysis syndrome

ESKD	end-stage kidney disease
EU	European Union
EVA	equine viral arteritis
F	systemic availability of a drug
FAB	French–American–British (classification of non-lymphoid leukemias)
FAD	flavin adenine dinucleotide
FAST	fluorescent allergosorbent test
FAT	fluorescent antibody test(ing)
FDA	Food and Drug Administration
FDP	fibrinogen degradation products
FEE	fractional electrolyte excretion
FFA	free fatty acids
FE	fractional excretion (of electrolyte)
FEI	Fédération Equestre Internationale
fL	femtoliter(s)
FMDV	foot-and-mouth disease virus
FPT	failure of passive transfer
FSH	follicle-stimulating hormone
ft	foot/feet
γ	gamma
g	gram(s)
G	gauge
GABA	γ-aminobutyric acid
GAD	glutamic acid decarboxylase
GC	gas chromatography
GC-MS	gas chromatography-mass spectrometry
GFR	glomerular filtration rate
GGD	generalized granulomatous disease
GGT	gamma glutamyltransferase
GH	growth hormone
GIT	gastrointestinal tract
GKX	guaifenesin-ketamine-xylazine combination
GM-CSF	granulocyte—monocyte colony-stimulating factor
GOT	glutamic oxalacetic transaminase
GnRH	gonadotropin-releasing hormone
GPT	glutamic pyruvate transaminase
GSH-px	glutathione peroxidase
GUS	gastric ulcer syndrome
Gy	gray (unit of absorbed dose of radiation)
h	hour(s)
H	hemagglutinin
ha	hectare
HA	hyaluronic acid
HBHA	Heinz body hemolytic anemia
HBLB	Horserace Betting Levy Board
hCG	human chorionic gonadotropin
HCO_3	bicarbonate
HDCV	human diploid cell vaccine
HETE	monohydroxyeicosatetraenoic acid
Hg	mercury
HI	hemagglutination inhibition (test)
HIE	hypoxic–ischemic encephalopathy
HMWK	high molecular weight kininogen
HPA	hypothalamus–pituitary–adrenal
HPLC	high performance liquid chromatography
HR	heart rate
HR_{max}	maximum heart rate
HV	Hendra virus
HYPP	hyperkalemic periodic paralysis
Hz	Hertz
IA	intra-articular(ly)
IAD	inflammatory airway disease
ICF	intracellular fluid
ICU	intensive care unit
IFAT	indirect fluorescent antibody test
IFN	interferon
Ig	immunoglobulin
IH	inhibiting hormone
IL	interleukin
IM	intramuscular(ly)
in	inch(es)
iNOS	inducible nitric oxide synthase
IOP	intraocular pressure
IPC	irrelevant plasma concentration
IPPV	intermittent positive pressure ventilation
ISCOMs	immune stimulating complexes
IT	intratracheal(ly)
ITP	idiopathic thrombocytopenia
IU	international unit
IU	intrauterine
IUC	irrelevant urinary concentration
IUGR	intrauterine growth retardation
IV	intravenous(ly)
J	joule(s)
JE	Japanese encephalitis
JEV	Japanese encephalitis virus
JFA	jaundiced foal agglutination (test)
κ	kappa
K	potassium
kcal	kilocalorie

KCl	potassium chloride
KCS	keratoconjunctivitis sicca
kDa	kilodalton(s)
keV	kilo electric volt
kg	kilogram(s)
kJ	kilojoule(s)
km	kilometer(s)
λ	lambda
L	liter(s)
LAK	lymphokine-activated killer (cell)
LC	larval cyathostominosis
LC–MS	liquid chromatography-mass spectrometry
LD_{50}	lethal dose that kills 50% of a test population
LDH	lactic dehydrogenase
LEM	leukoencephalomalacia
LH	luteinizing hormone
LMWH	low molecular weight heparin
LPS	lipopolysaccharide
LRS	lactated Ringer's solution
LRT	lower respiratory tract
LT	leukotriene
μ	mu
μg	microgram(s)
μL	microliter(s)
μm	micron(s)
m	meter(s)
MAD	modified acid fiber detergent
MAFF	Ministry of Agriculture, Fisheries and Food
MBq	megabecquerel(s)
MC3	third metacarpus
MCH	mean corpuscular hemoglobin
MCHC	mean corpuscular hemoglobin concentration
ME	metabolizable energy
mEq	milliequivalent(s)
min	minute(s)
mg	milligram(s)
MgO	magnesium oxide
MHC	major histocompatibility complex
MHz	megahertz
MJ	megajoule(s)
MLV	modified live vaccine
MAD	modified acid detergent
MDI	metered dose inhaler
MES	minimum effective strain
MIC	minimum inhibitory concentration
mL	milliliter(s)
mm	millimeter(s)
mmHg	millimetres of mercury
mmol	millimole(s)
MMP	matrix metalloproteinase
mo	month(s)
MPa	megapascal(s)
MPK	multiple punctate keratotomies
MPS	mononuclear phagocyte system
MRI	magnetic resonance imaging
MRLS	mare reproductive loss syndrome
MRSA	methicillin-resistant *Staphylococcus aureus*
MSH	melanocyte-stimulating hormone
MT3	third metatarsus
MW	molecular weight
N	neuramidase
N_2	nitrogen
Na	sodium
NAD	nicotinamide adenine dinucleotide
NADH	reduced NAD
NAIT	neonatal alloimmune thrombocytopenia
NB	nota bene (note well)
NaCl	sodium chloride
$NaHCO_3$	sodium bicarbonate
NDF	neutral detergent fiber
NE	net energy
NEC	necrotizing enterocolitis
NEFA	non-esterified fatty acids
NfE	nitrogen free extract
ng	nanogram(s)
NGT	nasogastric tube
NH_3	ammonia
NI	neonatal isoerythrolysis
NMDA	N-methyl-D-aspartate
NMS	neonatal maladjustment syndrome
NO	nitric oxide
NOS	nitric oxide synthase
NRC	National Research Council
ns	nanosecond
NSAID	non-steroidal anti-inflammatory drug
NSP	non-starch polysaccharide
NST	non-stress test
NV	Nipah virus
O_2	oxygen
OA	osteoarthritis
OBLA	onset of blood lactate accumulation

OC	organochloride; osteochondrosis
OCD	osteochondritis dissecans
OIE	Office International des Épizooties
OLWFS	Overo lethal white foal syndrome
OP	organophosphate
P	probability
Pa	pascal(s)
PAF	platelet-activating factor
PAGE	polyacrylamide gel electrophoresis
PAI	plasminogen activator inhibitor
PAS	periodic acid–Schiff (stain)
$PaCO_2$	partial pressure of arterial carbon dioxide
PaO_2	partial pressure of arterial oxygen
PCA	procoagulant activity
PCO_2	carbon dioxide tension
PCR	polymerase chain reaction
PCV	packed cell volume
PDA	patent ductus arteriosus
PDGF	platelet-derived growth factor
PEEP	positive end expiratory pressure
pg	picogram(s)
PG	prostaglandin
PGE	prostaglandin E
$PGF_{2\alpha}$	prostaglandin $F_{2\alpha}$
PGFM	13,14-dihydro-15-keto-prostaglandin-$F_{2\alpha}$
PGI_2	prostacyclin
PHF	Potomac horse fever
PHMB	polyhexamethylene biguanide
P_i	inorganic phosphate
PK–PD	pharmacokinetic—pharmacodynamic (modelling)
PL	phospholipid
PLGE	protein-losing gastroenteropathy
PLR	pupillary light reflex
PMMA	polymethyl methacrylate
PMSG	pregnant mare serum gonadotropin (eCG)
PN	parenteral nutrition
PO	per os (orally)
POMC	pro-opiomelanocortin
ppb	parts per billion
ppm	parts per million
PPM	persistent pupillary membranes
PPSC	pluripotent stem cells
PPV	positive pressure ventilation
PSGAG	polysulfated glycosaminoglycan
PSSM	polysaccharide storage myopathy
PT	prothrombin time
PTH	parathyroid hormone
PU/PD	polyuria–polydipsia
q	quaque (every)
q.i.d.	quater in die (4 times a day)
QUS	quantitative ultrasound
qs ad	quantum sufficiat ad (a sufficient quantity of)
q.v.	quod vide ("which see") – see elsewhere in this book for further information
rad	radiation absorbed dose
RAO	recurrent airway obstruction
RAST	radioactive allergosorbent test
RBC	red blood cell
RBF	renal blood flow
RCV	red cell volume
REM	rapid eye movement (sleep)
RER	recurrent exertional rhabdomyolysis
RH	releasing hormone
RID	radioimmunodiffusion (test)
RIG	rabies immune globulin
ROS	reactive oxygen species
RPE	retinal pigment epithelium
RQ	respiratory quotient
RS	respiratory secretions
RT–PCR	reverse transcriptase-polymerase chain reaction
RVV	recombinant vector vaccine
s	second(s)
SBC	subchondral cystic lesions
SC	subcutaneous(ly)
SCC	squamous cell carcinoma
SCID	severe combined immunodeficiency
S_{cr}	serum creatinine
SD	standard deviation
SDFT	superficial digital flexor tendon
SDH	sorbitol dehydrogenase
SE	standard error (of the mean)
SG	specific gravity
SGA	small for gestational age
SGOT	serum glutamic oxalacetic transaminase
SGPT	serum glutamic pyruvate transaminase
s.i.d.	semel in die (once a day)
SID	strong ion difference
SIMV	synchronized intermittent mandatory ventilation

SIRS	systemic inflammatory response syndrome
SLE	systemic lupus erythematosus
S_k	serum potassium
SN	serum neutralizing
SNT	serum neutralization test
SPA	staphylococcal protein A
SPAOPD	summer pasture associated obstructive pulmonary disease
SPF	specific-pathogen free
spp.	species
SRH	single radial hemolysis
STDV	standard deviation of data (over time range)
SVPD	supraventricular premature depolarization
SVT	supraventricular tachycardia
T_3	tri-iodothyronine
T_4	thyroxine
$t_{1/2}$	half-life
TB	Thoroughbred
Tc	technetium
TCA	tricarboxylic acid
TCO_2	total carbon dioxide (concentration)
TF	tissue factor
TGF	tissue growth factor
t.i.d.	ter in die (3 times a day)
TIMPS	tissue inhibitors of matrix metalloproteinases
TIVA	total intravenous anesthesia
TLC	thin layer chromatography
TMP/S	trimethoprim and sulfonamide
TNF	tumor necrosis factor
TP	total protein
TPP	total plasma protein
tPA	tissue plasminogen activator
TRH	thyrotropin-releasing hormone
TSH	thyroid-stimulating hormone
TT	thrombin time
TTA	transtracheal aspiration
TX	thromboxane
U	unit(s)
U_{cr}, uCr	urine creatinine
UFH	unfractionated heparin
U_K	urine potassium
UK	United Kingdom
URT	upper respiratory tract
US	ultrasound
USA	United States of America
USDA	United States Department of Agriculture
UTI	urinary tract infection
UV	ultraviolet
V_{200}	treadmill velocity that results in a heart rate of 200 bpm
V_d	volume of distribution
VE	Venezuelan encephalitis
VEV	Venezuelan encephalitis virus
VFA	volatile fatty acids
***V*La4**	see OBLA
VLDL	very low density lipoprotein
VN	virus neutralization
***V*O_2max**	the maximal rate of oxygen consumption
VPC	ventricular premature contractions
VPD	ventricular premature depolarization
VS	vesicular stomatitis
VSD	ventricular septal defect
VSV	vesicular stomatitis virus
VT	ventricular tachycardia
vWF	von Willebrand factor
WBC	white blood cell
WE	Western encephalitis
WEV	Western encephalitis virus
wk	week(s)
WNV	West Nile virus (*q.v.*)
XLA	X-linked agammaglobulinemia
yr	year(s)

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