Equine Ophthalmology

2ND EDITION

Brian C. Gilger, DVM, MS, DACVO
Professor of Ophthalmology
Department of Clinical Sciences
North Carolina State University
Raleigh, North Carolina

with 963 illustrations

ELSEVIER
SAUNDERS

ELSEVIER
SAUNDERS

3251 Riverport Lane
Maryland Heights, Missouri 63043

Equine Ophthalmology ISBN: 978-1-4377-0846-2

Library of Congress Cataloging-in-Publication Data

Gilger, Brian C.
Equine ophthalmology / Brian C. Gilger. – 2nd ed.
p. ; cm.
Includes bibliographical references and index.
ISBN 978-1-4377-0846-2 (hardcover : alk. paper) 1. Equine ophthalmology. I. Title.
[DNLM: 1. Eye Diseases–veterinary. 2. Horse Diseases. 3. Diagnostic Techniques, Ophthalmological–veterinary. SF 959.E93 G473e 2011]
SF959.E93G55 2011
636.089′77–dc22

2010015057

Vice President and Publisher: Linda Duncan
Acquisitions Editor: Penny Rudolph
Associate Developmental Editor: Lauren Harms
Publishing Services Manager: Catherine Jackson
Senior Project Manager: Rachel E. McMullen
Design Direction: Charlie Seibel

Printed in China
Last digit is the print number: 9 8 7 6 5 4 3 2 1

To my wife, Elizabeth, and daughter, Katherine—you are the light of *my* eyes

Contributors

Dennis E. Brooks, DVM, PhD, DACVO
Professor, Ophthalmology
College of Veterinary Medicine
Gainesville, Florida
Chapter 9: Glaucoma

Alison B. Clode, DVM, DACVO
Assistant Professor of Veterinary Ophthalmology
Department of Clinical Sciences
College of Veterinary Medicine
North Carolina State University
Raleigh, North Carolina
Chapter 5: Diseases and Surgery of the Cornea

Carmen M. H. Colitz, DVM, PhD, DACVO
Adjunct Associate Professor
College of Veterinary Medicine
North Carolina State University
Raleigh, North Carolina;
Adjunct Associate Professor
College of Veterinary Medicine
The Ohio State University
Columbus, Ohio;
Aquatic Animal Eye Care
Jupiter, Florida
Chapter 7: Diseases and Surgery of the Lens

Jennifer L. Davis, DVM, PhD, DACVIM, DACVCP
Assistant Professor of Equine Medicine
Department of Clinical Sciences
College of Veterinary Medicine
North Carolina State University
Raleigh, North Carolina
Chapter 13: Ocular Manifestations of Systemic Disease

Cornelia Deeg, DVM
Department of Veterinary Sciences
Ludwig-Maximilians-University
Institute for Animal Physiology
München, Germany
Chapter 8: Equine Recurrent Uveitis

Ann E. Dwyer, DVM
Genesee Valley Equine Clinic, PLLC
Scottsville, New York
Chapter 2: Practical General Field Ophthalmology
Chapter 14: Practical Management of Blind Horses

Susan Ewart, DVM, PhD, DACVIM
Department of Large Animal Clinical Sciences
Associate Dean for Research and Graduate Studies
College of Veterinary Medicine
Michigan State University
East Lansing, Michigan
Chapter 12: Inherited Ocular Disorders

Brian C. Gilger, DVM, MS, DACVO
Professor of Ophthalmology
Department of Clinical Sciences
North Carolina State University
Raleigh, North Carolina
Chapter 1: Equine Ocular Examination: Routine and Advanced Diagnostic Techniques
Chapter 3: Diseases and Surgery of the Globe and Orbit
Chapter 8: Equine Recurrent Uveitis

Elizabeth A. Giuliano, DVM, MS, DACVO
Associate Professor
Department of Veterinary Medicine and Surgery
College of Veterinary Medicine
University of Missouri
Columbia, Missouri
Chapter 4: Equine Ocular Adnexal and Nasolacrimal Disease

Steven R. Hollingsworth, DVM, DACVO
Associate Professor of Clinical Veterinary Ophthalmology
Department of Surgical and Radiological Sciences
School of Veterinary Medicine
University of California
Davis, California
Chapter 6: Diseases of the Uvea

Andy Matthews, BVMcS, PhD, DECEIM, FRCVS
McKenzie, Bryson and Marshall Veterinary Surgeons
Kilmarnock
Ayrshire, United Kingdom
Chapter 5: Diseases and Surgery of the Cornea

Richard J. McMullen, Jr., Dr. Med. Vet.
Assistant Professor of Veterinary Ophthalmology
Department of Clinical Sciences
College of Veterinary Medicine
North Carolina State University
Raleigh, North Carolina
Chapter 7: Diseases and Surgery of the Lens

Paul E. Miller, DVM, DACVO
Clinical Professor of Comparative Ophthalmology
Department of Surgical Sciences
School of Veterinary Medicine
University of Wisconsin-Madison
Madison, Wisconsin
Chapter 11: Equine Vision

Christopher J. Murphy, DVM, PhD, DACVO
Professor of Comparative Ophthalmology
Department of Ophthalmology and Vision Sciences
School of Medicine
Department of Veterinary Surgical and Radiological Sciences
School of Veterinary Medicine
University of California, Davis
Davis, California
Chapter 11: Equine Vision

Simon M. Petersen-Jones, DVetMed, PhD, DVOphthal, DECVO
Professor
Small Animal Clinical Sciences
College of Veterinary Medicine
Michigan State University
East Lansing, Michigan
Chapter 12: Inherited Ocular Disorders

Bernhard Spiess, Dr. Med. Vet, DACVO/ECVO
Associate Professor
Vetsuisse Faculty
Equine Department
Section of Ophthalmology
University of Zurich
Zurich, Switzerland
Chapter 8: Equine Recurrent Uveitis

Riccardo Stoppini, DVM
Equine Ophthalmology Practitioner
Brescia, Italy
Chapter 1: Equine Ocular Examination: Routine and Advanced Diagnostic Techniques

Mary E. Utter, DVM, PhD, DACVO
Assistant Professor of Ophthalmology
New Bolton Center
School of Veterinary Medicine
University of Pennsylvania
Kennett Square, Pennsylvania
Chapter 9: Glaucoma

David A. Wilkie, DVM, MS, DACVO
Professor
Veterinary Clinical Sciences
The Ohio State University
Columbus, Ohio
Chapter 10: Diseases of the Ocular Posterior Segment

Preface

It has been just over 5 years since the publication of the first edition of *Equine Ophthalmology*. In the preface to the first edition, I challenged equine clinicians, ophthalmologists, and researchers to further the science of equine ophthalmology. I encouraged organizations and researchers to fund and perform studies on equine ocular disease and for clinicians to report on their findings on clinical cases so that the use of evidence-based medicine to direct care of equine ocular disorders could be more comprehensively achieved.

This challenge has been partially met. In some areas, research was performed and reported that allowed equine clinicians to use this information for their patients. Some excellent examples include the development of the equine intraocular lens, studies of the inheritance of congenital stationary night blindness, work on the pathogenesis of equine recurrent uveitis, and clinical studies on the treatment of fungal keratitis. However, much work remains to be done, including study of the genetic basis of nearly all ocular disease in horses, pathogenesis and treatment of equine glaucoma, and practical therapy for infectious keratitis and equine recurrent uveitis.

In the past several years, veterinary ophthalmologists, equine general practitioners, and organizations such as the American Association of Equine Practitioners (AAEP) have recognized the importance of equine ophthalmology. This is demonstrated by the large number of equine ophthalmology abstracts at scientific meetings, special issues on equine ophthalmology in *Veterinary Ophthalmology* and the *Equine Veterinary Journal*, and recent equine ophthalmology symposia sponsored by the AAEP and The Havemeyer Foundation.

As our knowledge of equine ophthalmology grows and specific techniques, diagnostic and therapeutic, are developed knowledge and experience of general veterinary ophthalmology will soon not be sufficient to manage equine ophthalmology cases. Dedicated education and training on equine ophthalmology is needed. Furthermore, most equine ophthalmologists do not have the resources to perform basic or clinical research. Because of these challenges, the International Equine Ophthalmology Consortium (IEOC) was formed in 2007 with the core missions:

1. To promote the sharing of knowledge through organization of international symposia on equine ophthalmology
2. To promote development of multicenter clinical trials
3. To organize and share resources to perform multi-center collaborative research projects (see www.equineophtho.com).

The IEOC has held two symposia (April 2009 and June 2010) and one mini-symposium at the ACVO meeting (November 2009). The third IEOC annual symposium is scheduled for April 2011. With increased education, research organization, and an international coordination of effort, the IEOC has and will continue to enhance the science and education of equine ophthalmology.

I hope that this second edition of *Equine Ophthalmology* will be used as an educational tool to enhance clinical abilities, and as a basis for scientific research. There are approximately 50% more color clinical photographs, and all drawings have been recreated and colorized. The textbook has been reorganized to allow all veterinarians to improve their care of equine patients. The chapter on ocular examination was written with additional illustrations to make it useful for clinicians of all skill levels. The new second chapter, authored by Dr. Ann Dwyer, is a practical guide for the diagnosis and management of ocular disorders by veterinarians treating horses in the field. Other chapters, for example Chapter 12 on inherited ocular disorders, Chapter 7 on diseases and surgery of the lens, and Chapter 5 on corneal disease, help to "push the envelope" regarding the emerging research on these specific areas of equine ocular disease.

I encourage all of you who are interested in equine ophthalmology to understand the importance of reporting your clinical or research findings. From case reports, retrospective, prospective, and laboratory research—do it, present it, write it, and publish it. I know that we are all busy and the collection of data, the analysis, and writing of a study is time-consuming, but it is the only way that we are going to improve the science of equine ophthalmology. Use this book as your base—a springboard to discover the truths of equine ocular disease.

Brian Gilger
January 2010

Acknowledgments

This book could not be possible without the sacrifice and hard work of all the authors, who took time away from their families and professions to contribute. I sincerely thank you. I also thank Penny Rudolph, Jolynn Gower, and Lauren Harms at Elsevier for their talent, hard work, and belief in this second edition.

In addition, I thank my clinical ophthalmology technician team, Damian Launer, Erin Matheson, and Sandy Machon for everything you have done to make this textbook possible. You are the best!

I thank my good friends Drs. David Wilkie, Dennis Brooks, Riccardo Stoppini, Claire Latimer, and Andy Matthews for their advice, images, and contributions to this textbook. I thank my colleagues at North Carolina State University, Drs. Alison Clode and Richard McMullen, for their enthusiasm and support of this project—I could not ask for two better people to work with. I also thank my wonderful residents through the years—you have really made me look good.

I also thank Beth Salmon, not only for all of the extensive behind the scenes work in the research laboratory (for without you nothing would get done), but more importantly, I thank you for your friendship and for taking care of everything when I am gone.

I thank my many patients who have taught me so much—I promise that I will always continue to learn.

Finally, I thank my best friend, my wife Elizabeth, for her remarkable ability to put life into perspective and to remind me what is important. I appreciate her unrelenting support of this textbook and thank her for her unwavering belief in me. Without her I could not function. I also thank my daughter Katherine, whose beautiful music was heard while I wrote this book, and if you listen carefully, it can be heard when you read these pages. I also thank my dogs Luke, Riley, and Muffy who are always at my side. They do not care about late submissions or missed deadlines, just if I am scratching their head.

Chapter 1

Equine Ocular Examination: Routine and Advanced Diagnostic Techniques

Brian C. Gilger
Riccardo Stoppini

The basic and essential aspect of equine ophthalmology is a complete, thorough ocular examination. In this chapter, ophthalmic examination of the horse will be discussed, with emphasis on techniques, tools and instruments, and other diagnostic modalities. Understanding normal equine ocular anatomy is integral to interpreting the ocular examination. Anatomy of the equine eye (Fig. 1-1) is described in detail in subsequent chapters and will not be repeated here, although cross-references to relevant sections in the book will augment our discussion. Excellent reviews of equine eye and head anatomy can also be found in other sources.[1-6]

Both routine and advanced ophthalmic diagnostic techniques are described. Examination of the equine eye includes obtaining the history and signalment, inspecting the patient in a well-lit environment, examining the ocular structures in a darkened environment, facilitating the examination with restraint, sedation, and local nerve blocks, and collecting relevant diagnostic samples or data.[4,7-10] Indications and technique for advanced diagnostics—ultrasound, electroretinography, computed tomography, and magnetic resonance imaging—will also be discussed in this chapter.

MEDICAL HISTORY

A thorough medical history relevant to the ocular examination should include how the animal is used (e.g., pet or performance) and its living environment. Additional information that should be collected includes any history of travel, vaccination history, deworming schedule, and presence of concurrent or previous medical problems such as nasal discharge, presence of stridor, previous trauma to the head, and status of other horses on the premises with similar signs. Characterization of the primary complaint should include the onset and initial clinical signs, treatment given and response to that treatment, progression and duration of the ocular problem, and current

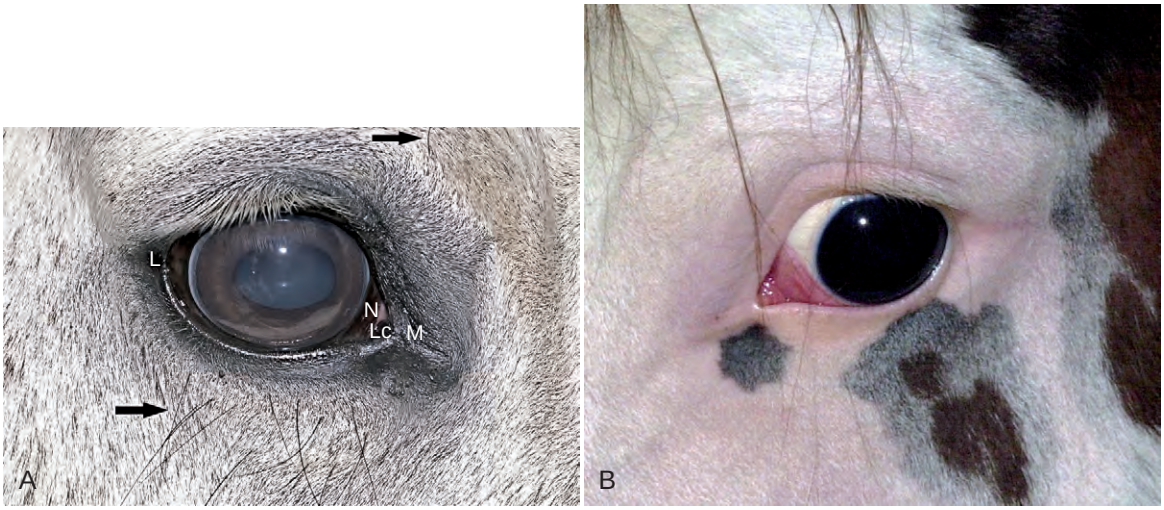


Figure 1-1. **A,** Normal external appearance of the equine eye. The horse's palpebral fissure, cornea, and pupil are oval horizontally. The lateral canthus (L) is more rounded than the medial canthus (M). There are prominent folds in the upper and lower eyelids. Numerous eyelashes are present along the lateral two-thirds of the upper eyelid, and vibrissae are located dorsonasal to the upper lid and ventral to the lower lid *(arrows)*. The leading edge of the third eyelid is usually partially pigmented (N). The lacrimal caruncle (Lc) is prominent. **B,** Normal external appearance of the equine eye when eyelid pigment is absent. Note the lack of pigment on the third eyelid, conjunctiva, and sclera as well.

Box 1-1 | **Equipment and Supplies for General Equine Ophthalmic Examination**

Routine Equipment and Supplies

- Bright focal light source: Finnoff halogen transilluminator
- Direct ophthalmoscope, PanOptic ophthalmoscope, or indirect ophthalmoscope with 20-diopter lens
- Sterile fluorescein dye strips
- Schirmer tear test
- Sterile culture swabs for cytology and culture
- Kimura platinum spatula, #10 to #15 sterile surgical blade (cytology)
- Glass slides (cytology)
- Sterile eyewash
- Ophthalmic lubricant, artificial tears ointment
- Proparacaine hydrochloride (HCl) 0.5% (Alcaine)—topical anesthetic
- Tropicamide HCl 1% (Mydriacyl)—short-acting dilating agent
- Detomidine HCl or xylazine—sedation
- Mepivacaine HCl (Carbocaine) or lidocaine HCl—local nerve blocks
- Graefe fixation forceps (to manipulate conjunctiva and third eyelid)
- Digital tonometer (TonoPen or TonoVet tonometer)
- Open-ended tomcat urinary catheter for nasolacrimal irrigation
- 1-mL and 3-mL syringes, 18- and 25-gauge needles
- 12-mL syringes for nasolacrimal irrigation

Advanced Equipment and Supplies

- All supplies and instruments for routine examination
- Handheld slit-lamp biomicroscope
- Binocular indirect ophthalmoscope and 15-, 20-, and 30-diopter lenses
- Ultrasound (7.5-, 10-, and 20-MHz probe)
- Sterile methocellulose gel for ultrasound
- Electroretinogram
- 3½-inch, 19-gauge spinal needle for retrobulbar block
- 27-gauge needle for aqueocentesis
- Digital camera (color and infrared)
- Advanced imaging: radiography, computed tomography, magnetic resonance imaging

therapy. Signalment can provide an important clue as to the cause of many ophthalmic conditions (e.g., congenital stationary night blindness in the Appaloosa, hereditary cataracts in the Morgan horse). Existing medical therapy can also greatly influence findings on ophthalmic examination. For example, a finding of mydriasis on the ophthalmic examination could be caused by use of topical atropine, which may result in mydriasis for up to 14 days in horses.[11] Depending on the specific complaint, further information may be required, such as a thorough description of vision loss (e.g., light versus dark, moving objections, one eye or both, etc.).

ROUTINE AND ADVANCED EQUIPMENT REQUIRED FOR THE OPHTHALMIC EXAMINATION

Prior to any examination, the proper equipment to perform the examination is needed. Although there are some differences in opinion and personal preferences among equine ophthalmologists, Box 1-1 lists the routine and advanced equipment a clinician should have available for the ophthalmic examination. Routine materials for the examination are shown in Figures 1-2 and 1-3. Indications and methods of use will be described in later sections of this chapter.

Figure 1-2. Materials and supplies for a routine ophthalmic examination in the horse. **A,** 18-Gauge, 1½-inch needle, 25-gauge, 1-inch needle, 1 mL and 3 mL syringes. **B,** Tranquilizer (detomidine). **C,** 2% Lidocaine HCl. **D,** Schirmer tear test strips. **E,** Fluorescein dye strips. **F,** 1% Tropicamide HCl. **G,** Sterile eyewash. **H,** Direct ophthalmoscope. **I,** Finnoff transilluminator. **J,** Indirect ophthalmoscopy lens (20 Diopter). **K,** Panoptic ophthalmoscope.

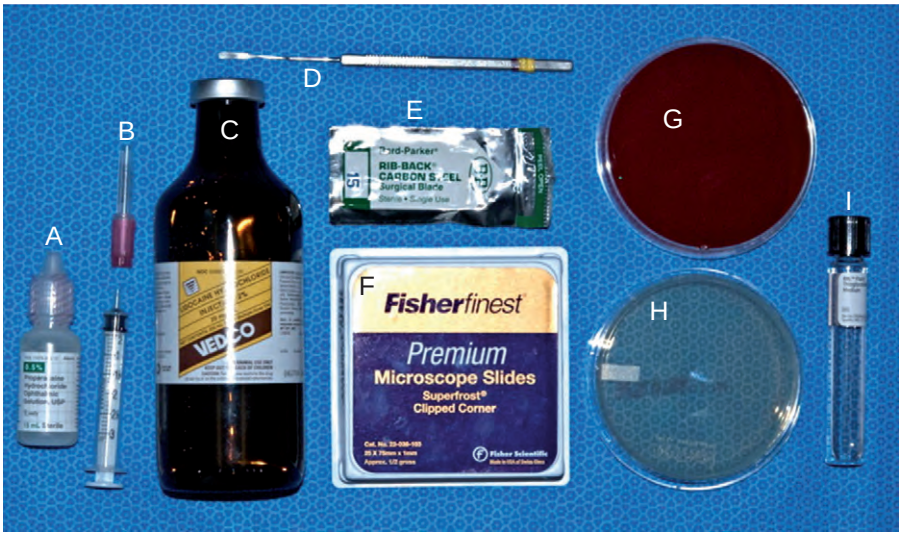


Figure 1-3. Materials for collection of corneal culture and cytology. **A,** 0.5% Proparacaine HCl. **B,** 25-Gauge, 1-inch needle and 3 mL syringe. **C,** 2% Lidocaine HCl. **D,** Kimura platinum spatula. **E,** #15 surgical blade. **F,** Microscope slides. **G,** Blood agar culture plate. **H,** Sabouraud agar culture plate. **I,** Thioglycolade culture broth.

OVERVIEW AND METHODS OF THE EQUINE OCULAR EXAMINATION

The ocular examination in the horse, like any physical examination, should be performed in a systematic manner. The general order of steps to be taken in the examination is listed in Box 1-2. The initial examination of the equine eye should occur prior to sedation and should take place in a well-lit area. The examination area should be quiet, away from distractions, and if possible away from other horses. The menace response and other subjective vision testing (e.g., maze testing) and evaluation of the pupillary light reflex (PLR) should be performed before sedation. For accurate evaluation of PLRs, a bright focal light source and a darkened examination area are often required. To adequately examine the cornea and internal structures of the eye, the horse must be examined in a darkened stall or in stocks in a room where the lights can be dimmed. Ideally, stocks are preferred because they will better protect the examiner from accidental (or purposeful!) movements of the horse, which can be exaggerated and unpredictable when the horse is tranquilized.

A thorough ocular examination usually requires appropriate restraint, tranquilization, regional nerve blocks, and topical anesthesia. Methods of restraint required to examine the ocular structures of the horse range from a halter and lead rope to mechanical restraint in stocks with use of a lip twitch. Use of restraint is dependent on temperament of the horse and experience of the handlers and examiner. Use of a tranquilizer is generally recommended, and frequently needed, to facilitate the routine ophthalmic examination.

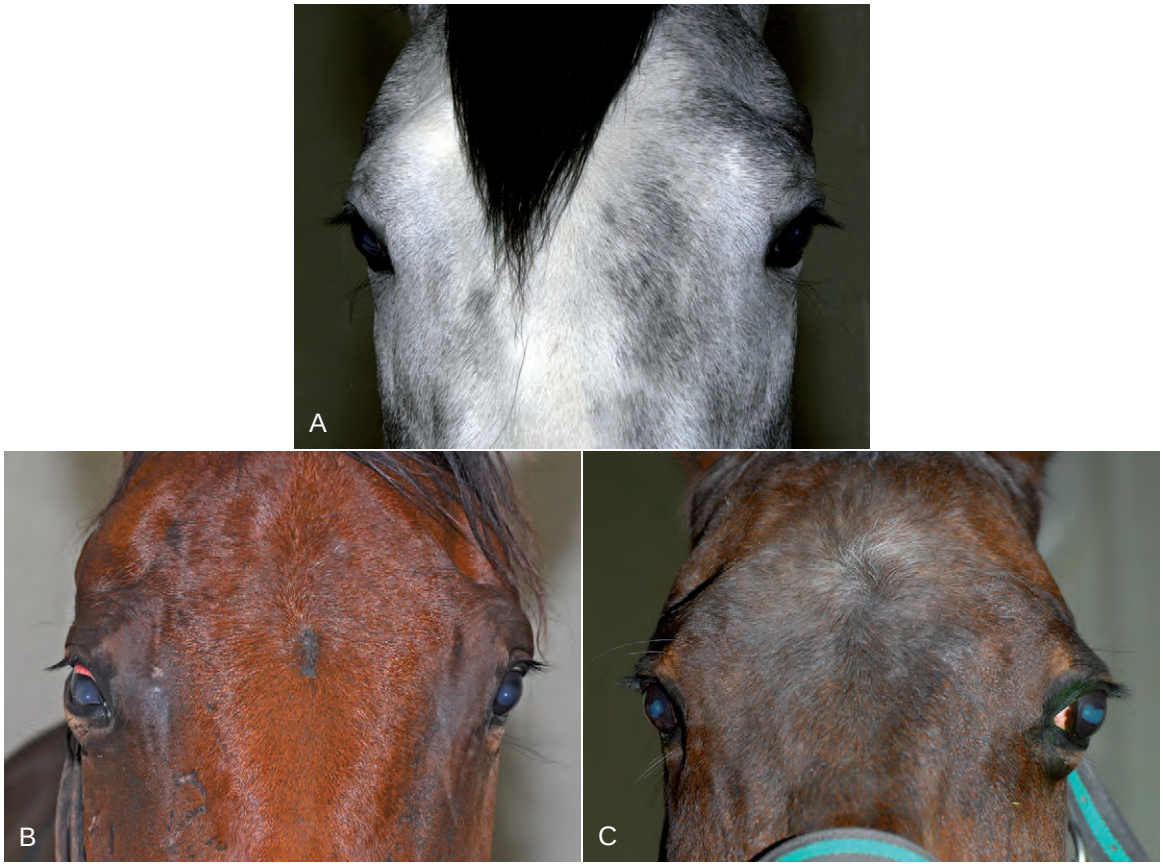


Figure 1-4. **A,** The head (including ears and nostrils), bony orbits, eyelids, globes, and pupils should be examined for symmetry, with the examiner positioned in front of the horse. **B,** Horse with orbital asymmetry due to an orbital fracture on the right side. **C,** Horse with asymmetry due to a retrobulbar mass resulting in exophthalmos on the left side.

Box 1-2 | **General Order of Steps in the Routine Equine Ocular Examination**

1. Obtain medical and ocular history.
2. Examine horse in its environment.
   - Observe walking on a lead or loose in a stall or round pen.
   - Observe horse performing activity such as jumping, cutting, etc.
3. Evaluate for symmetry from the front of the head.
   - Observe globe, orbit, pupils, eyelash direction, ear and lip position.
4. Perform vision testing.
   - Menace response, dazzle reflex, maze testing.
5. Perform palpebral and pupillary light reflexes.
6. Perform Schirmer tear test if indicated.
7. Administer sedation if required.
8. Perform palpebral nerve block.
9. Use direct transillumination for gross disease of eyelids, cornea, anterior chamber, and iris.
10. Collect samples for culture and cytology if indicated.
11. Perform detailed examination of the eyelids, cornea, anterior chamber, and iris with transillumination and biomicroscopy.
12. Test corneal reflex.
13. Apply topical fluorescein and examine the cornea.
14. Apply topical anesthesia if indicated.
15. Perform tonometry.
16. Induce mydriasis (tropicamide HCl) if not contraindicated.
17. Perform detailed examination of the lens and vitreous, via transillumination, retroillumination, and biomicroscopy.
18. Perform direct and/or indirect ophthalmoscopy.
19. Irrigate nasolacrimal duct(s) if indicated.

INITIAL EXAMINATION

With the examiner positioned in front of the horse, the head, bony orbits, eyelids, globes, and pupils should be examined for symmetry (Fig. 1-4) before touching the eyelids, giving sedation, or use of eyelid nerve blocks. Ocular comfort may be assessed by evaluation of palpebral fissure size and symmetry, position of the eyelashes, ocular discharge, and blink rate.[4,8,9]

The upper eyelashes of the healthy horse are nearly perpendicular to the cornea (Fig. 1-5, *A*).[8] A ventral or downward direction of the eyelashes in relation to the cornea may indicate blepharospasm, enophthalmos, or ptosis (see Fig. 1-4, *B*), while an upward deviation may indicate exophthalmos or an enlarged eye (see Fig. 1-4, *C*).[8]

The examiner should then be positioned at the side of the horse's head to examine each eye individually. An assistant

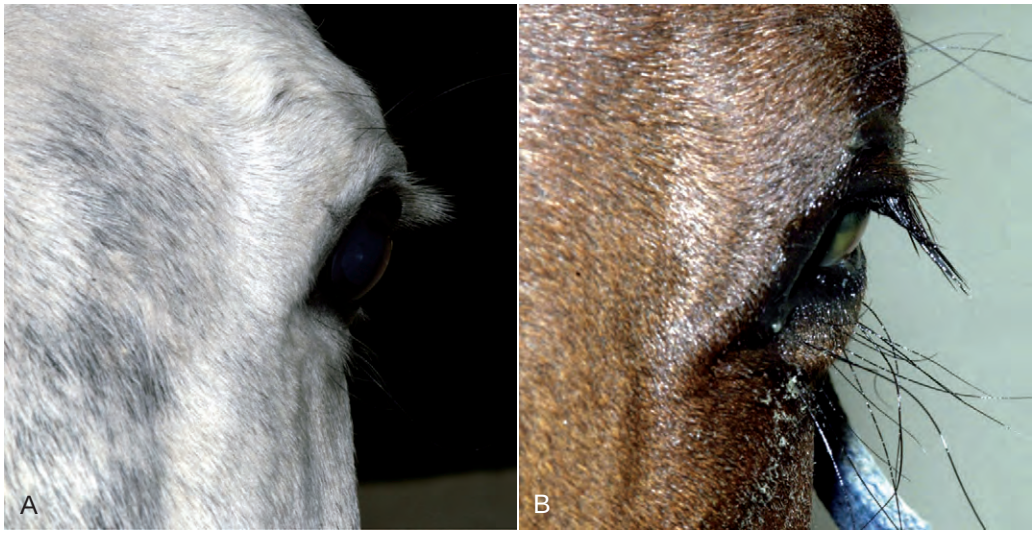


Figure 1-5. **A,** The cornea and eyelids as viewed from the front in a healthy horse. The upper eyelashes are nearly perpendicular to the cornea. **B,** The cornea and eyelids as viewed from the front in a horse with ocular pain. The eyelashes are no longer at 90 degrees from the corneal surface but are pointed downward.

may be required to elevate the head of a sedated horse to the same level as the examiner's eyes. The examiner may need to use a stool for an extremely tall horse or kneel on the ground for an extremely short horse (e.g., miniature horse), although this should be done with great caution and never directly in front of the horse.

A cranial nerve evaluation (specifically, cranial nerves II, III, IV, V, VI, VII) is then performed before any sedation is induced. These cranial nerves are assessed via the menace response, pupillary light and dazzle reflexes, globe and eyelid position and mobility, and sensation of ocular and adnexal structures.[8,9] Examination of the cranial nerves is discussed in more detail in the following section.

The cornea should be examined for abnormalities (e.g., opacities, ulceration, blood vessels, edema) by using transillumination and/or slit-lamp biomicroscopy. Evaluation of resting pupil size, shape, and mobility and appearance of the anterior chamber structures should follow, including the assessment for aqueous flare. The attachment of the iridocorneal angle pectinate ligaments to Descemet's membrane (i.e., gray line) can be observed medially and laterally in the adult horse (Fig. 1-6) and allows for direct visualization of the horse's iridocorneal angle. Collection of cultures and Schirmer tear values are performed when indicated prior to placing any medications into the eyes. When indicated, cytology is collected next, usually after application of 0.5% proparacaine hydrochloride (HCl) topical anesthetic (Alcaine 0.5% [Alcon Laboratories, Fort Worth, TX]). Fluorescein staining of the cornea is then performed. Examination of the nasolacrimal system, third eyelid, and conjunctiva is performed concurrently. Fluorescein staining is followed by induction of topical anesthesia with proparacaine if not already given to collect cytology and perform tonometry. The ocular media (cornea, aqueous humor, lens, and vitreous) are evaluated for clarity and transparency by transillumination and ophthalmoscopy.[4,9] The anterior surface of the third eyelid can be examined by gently retropulsing the globe to produce passive prolapse of the nictitans. For evaluation of the posterior surface, the third eyelid can be gently grasped with Graefe fixation forceps or manipulated with a strabismus hook.

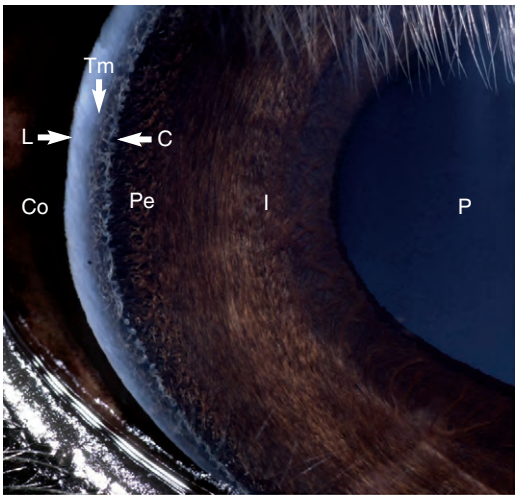


Figure 1-6. The attachment of the iridocorneal angle pectinate ligament to Descemet's membrane (i.e., gray line) can be observed medially and laterally in the adult horse. Pupil (P), iris (I), pectinate ligaments (Pe), attachment of pectinate ligaments to corneal endothelium (C), trabecular meshwork (Tm), limbus (L), and conjunctiva (Co).

For complete examination of the lens and posterior segment, mydriasis is required. The most common mydriatic used is tropicamide (Mydriacyl 1% [Alcon]), which takes effect in approximately 10 to 20 minutes and lasts 4 to 6 hours.[12,13] In the case of severe intraocular inflammation or reflex uveitis because of corneal disease or trauma, a single application of tropicamide may not be sufficient to dilate the pupil. Topical phenylephrine (2.5% or 10%) does not cause mydriasis in normal horses, nor does it enhance the mydriatic effect of tropicamide.[14,15] The use of atropine for routine examination is not recommended because of its longer duration of action and potential adverse effects in the horse.[11,16] After mydriasis has been achieved, the clarity, position, and size of the lens,

vitreous body, optic nerve, retinal blood vessels, and the tapetal and nontapetal fundus are evaluated. With full mydriasis, the edge of the lens and attachment of the zonular fibers may be visible.[17]

CRANIAL NERVE EXAMINATION

For a breakdown of the cranial nerve (CN) examination, see Table 1-1.

VISION TESTING

Vision testing in horses is subjective. Environmental observation, menace response, dazzle reflex, and maze testing provide only rough data. Determining total blindness is possible with these tests, but determining whether a horse has decreased vision is not easily done. Advanced diagnostic testing such as electroretinography (see later), may help determine if there are abnormalities in retinal electrical function but do not test vision per se. If visual function is in doubt in one or both eyes, the horse can have a unilateral blindfold and be subjected to a maze test. However, horses that are depressed, ataxic, or have vestibular disease may stumble over objects despite having vision.[9] Equine vision and vision testing are discussed more extensively in Chapter 11.

MENACE RESPONSE

The menace response is a learned protective response in which a menacing movement toward the eye results in closure of the eyelids and possibly retraction of the globe or an avoidance movement of the head.[12] The threatening movement can be performed with the examiner's hand, but care should be taken to avoid contacting the vibrissae and to avoid causing an air current that could be detected even in a blind eye. For detection of a visual deficit in one field, the menacing gesture is directed first toward the nasal visual fields and then toward the temporal visual fields.[18] However, partial visual deficits can be extremely difficult to detect using a menace response. The afferent arm of the menace response is the retina and CN II, and the efferent arm is the palpebral branch of CN VII, which innervates the orbicularis oculi muscle (Fig. 1-7).[19] A horse that has intact vision but is extremely stoic, depressed, or frightened may have a diminished menace response. Lightly tapping the medial or lateral canthus before attempting to induce the menace response again may heighten the response from an uninterested, stoic horse. A pathologic lack of menace response may result from a lesion in the retina, CN II, the visual cortex, or CN VII (see Fig. 1-7).[19] Cerebellar disease can also cause bilateral deficiency in the menace response in the absence of blindness or CN VII paralysis, possibly because of a loss of cerebellar modulation of cerebral visual function.[18,19]

PUPILLARY LIGHT REFLEXES

Both eyes should be examined for pupil size and symmetry and for abnormalities such as synechia that may affect the PLR. One method to observe pupil symmetry in the horse is to use an indirect or direct ophthalmoscope directed at the center of the horse's head from a distance of 6 to 8 feet. This technique will illuminate the pupils via both tapetal reflexes and make it possible to evaluate pupil symmetry (Figs. 1-8 and 1-9).[20] Anisocoria may be a normal finding in horses with bilateral heterochromia iridis or unilateral heterochromia iridis in which the larger pupil is ipsilateral to the heterochromic eye (Fig. 1-10).[6]

When stimulated by light during the PLR, vertical movement of the pupil is much faster and excursion is greater than horizontal movement. The pupil's shape is a horizontal ellipse that becomes rounder when dilated (Figs. 1-11 and 1-12).[21] Pupillary light reflexes can be used to simultaneously evaluate function of the retina, CN II, midbrain, and CN III.[18-20] Light directed into one eye should result in constriction of both that pupil (direct response) and the pupil of the contralateral eye (indirect or consensual response). This results from bilateral excitation of the parasympathetic component of CN III in the pretectal region (see Fig. 1-7).[18-20] The normal equine pupil responds somewhat sluggishly and incompletely to light, in a biphasic manner.[8,19] The first part is a brisk but small reaction, followed by the second slower complete movement. The mag-

Table 1-1 | **Cranial Nerve Examination**

CN	NAME	MOTOR (M) OR SENSORY (S)	FUNCTION	DYSFUNCTION	ASSESSMENT
II	Optic	S	Vision Pupillary light pathway	Blindness	Menace response Pupillary light reflex Dazzle reflex
III	Oculomotor	Medial, dorsal, ventral rectus (M) Pupillary sphincter muscle (M) Levator palpebrae superioris (M)	Globe movement Pupillary function Upper eyelid elevation	Lateral strabismus Mydriasis Ptosis	Eye position Pupillary light reflexes
IV	Trochlear	Superior oblique (M)	Globe movement	Dorsomedial strabismus	Move head and observe eye position
V	Trigeminal	Maxillary branches: skin of face/eyelid (S) Ophthalmic branches: eye (S)	Sensation of skin, eyelids, and cornea	Neurotrophic keratitis	Corneal reflex
VI	Abducens	Lateral rectus (M)	Globe movement	Medial strabismus	Move head and observe eye position
VII	Facial	Orbicularis oculi (M) Lacrimal gland (M)	Close palpebral fissure Stimulate tear production	Exposure keratitis Keratoconjunctivitis sicca	Observation Palpebral reflex Schirmer tear test
VIII	Vestibulocochlear		Equilibrium	Spontaneous nystagmus	Observation

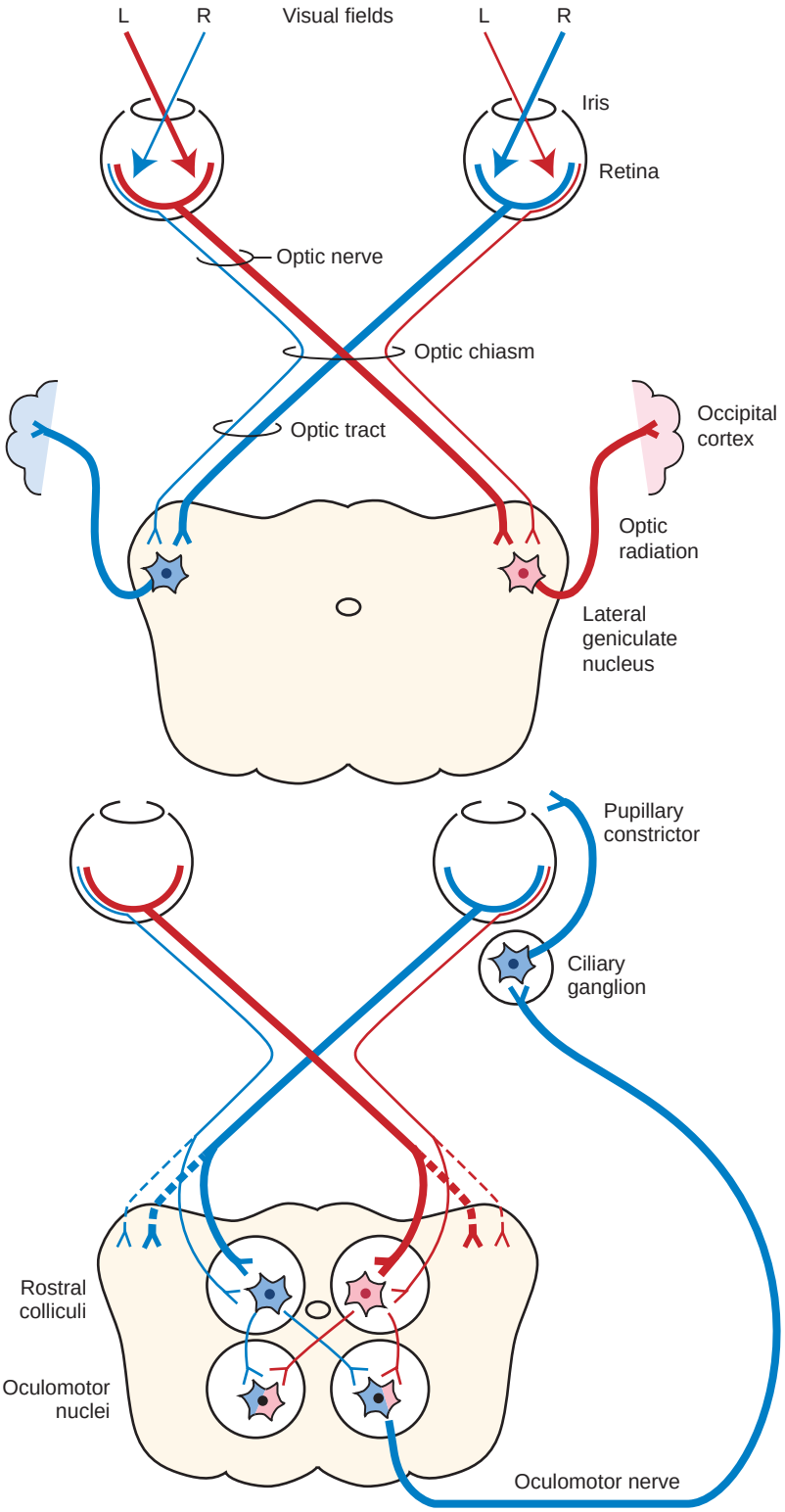


Figure 1-7. Central visual pathway/pupillary light reflex (PLR) pathway.

nitude and time of response depends on the brightness of the light source and the mental state of the horse. A very focal and bright light source is required to stimulate a rapid and complete response. Pupillary light responses are most vigorous if the beam is directed towards the visual streak in a direction that is temporal (lateral) and slightly dorsal to the optic disc. Consensual responses can be difficult to evaluate in the horse because they tend to be weaker than the direct response and can be awkward for an examiner to determine alone. The indirect PLR is less prominent because of decussation at the chiasm (75%)

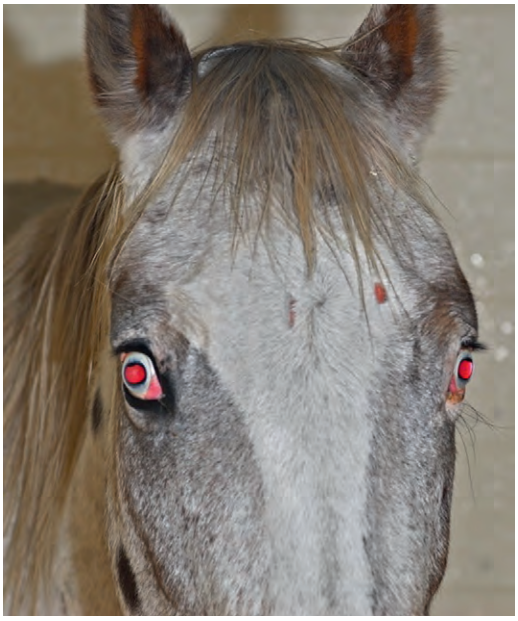


Figure 1-8. With the examiner 6 to 8 feet in front of the horse, an indirect ophthalmoscope directed at the center of the horse's head should illuminate both tapetal or red reflexes and make it possible to determine pupil symmetry.

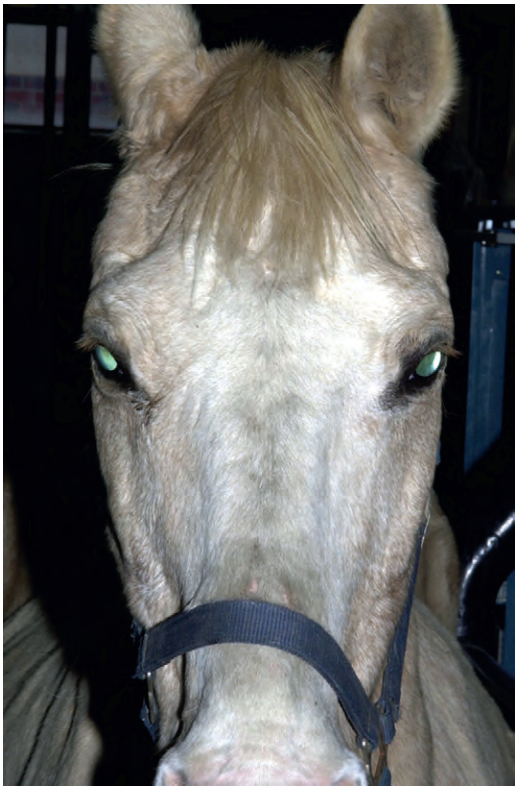


Figure 1-9. With the examiner 6 to 8 feet in front of the horse, an indirect ophthalmoscope directed at the center of the horse's head should illuminate both tapetal reflexes and make it possible to determine pupil symmetry. In the adult horse, a greater distance is required to view both pupils. Supraorbital fat atrophy can also be seen in this aged horse.

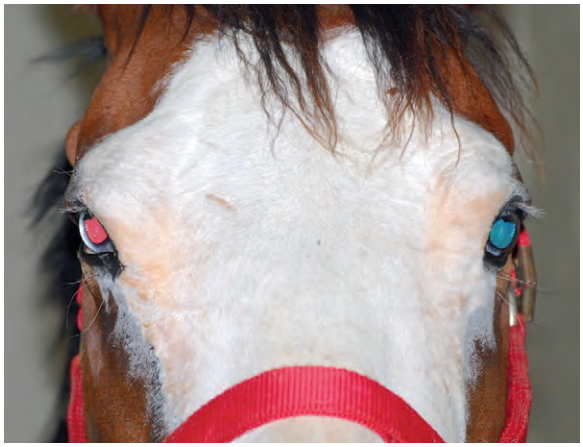


Figure 1-10. Anisocoria may be a normal finding in horses with bilateral heterochromia iridis or unilateral heterochromia iridis in which the larger pupil is ipsilateral to the heterochromic eye.

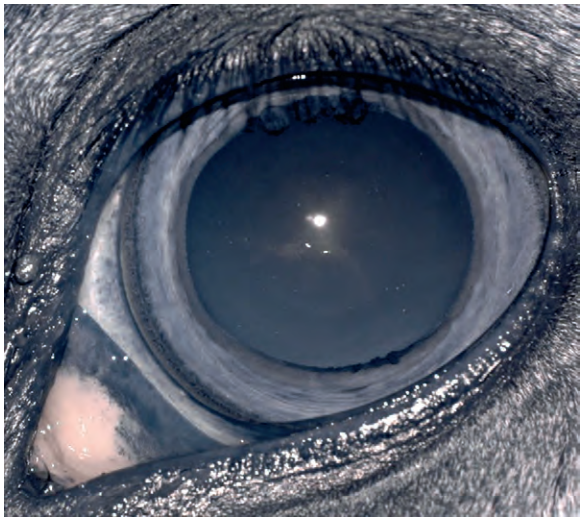


Figure 1-11. Pupil of the adult horse appears rounder when dilated (infrared photograph).

in the horse, which results in more efferent pupillomotor fibers that return to the ipsilateral side of the brain (see Fig. 1-7).[6,20] This is referred to as *dynamic contraction anisocoria*.[17] Evaluation for the consensual light reflex is unnecessary if the horse has vision and a direct response in both eyes. The consensual light reflex can be extremely valuable in evaluating problems when the posterior segment cannot be visualized (e.g., corneal edema, hyphema) for assessment of retinal function in the affected eye. Pupillary escape, a slight dilation that follows constriction under direct light stimulation, is a normal response in the horse.[20]

DAZZLE REFLEX

The dazzle reflex, in contrast to the cortically mediated menace response, is a subcortical reflex that requires function of the retina, CN II, CN VII, rostral colliculus, possibly the supraoptic nuclei of the hypothalamus, and orbicularis oculi.[18-20] A very bright focal light source is directed into the eye, and blinking

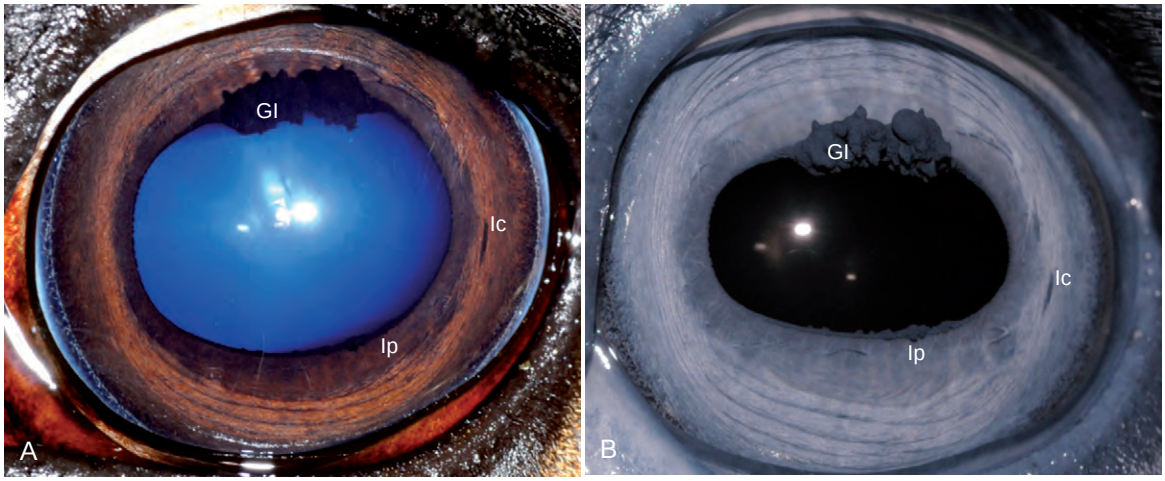


Figure 1-12. Normal anatomy of the pupil and corpora nigra in a horse. Granula iridica (GI) are present on the dorsal and ventral pupillary margins but are normally more prominent on the dorsal margin. The iris can be separated into a pupillary zone (Ip) and a more peripheral ciliary zone (Ic). **A,** Color photograph. **B,** Infrared photograph.

or blepharospasm is a normal response. Care should be taken if the light source generates heat, because this can be detected by the horse if the light source is close to the cornea and can also result in blepharospasm.

PALPEBRAL REFLEX

Horses normally blink approximately 5 to 25 times per minute at rest.[22] The blink is synchronous between both eyes approximately 30% to 100% of the time.[22,23] Two types of normal blinking occur in the horse at rest: complete and incomplete.[23] Incomplete blinking is most common and consists predominantly of upper eyelid motion downward.[23] Complete blinking is associated with an upward movement of the lower lid to meet the upper lid and is highly variable in occurrence.[23] The blink rate slows when the horse is sedated, anxious, or focused on an object of interest.

The palpebral reflex is elicited by touching the medial and lateral canthi and results in closure of the eyelids.[18-20] If CN V or CN VII is abnormal (e.g., facial nerve paralysis) or if the eyelids are unable to close (e.g., with severe trauma and swelling), the blink may be absent or incomplete.

CORNEAL REFLEX

The corneal reflex is elicited by lightly touching the unanesthetized cornea with a sterile cotton-tipped swab and results in closure of the eyelid and retraction of the globe.[18-20] This subcortical reflex occurs in response to a tactile or painful stimulus to the cornea. The afferent pathway of the corneal reflex is via the ophthalmic branch of CN V.[20] The result should be closure of the eyelid and retraction of the globe, mediated by CN VII and CN VI, respectively.[20] If CN V or CN VII is abnormal or if the eyelids are unable to close, the blink may be absent or incomplete. Corneal sensitivity can be quantitated by a technique called *corneal esthesiometry,* which is described later in this chapter. Lack of corneal sensation may be the cause of corneal ulceration and other corneal abnormalities (see Chapter 5).

AUTONOMIC (SYMPATHETIC AND PARASYMPATHETIC) NERVOUS SYSTEM

The autonomic nervous system is composed of two main divisions: the sympathetic and parasympathetic nervous systems. The sympathetic nervous system (Fig. 1-13) begins in the hypothalamus and extends down the intermediolateral cell columns of the spinal cord to synapse at C8 to T3. The axons from these cells exit the anterior nerve root of the spinal cord through the white ramus. The fibers (preganglionic fibers) course through the brachial plexus, through the thoracic inlet, ascend in the sympathetic trunk (with the jugular vein), and synapse at the cranial cervical ganglion. Postganglionic fibers proceed rostrally between the tympanic bulla and petrous temporal bone through the orbital fissure and form the sympathetic root of the ciliary ganglion.[18-20] Short ciliary nerves (along with contributory fibers to the long ciliary nerves) extend from the ciliary ganglion to the dilator muscle of the iris (see Fig. 1-13).

The sympathetic nervous system controls dilation of the pupils and other motor functions of the eyes and face. Damage to sympathetic innervation to the head may result in Horner's syndrome (miosis, ptosis, enophthalmos, increased sweating on the face and ear of the affected side, ipsilateral distention of facial blood vessels, and ipsilateral hyperemia of the conjunctiva and nasal mucosa).[24-30] Chapter 13 offers a detailed description of the clinical signs and diagnosis of Horner's syndrome in horses. Causes reported in the horse include jugular vein and carotid artery injections, cervicothoracic spinal cord injury, cervical abscesses, guttural pouch disease or surgery, neoplasia or trauma of the neck and thorax, trauma to the vagosympathetic trunk, middle ear disease, traumatic lesions of the basisphenoid area, polyneuritis equi syndrome, equine protozoal myelitis of the cervical spinal cord, esophageal rupture, and trauma to the neck and thorax.*

The parasympathetic nervous system to the eye originates in the oculomotor nucleus in an area called the *Edinger-*

*References 8, 20, 24, 26, 27, and 29-31.

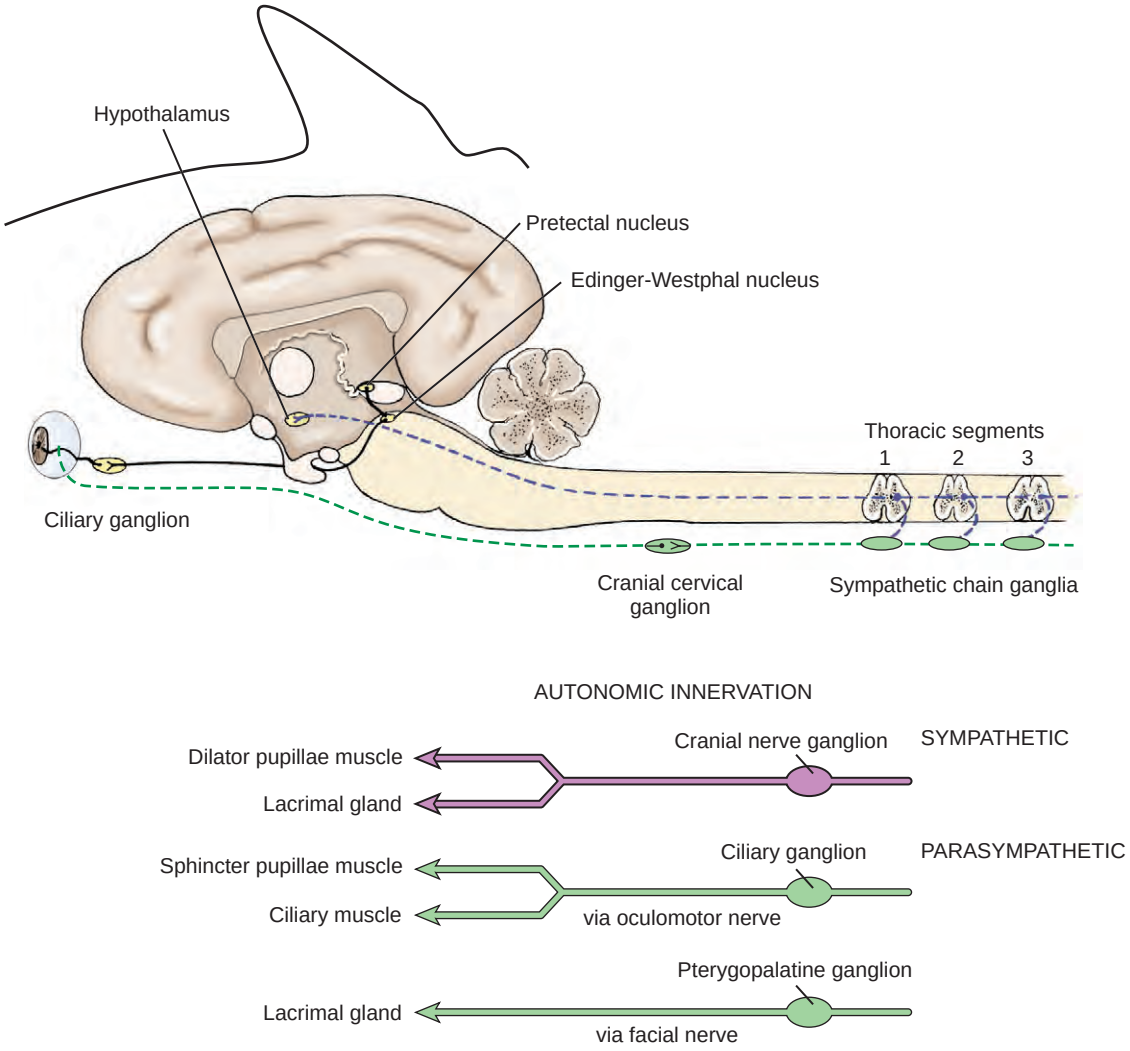


Figure 1-13. Sympathetic and parasympathetic nervous system.

Westphal nucleus. The fibers from this nucleus travel with the oculomotor nerve (CN III) and exit in the motor root of the ciliary ganglia where they synapse. The postsynaptic fibers travel to the eye in the short ciliary nerves to the constrictor muscles of the iris (see Fig. 1-13). Parasympathetic fibers also run with the facial nerve (CN VII) to the lacrimal gland to result in lacrimation when stimulated.

RESTRAINT AND SEDATION

Some horses can undergo an ocular examination without sedation, but most horses require sedation for a complete, detailed ophthalmic examination. Use of restraint and sedation depends on the temperament of the horse, availability of equipment, and comfort level of the handlers and examiner. Tranquilization with detomidine HCl (Dormosedan [Pfizer Animal Health, New York, NY]) 0.02 to 0.04 mg/kg, administered intravenously [IV]) is preferred for ophthalmic examinations because it provides rapid tranquilization without an excitation phase (either on induction or during recovery) and a steady and low head position without movement (i.e., fine tremors). Xylazine 0.5 to 1 mg/kg IV with or without butorphanol tartrate (Torbugesic [Fort Dodge Animal Health, Overland Park, KS] 0.01 to 0.02 mg/kg IV) can also be used.[8,9] Butorphanol is commonly added for painful procedures or additional restraint.[8,9] However, xylazine can have a profound excitation phase on induction or recovery. Both butorphanol and xylazine are associated with fine head tremors, or head "jerks," which can be very disruptive during slit-lamp biomicroscopy and minor procedures around the eye such as cytology collection. Addition of acepromazine (0.02 to 0.04 mg/kg IV; 20 mg IV in a 500-kg horse)[32] 10 to 15 minutes prior to the detomidine is recommended to avoid the fine tremors when additional tranquilization is needed for extended examination or minor standing surgical procedures. Additional restraint includes lip (rope or chain) and neck twitch (manual). Although these techniques are generally very effective for short-term restraint (i.e., less than 10 minutes), some horses react adversely to these techniques, so caution is advised when using them.

REGIONAL NERVE BLOCKS

Two ophthalmic nerves are frequently denervated ("blocked") during the equine ocular examination: the auriculopalpebral, or more precisely the palpebral branch of the facial nerve (CN VII), and the frontal (supraorbital) branch of the trigeminal nerve (CN V).[33,34] When these nerves are blocked, akinesia and anesthesia, respectively, of the upper eyelid occurs.

REGIONAL AKINESIA

The most common nerve blocked is the palpebral branch of the auriculopalpebral nerve, which innervates the orbicularis oculi muscle, responsible in part for eyelid closure. The orbicularis oculi muscle in horses is very strong, and therefore akinesia of this muscle is required to open the eyelid for examination in many horses, especially horses that are painful. It is extremely important in conditions in which the structural integrity of the globe is compromised, because the pressure applied by the muscle during manipulation for examination or during blepharospasm could result in rupture of the globe. Akinesia of the eyelids may be induced for routine eye examination, diagnostic procedures (e.g., corneal cytology and culture), therapy (e.g., subconjunctival injections, placement of a subpalpebral lavage), and standing surgeries.[33,34]

A volume of 1 to 2 mL of an anesthetic is injected subcutaneously with a 25-gauge, ⅝-inch needle adjacent to the nerve, and the injection site is massaged to facilitate anesthetic diffusion.[8,9,12,33,34] Anesthetics most frequently used for eyelid blocks include 2% lidocaine HCl, which has an onset of action of 4 to 6 minutes and a duration of 60 to 90 minutes, and 2% mepivacaine (Carbocaine [Pharmacia & Upjohn Company, Division of Pfizer Inc., New York, NY]), with an onset of action of 3 to 5 minutes and a duration of 90 to 120 minutes.[8,9,12] Procaine or bupivacaine can also be used. Repeated injections of anesthetic may result in a refractory phenomenon, requiring higher volumes of drug and longer times to achieve akinesia.[12] The auriculopalpebral nerve block results in paralysis of the orbicularis oculi muscle of the upper eyelid and variable paralysis of the lower eyelid for approximately 1 to 2 hours.[8,9,12] Duration of anesthesia can be prolonged with the addition of 1:10,000 epinephrine,[12] but this is not usually required for most examinations or minor surgical procedures. Ptosis, narrowing of the palpebral fissure, and easy manual elevation of the upper eyelid should result.[8,9,12] Sensation to the eyelids and some palpebral function remains intact, so the horse can usually blink and continue to protect the cornea. Once the examination is concluded, if the horse is not blinking well, topical ophthalmic ointments should be used every 30 minutes to protect the cornea until palpebral function returns.

The auriculopalpebral nerve branches from the main trunk of the facial nerve, where it is protected by the parotid gland for the full length of the caudal border of the ramus of the mandible.[12,20] It then emerges from beneath the gland just caudal to the caudal border of the condyle of the mandible, where it is covered by thin facial muscles and lies close to the rostral auricular artery and vein.[12] The branches then pass rostrally and dorsally to reach their destination (Fig. 1-14).

The auriculopalpebral nerve can be blocked subfascially in the depression just anterior to the base of the ear where the caudal border of the coronoid process of the mandible meets the zygomatic process of the temporal bone. At this point, the nerve emerges from the parotid salivary gland and becomes subcutaneous on the lateral aspect of the dorsal tip of the coronoid process (see Fig. 1-14).[12,33,34]

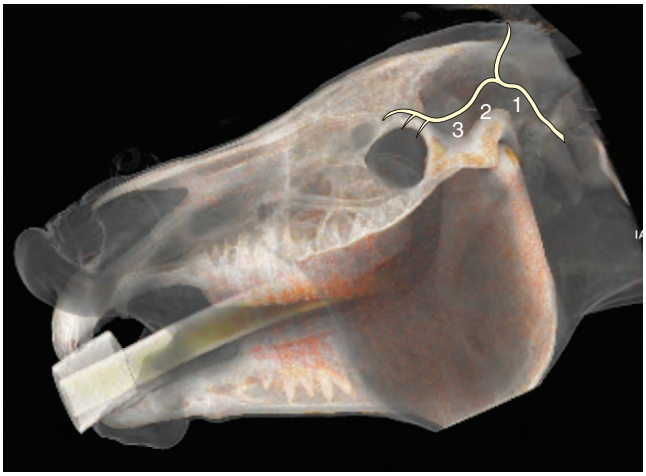


Figure 1-14. Three sites at which the auriculopalpebral nerve can be blocked: caudal to the posterior ramus of the mandible *(1)*, dorsal to the highest point of the zygomatic arch *(2)*, and where it lies on the zygomatic arch caudal to the bony process of the frontal bone *(3)*.

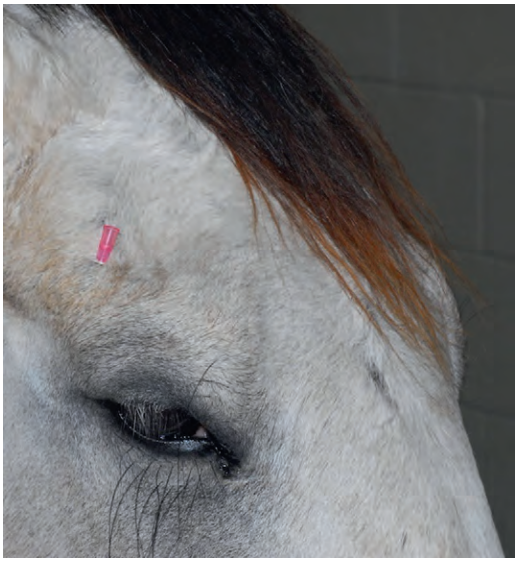


Figure 1-15. Location of the palpebral nerve block. A 25-gauge needle is inserted, and 1-2 mL of lidocaine or Carbocaine is injected subcutaneously.

The palpebral branch of the auriculopalpebral nerve can be blocked just lateral to the highest point of the caudal zygomatic arch, where the nerve can be palpated through the skin by running a finger forcefully over the dorsal border of the bone (Fig. 1-15, see Fig. 1-14).[33,34] The palpebral branch of the auriculopalpebral nerve can also be blocked where it lies on the zygomatic arch caudal to the bony process of the frontal bone (see Fig. 1-15).[33,34]

REGIONAL ANESTHESIA AND ANALGESIA

Sensation to the eyelids is provided by the ophthalmic and maxillary divisions of the trigeminal nerve (CN V) (Fig. 1-16).[12]

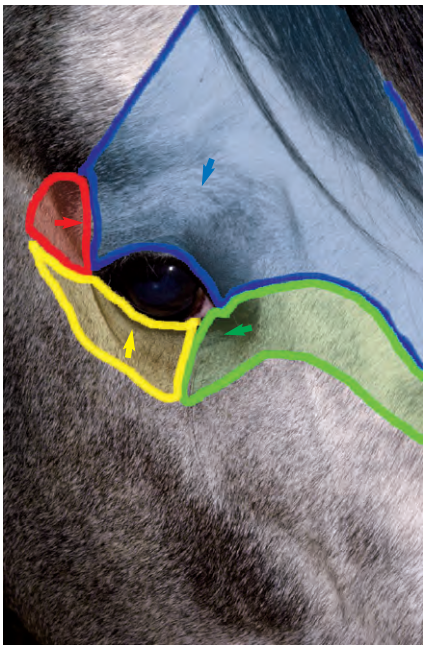


Figure 1-16. Sensation to the eyelids is provided by the ophthalmic and maxillary divisions of the trigeminal nerve (CN V). The frontal, lacrimal, and infratrochlear nerves arise from the ophthalmic branch of CN V, whereas the zygomatic nerve arises from the maxillary branch of CN V. The approximate areas of sensation that would be blocked with each nerve are indicated as follows: frontal *(blue)*, lacrimal *(red)*, zygomatic *(yellow)*, infratrochlear *(green)*.

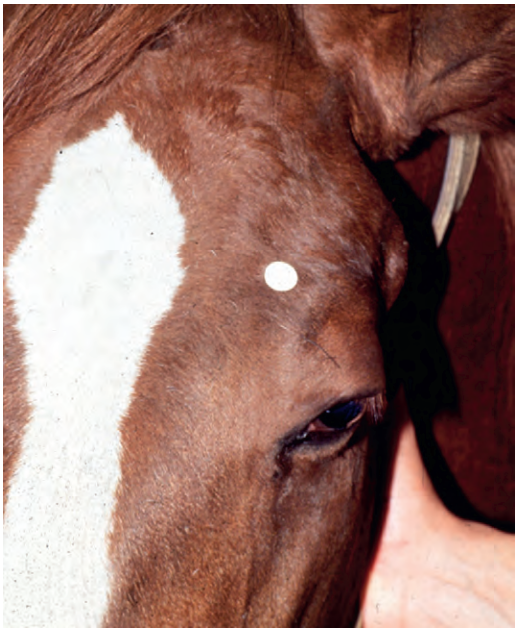


Figure 1-17. The frontal (supraorbital) nerve is blocked as it emerges from the supraorbital foramen within the frontal bone, as indicated by the white dot.

The frontal, lacrimal, and infratrochlear nerves arise from the ophthalmic branch of CN V, and the zygomatic nerve arises from the maxillary branch of CN V.[6,12] The frontal (supraorbital) nerve innervates most of the central upper eyelid and is the only sensory block normally required for examination.[12] The lacrimal nerve provides sensory innervation for the lateral upper eyelid.[12] The infratrochlear nerve provides sensory innervation for the medial canthus.[12] The zygomatic nerve innervates the majority of the lateral lower eyelid.[12] The nasociliary nerve, a branch of the maxillary branch of CN V, provides sensory innervation to the cornea.[12] Anesthesia of these nerves is sometimes necessary for eyelid and conjunctival biopsies or simple surgeries, as well as subpalpebral lavage placement in the horse. The anesthetics most frequently used are the same as those used for akinesia and include lidocaine HCl and mepivacaine.

The four main sensory nerve branches can be blocked directly as follows: The frontal (supraorbital) nerve is blocked as it emerges from the supraorbital foramen within the frontal bone (Figs. 1-17 and 1-18).[12,17] This foramen can be palpated if the examiner places his or her thumb below the dorsal orbital rim and the middle finger in the supraorbital fossa. The examiner then places the index finger straight down midway between the thumb and middle finger to locate the supraorbital foramen (see Fig. 1-18). A depression is usually palpable. A 25-gauge, ⅝-inch needle is then inserted subcutaneously over the foramen, and 1 to 2 mL of anesthetic is injected (Fig. 1-19). Passing the needle into the foramen is not recommended because this may damage the supraorbital artery and vein, which exit the skull through the supraorbital foramen. Furthermore, if the needle

Figure 1-18. The supraorbital foramen can be palpated if the examiner places his or her thumb below the dorsal orbital rim and the middle finger in the supraorbital fossa. The examiner then places the index finger straight down midway between the thumb and middle finger to locate the supraorbital foramen.

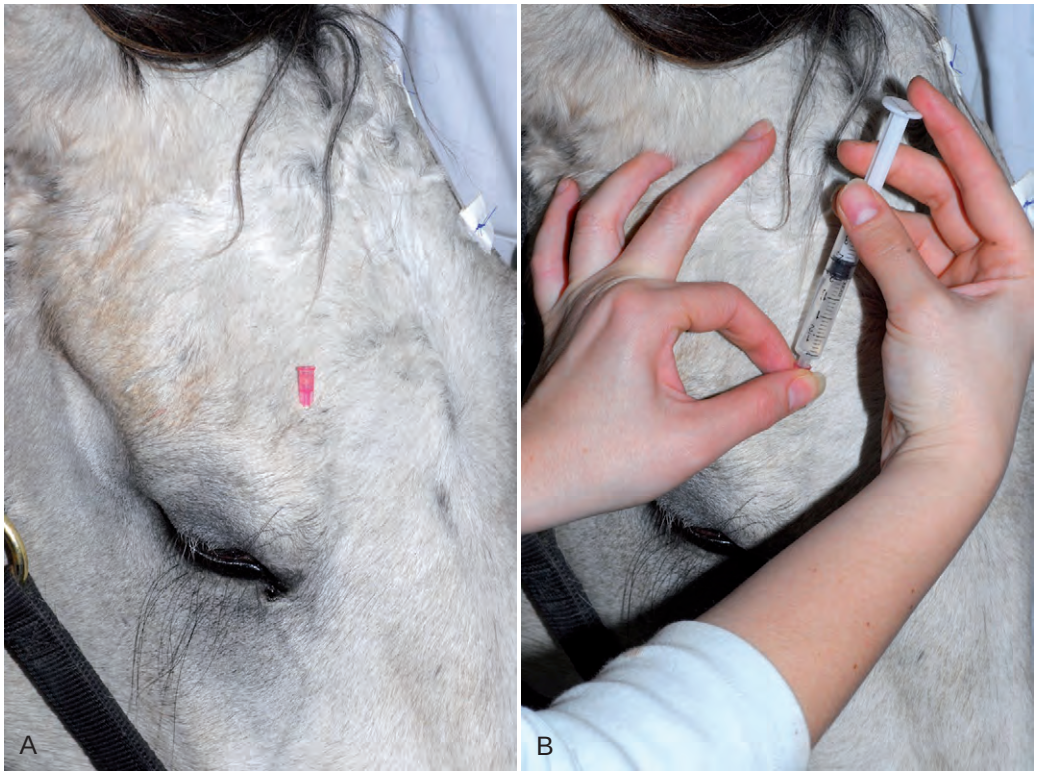


Figure 1-19. **A,** A 25-gauge, ⅝-inch needle is inserted into or just over the foramen. **B,** Inject 1 to 2 mL of anesthetic.

Figure 1-20. The lacrimal nerve can be blocked by using a line block along the lateral third of the dorsal orbital rim.

Figure 1-21. The zygomatic nerve can be blocked with a line block along the ventrolateral orbital rim.

inadvertently enters the periosteum surrounding the supraorbital foramen, this can be painful and the horse may react negatively. The frontal nerve is mainly sensory, but this block can result in partial upper eyelid akinesia as well, likely by further denervating the branches of the palpebral nerve.[9]

The lacrimal nerve can be blocked by injecting 1 mL of lidocaine adjacent to the lacrimal notch, a depression that can be palpated on the dorsolateral boney orbital rim, or by using a line block along the lateral third of the dorsal orbital rim (Fig. 1-20 and see Fig. 1-16).

The zygomatic nerve can be blocked with a line block along the ventrolateral orbital rim (Fig. 1-21 and see Fig. 1-16).

The infratrochlear nerve can be blocked as it runs through the trochlear notch located medially on the dorsal orbital rim (Fig. 1-22 and see Fig. 1-16). The notch can be palpated along the orbital rim.

GLOBE AND ORBIT EXAMINATION

Anatomy of the globe and orbit is reviewed in detail in Chapter 3. Initial examination of the globe and orbit should be made with the examiner positioned in front of the horse (see Fig. 1-4), where symmetry between the eyes is carefully assessed. Palpebral fissure size and symmetry, relative globe position, and

Figure 1-22. The infratrochlear nerve can be blocked as it runs through the trochlear notch, located medially on the dorsal orbital rim. The notch can be palpated.

Figure 1-24. Exophthalmos of the right eye of a horse with a retrobulbar mass.

Figure 1-23. Enlarged left eye of a horse with chronic glaucoma.

Figure 1-25. Corneal globosa of a Rocky Mountain horse with multiple congenital ocular anomalies. (Photograph courtesy Dr. David Ramsey.)

direction of the eyelashes are evaluated. The upper eyelashes of the healthy horse are nearly perpendicular to the cornea (see Fig. 1-5).[8] A change in the angle between the eyelashes and the cornea may indicate blepharospasm, enophthalmos, exophthalmos, or ptosis (see Fig. 1-5).[8]

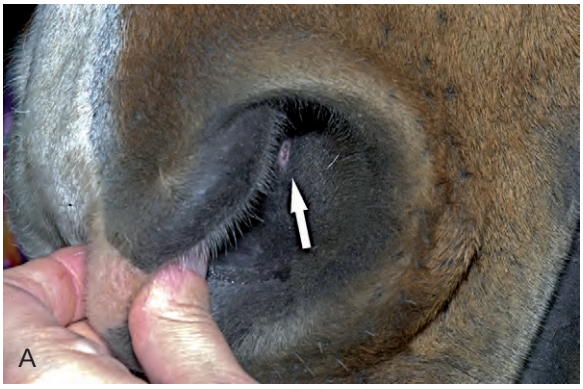
Apparent changes in globe size (e.g., hydroophthalmus [Fig. 1-23]) should be differentiated from changes in globe position (e.g., exophthalmos [Fig. 1-24]). Cornea globosa (Fig. 1-25) has been reported in the Rocky Mountain horse and may be difficult to distinguish from hydroophthalmus.[35,36] The orbit should be examined by observation, palpation of the bony orbital rim, and retropulsion of the globe through a closed eyelid.[4,8,9] Forceful manipulation of the eyelid and retropulsion should not be performed if the structural integrity of the cornea or globe may be compromised.

EYELIDS AND CONJUNCTIVA EXAMINATION

Anatomy of the eyelids and conjunctiva is reviewed in detail in Chapter 4. Examination of the eyelid should include assessment of function and detailed examination using diffuse illumination with magnification (e.g., using a slit-lamp biomicroscope). The periocular tissues including the eyelids, conjunctiva, sclera, and nictitans should be inspected with transillumination,[17] the technique of direct focal illumination for inspection of the anterior structures of the eye. It can be performed with a Finnoff transilluminator (Welch-Allyn, Skaneateles Falls, NY), direct ophthalmoscope, slit-lamp biomicroscope, or even a penlight. Eyelids should be examined for position, movement, and conformation prior to the use of eyelid blocks.[4,8,9] Attempts to forcefully elevate the upper eyelid should be avoided if a palpebral nerve block has not yet been performed, and each eye should be examined with minimal handling of the adnexal tissues. Culture and cytology should be collected prior to instillation of any medications (see detailed information on culture and cytology in this chapter and in Chapter 2). Biopsy of the eyelid or conjunctiva should be considered if indicated (see later and in Chapter 4).

LACRIMAL AND NASOLACRIMAL SYSTEM EXAMINATION

Please see anatomy of the lacrimal and nasolacrimal system in Chapter 4. Assessment of the lacrimal system is done by microscopic examination of the tear film via slit-lamp biomicroscopy (or other means of magnification) and adjunctive diagnostic



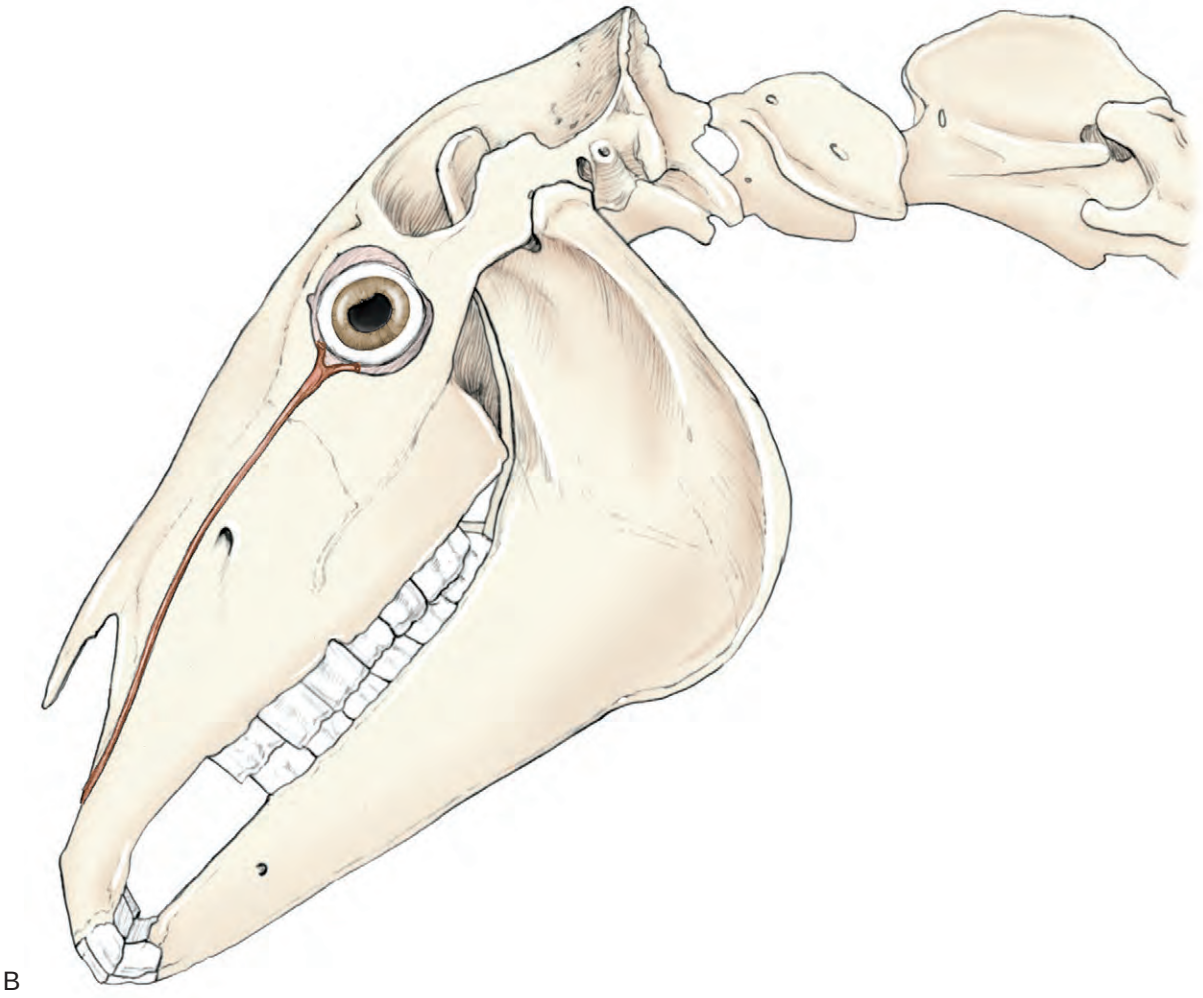


Figure 1-26. **A,** Normally a single distal punctum of the nasolacrimal system is present and can be located in the skin of the floor of the nostril near the mucocutaneous junction *(arrow)*. **B,** Normal anatomy of the equine nasolacrimal duct. Two proximal lacrimal puncta, one in each eyelid, are present along the medial inner eyelid margin. A canaliculus leads from each punctum toward the medial canthus and ends in the lacrimal sac, which is poorly developed in the horse. The lacrimal sac is the expanded beginning of the approximately 22- to 30-cm–long nasolacrimal duct. The course of the nasolacrimal duct follows a line drawn from the medial canthus of the eye to a point just dorsal and rostral to the infraorbital foramen.

tests, such as the Schirmer tear test. The examiner should also inspect the openings of the proximal (eyelid) and distal (nasal) nasolacrimal puncta (Fig. 1-26).

The Schirmer tear test (STT) is used commonly to measure aqueous tear production.[37-40] In the test, a filter paper strip is placed in the conjunctival sac, and wetting is then measured in millimeters per 60 seconds (Fig. 1-27). Commercial filter paper strips available include standardized Sno-Strips (Akorn) and Color Bar (Eagle Vision/Schering-Plough, Kenilworth, NJ). Strips can also be made from Whatman filter paper (No. 40,

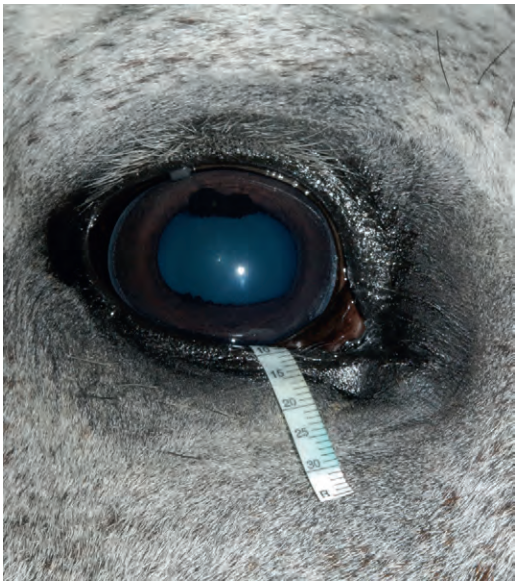


Figure 1-27. The Schirmer tear test (STT) is used to measure aqueous tear production. In the test, a filter-paper strip is placed in the conjunctival sac, and wetting is then measured in millimeters per 60 seconds.

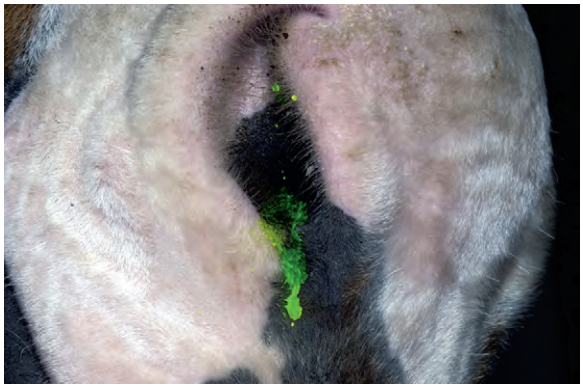


Figure 1-28. Passage of fluorescein dye to the distal punctum in the nares (Jones test) is timed and should occur within 5 minutes but may take up to 20 minutes in the horse.

5 × 40 mm with a notch 5 mm from the end).[12] The Schirmer I test, in which no topical anesthesia is used, measures the approximate amount of basal and reflex tearing. The Schirmer II test, performed after the application of topical anesthesia, theoretically only measures basal secretion of aqueous tears. Some residual tear volume may make both of these measurements slightly inaccurate. The STT should be performed before manipulation of the eye and orbit during examination to minimize reflex tearing. There are no reports of the effect of an auriculopalpebral nerve block on the STT in horses.

Deficiencies in aqueous tear production have rarely been reported in the horse.[23,38,40-46] Possibly this is because the STT is not a part of the routine ophthalmic examination in the horse, but it should be. Specific indications to perform STT include evidence of CN VII dysfunction (e.g., after trauma, facial paralysis), desiccated cornea or conjunctiva, presence of tenacious mucoid discharge, and presence of unexplained corneal vascularization or ulceration. Keratoconjunctivitis sicca is most commonly the result of CN V or VII trauma but has also been reported in cases of fractures of the mandible and stylohyoid bone, post anesthesia, locoweed poisoning, eosinophilic dacryoadenitis, hypothyroidism, and in association with corneal stromal sequestration.[23,38,40-46]

The effects of age, season, gender, environment, sex, time of day, and placement of strips on STT results in healthy horses and ponies have also been reported.[37,39] In general, the STT value in the horse is much greater than that in cats and dogs.[38,47,48] STT values are highly variable between eyes and between the same eye during different times of the day, and this appears to be unrelated to signalment, housing, or season.[37] One study found a diurnal variation in horses housed in a 12-hour light and 12-hour dark setting.[39] These horses had STT values that gradually increased during the light phase, peaked at 4 to 6 hours, then decreased during the dark phase.[39] Healthy horses have been reported to have an STT I range of 11 to greater than 30 mm wetting/min and 15 to 20 mm/30 sec. Both sick and healthy neonatal foals have been reported to have lower STT values than adults.[49,50] STT I values for sick neonatal foals (14.2 ± 1 mm of wetting/min) and healthy neonatal foals (12.8 ± 2.4 mm/min) were not significantly different but were lower than STT I values from healthy adult horses (18.3 ± 2.1 mm/min).[49,50]

Comparisons of STT I and STT II values revealed minimal differences in one study (i.e., STT I and STT II values of 12.7 ± 9.1 mm wetting/min and 9.9 mm ± 4.25 mm wetting/min),[48] while the second did not reveal a difference between STT I and STT II values.[37] This is in contrast to the dog, in which the STT I value is significantly higher than the STT II value.[51] Sedation with xylazine does not affect the STT value; however, general inhalant anesthesia with halothane does lower the STT value for up to 3 hours.[38]

Borderline STT measurements (e.g., measurements of 10 to 15 mm wetting/min) should always be repeated. Comparison of tear test results between the two eyes should be cautiously interpreted in clinical assessment of decreased tearing.[37] In general, repeatable measurements of less than 10 mm wetting/min should be considered abnormal in conjunction with clinical signs.[4] Please see Chapters 4 (adnexa and lacrimal) and 5 (cornea) for more information on keratoconjunctivitis sicca.

NASOLACRIMAL DUCT PATENCY

The physiologic patency of the nasolacrimal system can be evaluated with topical sodium fluorescein, which is not rinsed from the eye.[12] Passage of the fluorescein to the distal puncta in the nares (Jones test) is timed and should occur within 5 minutes but may take up to 20 minutes (Fig. 1-28).[17] The required time for passage is influenced by the amount of fluorescein placed, tear production, and length of the individual horse's nasolacrimal system.[17] A positive test result is definitive for a patent nasolacrimal duct but does not prove that both proximal puncta are patent.[17] A negative test result is only suggestive of a problem and may even be normal in the horse because of the large volume capacity of the nasolacrimal duct.[17,52,53] However, the nasolacrimal duct should be irrigated if the dye fails to appear and clinical signs suggest a problem such as epiphora (watery ocular discharge) without an obvious cause, mucopurulent ocular or nasal punctal discharge, or dacryohemorrhea.[17,52,53]

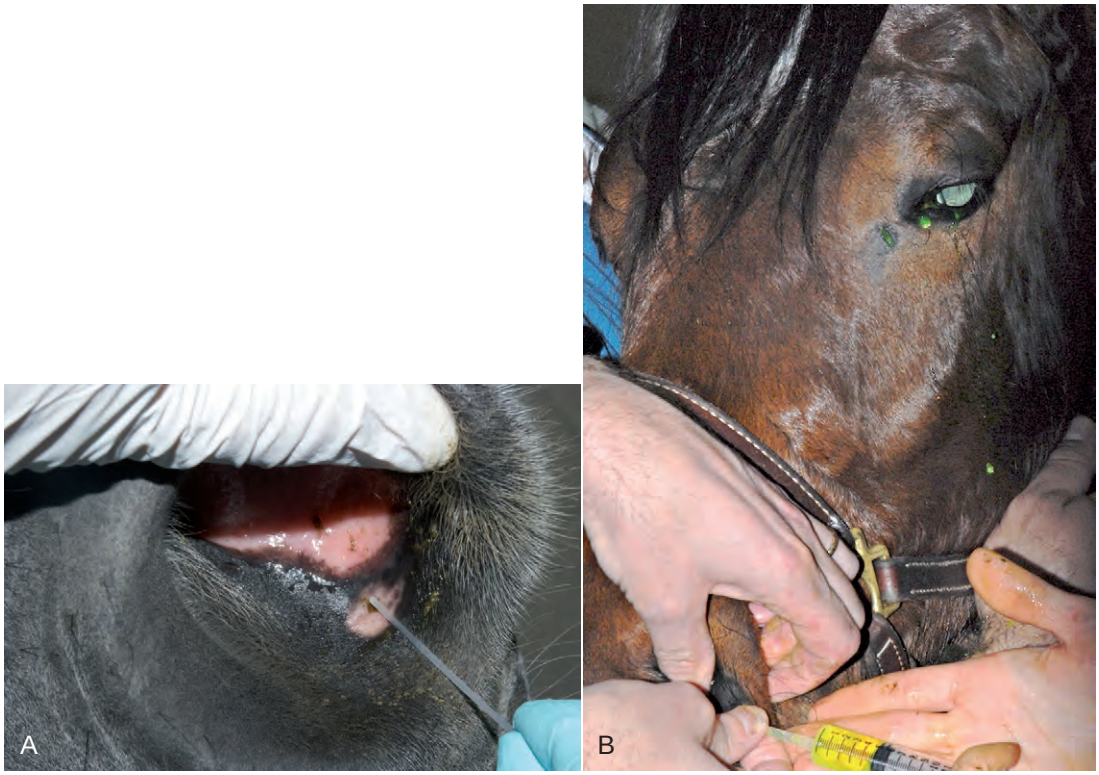


Figure 1-29. Retrograde irrigation through the distal opening to the nasolacrimal duct is easiest to perform. **A,** The tip of the catheter, after it has been coated with lidocaine gel, is inserted into the distal punctal opening. Digital pressure should be applied to the opening to prevent normograde loss of fluid. **B,** The 12-mL syringe, previously filled with eyewash, is attached; gentle irrigation of the nasolacrimal duct is performed until fluid exits the proximal punctum near the medial canthus of the eye.

Irrigation of the nasolacrimal duct can be performed retrograde (i.e., from the distal nares opening) or normograde (i.e., from the proximal eyelid puncta).[12] Sedation is usually required to perform either procedure in the horse. Retrograde irrigation through the distal opening to the nasolacrimal duct is easiest to perform (Fig. 1-29) because of the larger size of the opening.[17,53] The distal nasolacrimal puncta can usually be cannulated by a No. 5 or 6 polyethylene urinary catheter.[17] Suitable catheters are 4 to 6 Fr canine urinary catheters, 5 Fr feeding tubes, or polyethylene tubing.[17] The largest catheter that will pass through the bony canal in an adult is a 6 Fr urinary catheter.[17] The tip of the catheter, after it has been coated with lidocaine gel, is inserted into the distal punctal opening for a distance of at least 5 cm. Digital pressure should be applied to the opening to close it and prevent normograde loss of fluid. A 12- to 20-mL syringe previously filled with eyewash is attached, and gentle irrigation of the nasolacrimal duct is performed until fluid exits the proximal punctum near the medial canthus of the eye. Sneezing by the horse is common during this procedure and may be violent. A list of supplies needed to perform nasolacrimal duct irrigation can be found in Box 1-3.

If retrograde irrigation is unsuccessful, then normograde irrigation from the proximal puncta should be attempted with a lacrimal canula, open-ended tomcat catheter, or teat tube syringe (Fig. 1-30).[17] The puncta in the lower eyelid are usually slightly larger and easier to cannulate than the puncta in the upper eyelid.[17] Gentle pulse pressure may be required to unblock an obstructed duct. Excessive force in the placement of the catheter or during irrigation should be avoided because significant damage to the nasolacrimal duct could result.[17] Ducts that are compromised by a foreign body or other anatomic obstruction (e.g., after trauma, mass effect) may not be effectively irrigated.[54] Skull radiographs or CT scans and a contrast dye study (e.g., dacryocystorhinography) should be performed next if the duct cannot be irrigated. See descriptions of these diagnostic techniques later in the chapter.

Box 1-3 | **Supplies Needed for Irrigation of the Nasolacrimal Duct**

Retrograde Irrigation

- Lidocaine gel
- Open-ended tomcat catheter, 4 to 6 Fr polyethylene urinary catheter, 5 Fr feeding tubes, or polyethylene tubing
- A 12- to 20-mL syringe
- Sterile eyewash or balanced salt solution

Normograde Irrigation

- Topical anesthetic (proparacaine HCl)
- Open-ended tomcat catheter, lacrimal canula
- A 12- to 20-mL syringe
- Sterile eyewash or balanced salt solution

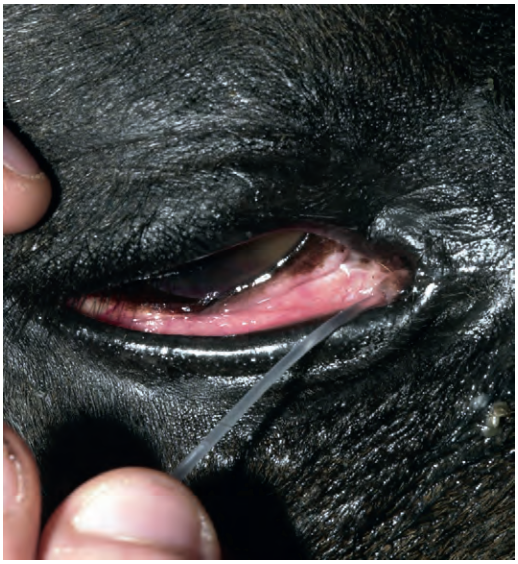


Figure 1-30. Normograde irrigation from the proximal puncta should be attempted if the result of the Jones test is negative and the duct cannot be irrigated from the distal nasal puncta. Catheterization of the proximal punctum using an open-ended tomcat catheter in the lower eyelid is demonstrated.

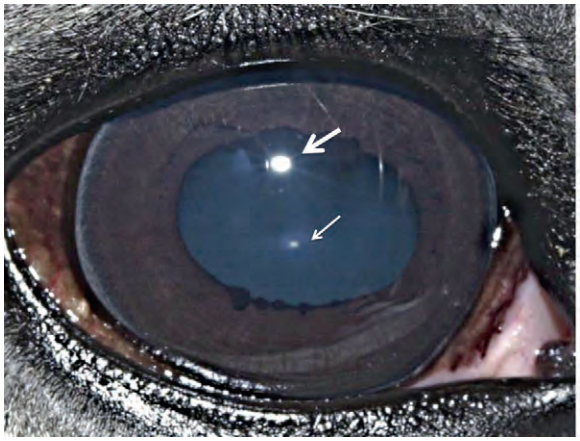


Figure 1-31. The Purkinje-Sanson reflexes are three reflections produced by the light source during transillumination. The largest is produced by the cornea *(larger arrow)*. The second is produced by the anterior lens capsule *(smaller arrow)*. The third is not easily visible and is produced by the posterior lens capsule.

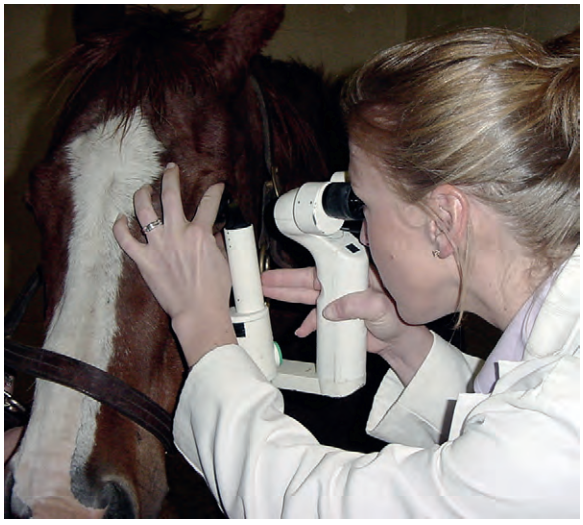


Figure 1-32. Biomicroscopy with the battery-operated Kowa SL-14 biomicroscope.

CORNEA AND SCLERA EXAMINATION

The anatomy and diseases of the equine cornea are described in Chapter 5. To examine the cornea of the horse, diffuse and focal direct illumination (or transillumination) with magnification is used first, followed in most cases by biomicroscopy using a slit-lamp. The corneal examination should be performed with the observer located rostral to the eye. Light directed diagonally across the cornea will reveal opacities of the cornea against the dark background of the pupil.[17]

The Purkinje-Sanson reflexes are three reflections from the eye produced by the light source during transillumination (Fig. 1-31).[17] Disease may alter the sharpness and location of these reflexes. The first, largest, and most anterior originates from the cornea. The second originates from the anterior lens capsule, and the third and most posterior originates from the posterior lens capsule. If a slit-lamp biomicroscope is used, two corneal reflexes are seen, one from the anterior surface and the other from the endothelium.[17] The corneal and anterior lens capsule reflexes are virtual and noninverted and will move in the same direction as a change in the light position. The image on the posterior surface is real and inverted and will move in the opposite direction to the light.[17] The images are valuable in determining corneal clarity, depth of the anterior chamber, thickness and position of the lens (after mydriasis), and in locating lesions within the lens.[17]

BIOMICROSCOPY FOR CORNEAL EXAM

The technique of biomicroscopy, in which a slit-lamp binocular microscope with an external pivoting light source is used, is the same for horses as for humans and small animals and has been well described elsewhere.[12,55-58] Slit-lamp biomicroscopy improves visualization and localization of lesions of the cornea, anterior chamber, lens, and anterior vitreous by means of transillumination and retroillumination.[12] It can also be used to assess corneal thickness (i.e., pachymetry), anterior chamber depth, and aqueous flare.[12]

The availability of portable handheld models of the slit-lamp biomicroscope has made biomicroscopy for equine ophthalmology easy and efficient. Portable models are available from Clement-Clark, Kowa, Nippon, Dioptrix, and Zeiss. The Kowa SL-14 or SL-15 (×10 or ×16 magnification) is light and powered by a rechargeable battery, and therefore of excellent use in examination of a horse (Fig. 1-32). However, lack of magnification above ×16 and inherent movement of the examiner and horse limits the ability to see fine structure and lesions. An alternative to a biomicroscope is using magnification (i.e, ×2.3 magnifying head loupes) and the slit beam on the direct ophthalmoscope. Very small "slit-lamps" are also made by Heine (HSL 150 [Heine USA, Dover, NH]; Eidolon Hand Held Slit Lamp Model 510L [Eidolon Optical LLC, Natick, MA]) that resemble a penlight with a magnifier on the end (Fig. 1-33). Although these instruments are inexpensive and portable,

Figure 1-33. Use of a small, portable slit-lamp (Heine Handheld Slit Lamp, Heine USA, Dover, NH). (Photograph courtesy Dr. David Wilkie.)

Figure 1-34. The light beam of the biomicroscope should be angled at 20 to 45 degrees from the axis of the microscope and thus the visual plane of the observer.

their lack of magnification and illumination limits their usefulness.[12]

The light beam of the biomicroscope should be angled at 20 to 45 degrees from the axis of the microscope and thus the visual plane of the observer (Fig. 1-34). The light beam width, length, orientation, and color can then be modified by a series of diaphragms and filters.[12] The focal distance of the instrument is 7 to 10 cm, and fine focus is achieved by moving either toward or away from the eye within this range.[12]

The initial examination of the horse should proceed with diffuse illumination: a wide, low-intensity slit beam should be used, and the microscope should be defocused from the light.[12] The surfaces of the eyelids, cornea, conjunctiva, and iris should be inspected. With the use of low magnification, a broad slit beam is focused on the cornea, creating a parallelepiped (i.e., a three-dimensional section) of illuminated tissue.[12,55] This allows visualization of transparent structures such as the cornea and lens in three dimensions. In the cornea, the anterior surface, stroma, and posterior surface of the cornea can be visualized.[55] Nontransparent structures such as the sclera only yield a magnified two-dimensional surface or external view. The slit beam is then narrowed and intensified to reveal a two-dimensional cross-section of the cornea and lens, allowing the examiner to accurately determine lesion depth and axial positioning.[55] This is extremely important in evaluating the depth of corneal lesions (e.g., stromal ulcerative keratitis, stromal abscesses) in the horse.

Direct and indirect retroillumination are performed by reflecting the slit beam from deeper structures while focusing on more superficial structures.[55] Other techniques that can be performed with slit-lamp biomicroscopy, such as specular reflection, are difficult to impossible in a horse because of continuous slight ocular movements.

CULTURE OF CORNEAL LESIONS

Culture and sensitivity testing can aid in the diagnosis of infectious keratitis and help to determine antimicrobial therapy. Specimens for culture should be obtained as early as possible in the examination, before the administration of topical preparations (e.g., proparacaine, fluorescein). Because topical anesthesia is routinely used in the workup of painful ocular disease in the horse, it is important to note that some topical drugs (e.g., proparacaine, tetracaine) have been reported to inhibit organism growth.[59] However, it has also been shown that a single application of proparacaine is unlikely to affect culture results.[60] In reality, some horses are in so much pain that even with sedation and regional nerve blocks, they will not allow the examiner to obtain an appropriate sample without application of topical anesthesia.

Culture of the ocular surface can be performed with sterile, moistened, Dacron-tipped swabs or the blunt end of a sterile surgical blade. The Dacron-tipped swab is rubbed or rolled (Fig. 1-35) over the area to be cultured, and the blunt end of the surgical blade is used in a scraping motion (Fig. 1-36). The eyelids should be retracted to prevent contamination of the sample if the eyelids are not the object of sample collection. Samples should be taken from the edges of a corneal ulcer to avoid possible deep or fragile areas of the cornea.

Type of culture and choice of antibiotic sensitivities should be made on the basis of clinical signs and the region and environment in which the horse is living. Both aerobic and fungal culture and sensitivity testing are usually indicated for most cases. Anaerobic testing may be indicated in some circumstances, but fungal testing is not necessary in nonendemic areas such as the southwestern United States. Fungal pathogens of the equine eye are usually saprophytic fungi that require enriched media such as Sabouraud dextrose agar or blood agar.[8] Fungal or bacterial pathogens can be so deep within the cornea that a diagnostic sample cannot be obtained, especially in the case of a stromal abscess. Culture of equine herpesvirus 2 (EHV-2) from the cornea has also been reported.[61,62] Viral culture or isolation usually requires that the sample be placed in a sterile saline solution in an Eppendorf tube, but instructions should be obtained directly from the testing laboratory. See Chapter 5 for more information regarding indications for culture and pathogens to consider for equine keratitis.

Figure 1-35. Culture of the ocular surface can be performed with sterile, moistened Dacron-tipped swabs. The Dacron-tipped swab is rubbed or rolled over the area to be cultured.

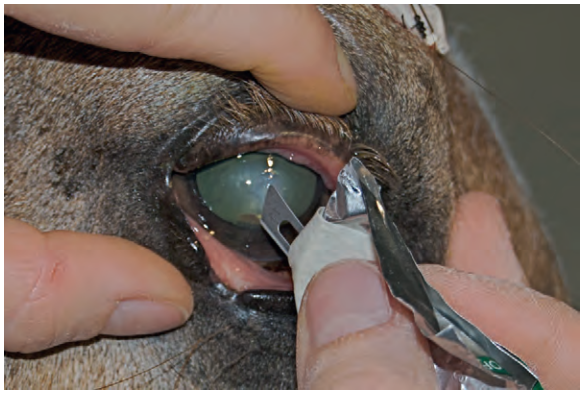


Figure 1-36. Culture of the ocular surface can be performed with a sterile surgical blade; the blunt end of the surgical blade is used in a scraping motion.

CYTOLOGY

Cytology is a quick, simple, and indispensable method for characterizing the type of inflammatory (i.e., neutrophilic, lymphocytic, or eosinophilic) process present and may also assist in making a diagnosis (e.g., bacteria or fungal hyphae). Cytology is indicated in all cases of ulcerative keratitis in the horse. Cytology can provide rapid results that may guide the immediate course of therapy.[63-65] Tools for collecting cytologic samples include instruments that are also used to obtain samples for culture (i.e., Dacron-tipped swabs, blunt end of a sterile scalpel blade), as well as cytobrushes and spatulas.[8] Topical anesthetic, microscope slides, slide stain, and a microscope are also required. A microscope slide alone can be used to perform "impression" cytology. This method is probably not effective in identifying pathologic organisms in the case of corneal disease but may be helpful in situations such as the presence of an ulcerative eyelid mass.

The cotton-tipped or Dacron-tipped swab provides the least traumatic method of retrieving adequate exfoliative samples.[63] This technique is recommended when excessive manipulation

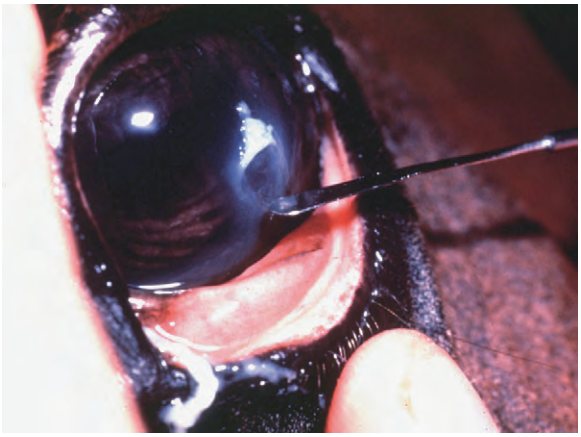


Figure 1-37. Use of a Kimura spatula provides a more precise method of collecting cells from specific areas, and greater numbers of deeper cells can usually be obtained.

is contraindicated (e.g., deep or melting corneal ulceration). Use of a spatula or the blunt end of a scalpel blade is a more precise method of collecting cells from specific areas, and greater numbers of deeper cells can usually be obtained (Fig. 1-37).[12] As in the collection of samples for culture, topical anesthetic is usually required regardless of instrument used. The cytobrush has proved to be superior in all cytologic parameters studied when compared with cotton-wool tips and two different spatulas in dogs, cats, sheep, goats, cattle, and horses.[63,66] The large size of the cytobrush is a disadvantage in the eyes of small animals but not in the large equine eye. A cytobrush was used to obtain a cytologic sample in a report in which a *Histoplasma* species was identified in a case of equine keratitis.[66]

During collection or transfer to slides, care must be taken with all samples to prevent cell damage and gently form a monolayer. The examiner should roll the swab gently, should not "spin" the cytobrush, and should not use excessive force with the blade edge, because this leads to greater cell damage.[63] Commonly used stains include the Gram stain and various Romanowsky-type stains (e.g., Diff-Quik, Wright-Giemsa stain) (Fig. 1-38). The Romanowsky-type stains can be used for quick "screening" in cases of ulcerative keratitis when information is needed to formulate an initial therapeutic plan. The Romanowsky-type stains are generally satisfactory for detection of bacteria, fungal hyphae, yeast bodies, inflammatory cells, and neoplastic cells. The Gram stain is indicated to provide further information about identified bacteria. Fungal hyphae may be difficult to identify on routine staining and may require more specialized stains for fungal elements, which include periodic acid-Schiff (Fig. 1-39) and Gomori's methenamine silver stain (Fig. 1-40).[67] In addition to routine staining, newer tests are becoming available for infectious diseases in the horse. These include the polymerase chain reaction (PCR) and immunofluorescent antibody test for herpes (i.e., EHV-1, EHV-2, EHV-4) and fungal DNA on corneal or conjunctival cytologic and histopathologic specimens.[68] Careful interpretation of these sensitive tests is required by the clinician, as demonstrated in one study in which EHV-2 DNA was detected by PCR in 22 out of 77 (28.6%) ocular swabs of normal horses and positive in only 4 out of 48 (8.3%) samples from diseased

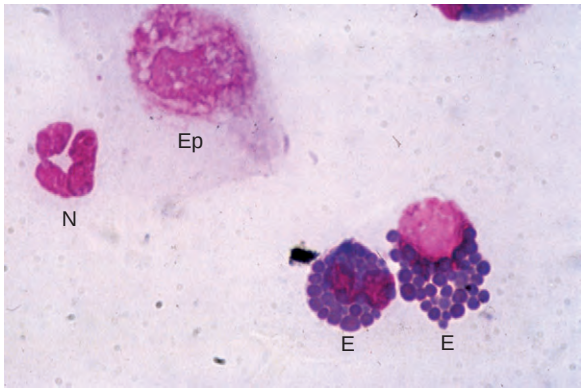


Figure 1-38. Commonly used stains include the Gram stain and various Romanowsky-type stains (e.g., Diff-Quik, Wright-Giemsa stain). Two equine eosinophils *(E)* are present on this Wright-Giemsa–stained slide. The equine eosinophil is unique in appearance and is not a routine finding. An epithelial cell *(Ep)* and a neutrophil *(N)* are also seen.

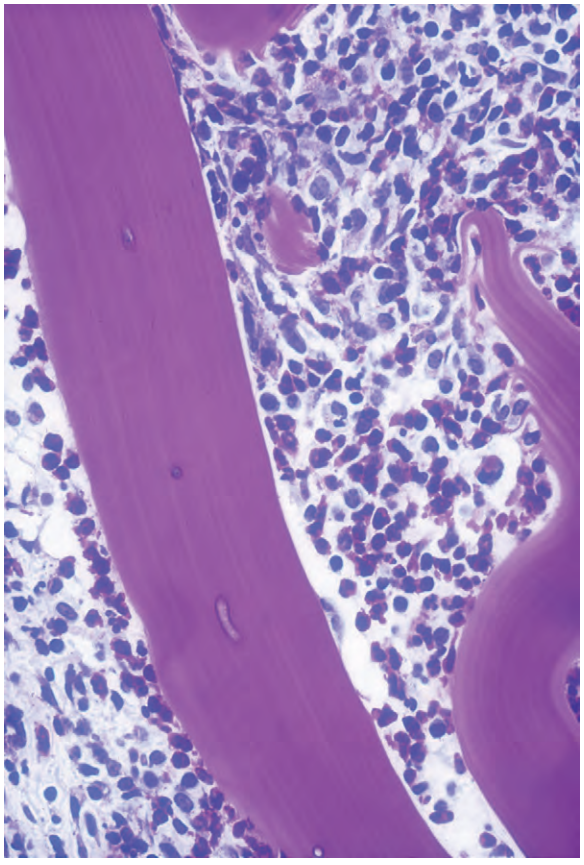


Figure 1-39. Fungal hyphae may be difficult to identify on routine staining. More specialized stains for fungal elements include periodic acid-Schiff. Descemet's membrane and the epithelium stain a dark pink with periodic acid-Schiff. The fungal hyphae can be seen as clear bodies within Descemet's membrane in this histologic section of cornea.

horses.[69] Topical fluorescein staining can interfere with test results (i.e., cause false-positive results), and therefore samples for immunofluorescent antibody testing should be collected before fluorescein staining.[70] For more information on collecting and interpreting ocular cytology, see Chapter 2.

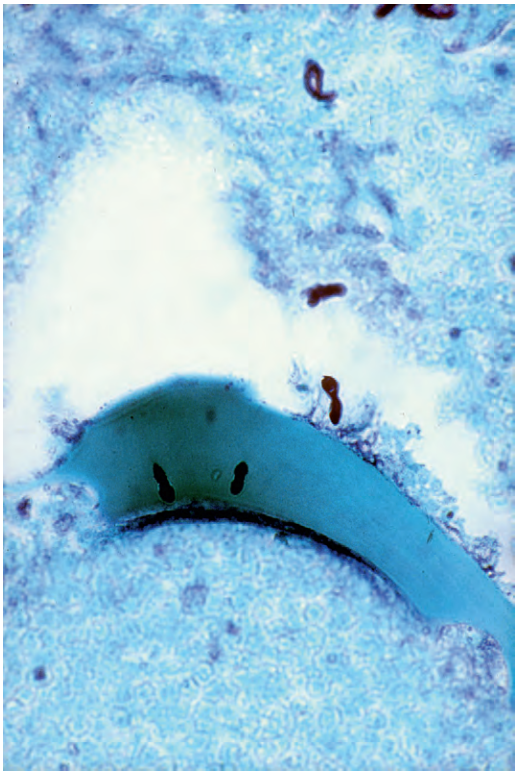


Figure 1-40. Fungal hyphae may be difficult to identify on routine staining. More specialized stains for fungal elements include Gomori's methenamine silver stain. The cornea stains blue-green, and the fungal hyphae stain black or dark brown in this histologic section of cornea.

OPHTHALMIC DYES

SODIUM FLUORESCEIN

Topical ophthalmic dyes are routinely used in veterinary medicine to aid in the diagnosis of corneal, conjunctival, and nasolacrimal diseases. Commonly used topical ophthalmic dyes include sodium fluorescein, rose bengal, Alcian blue, Trypan blue, and methylene blue.[12,71-73] Sodium fluorescein and rose bengal are the two most commonly used stains in clinical veterinary ophthalmology.[12,72,74,75] Indications for the use of topical ophthalmic dyes in the horse include determining the health and integrity of the corneal and conjunctival epithelium and the physiologic flow of the nasolacrimal system. Intravenous sodium fluorescein is used to perform fluorescein angiography and is discussed later in this chapter.

The most common use for topical sodium fluorescein is detecting ulcerative keratitis, but it will also stain conjunctival ulcerations and abrasions. In a corneal ulceration, the hydrophilic fluorescein binds to the corneal stroma but not to the lipophilic epithelium or to Descemet's membrane (Fig. 1-41). Small quantities can also pool or diffuse through intact epithelial cell intercellular spaces to reveal weakly staining epithelial microcysts and partial-thickness microerosions.[12,73] From the stroma, the dye can then readily pass through Descemet's membrane and the corneal endothelium to enter the aqueous humor and can be quantified (e.g., by fluorophotometry).

Fluorescein staining of the cornea is indicated for almost every condition in the horse involving its eye and orbit—a red

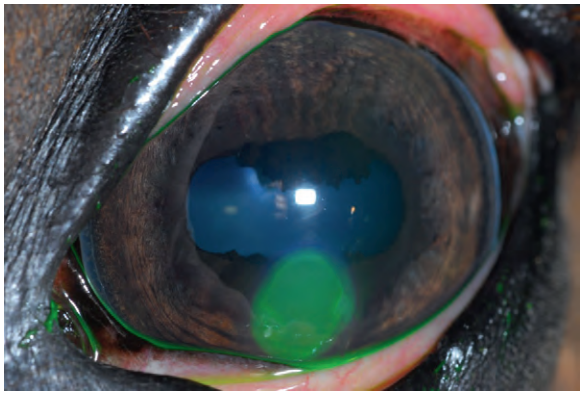


Figure 1-41. In a corneal ulceration, the hydrophilic fluorescein binds to the corneal stroma but not to the epithelium or to Descemet's membrane, resulting in a green stain.

Figure 1-42. The easiest method of applying topical fluorescein to horses is to place a sterile fluorescein strip in a 3-mL syringe, fill the syringe with sterile eyewash, replace the plunger, then squirt the solution through the hub of a 25-gauge needle from which the needle has been manually broken off.

or painful eye, discharge from the eye, an obvious corneal irregularity, history of ocular trauma—and for assessment of physiologic nasolacrimal function. Fluorescein is available as a sterile 0.5% to 2% alkaline solution or as a sterile impregnated paper strip.[76] The impregnated paper strips should be used for topical application, because the solutions have been associated with bacterial contamination.[77] Other equipment needed to perform the stain includes sterile eyewash solution and a 3-mL syringe with a 25-gauge needle. The easiest method of applying topical fluorescein to horses is to place a sterile fluorescein strip in a 3-mL syringe, fill the syringe with sterile eyewash, replace the plunger, and then squirt the solution through the *hub* of a 25-gauge needle from which the needle has been manually broken off (Fig. 1-42).[8,17] After application, the eyelids should be closed or the animal allowed to blink to distribute the stain evenly across the ocular surfaces. Excess fluorescein can be removed with gentle irrigation with eyewash if required. Alternatively, undiluted fluorescein applied topically may allow for better visualization of corneal epithelial erosions or early corneal trauma.* The use of an ultraviolet or blue light, usually available on a direct ophthalmoscope or the slit-lamp biomicroscope, may improve visualization of the stain. False-positive results may occur after the use of proparacaine topical anesthesia or if direct contact between the paper strip and cornea occurs, which may leave a mark that resembles a corneal defect.[12,17]

Fluorescein may also be used to detect leakage of aqueous humor through the cornea (i.e., Seidel test).[12,17] The Seidel test can be used to detect full-thickness corneal injuries or determine whether a corneal suture is leaking. The application of sodium fluorescein without subsequent irrigation results in a high dye concentration in which the dye fluoresces at wavelengths closer to the yellow and orange spectra. With or without gentle pressure on the cornea, aqueous leakage locally dilutes the fluorescein, and the dye fluoresces green.[12]

*Dr. Dennis Brooks, personal communication, 2009.

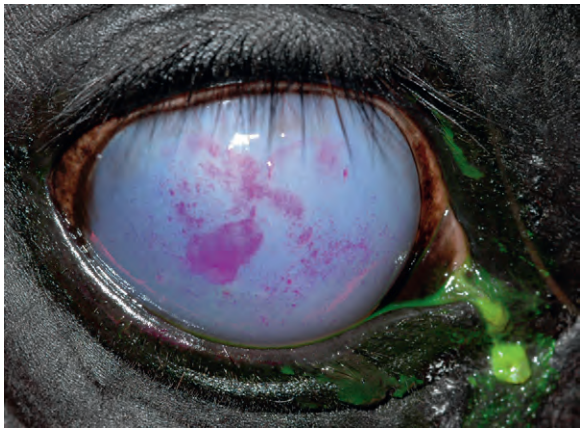


Figure 1-43. Rose bengal has been used to aid in the diagnosis of preocular tear film disorders, mucin preocular film deficiencies, and superficial corneal epithelial abnormalities in horses. Rose bengal stains dead and degenerating cells and mucus. (Photograph courtesy Dr. Dennis Brooks.)

ROSE BENGAL

Rose bengal (i.e., dichlorotetraiodo fluorescein) has been used to aid in the diagnosis of preocular tear film disorders, mucin preocular film deficiencies, and superficial corneal epithelial abnormalities in horses (Fig. 1-43). It can be used primarily or after sodium fluorescein application. Rose bengal stains dead and degenerating cells and mucus.[73] However, rose bengal has a dose-dependent ability to stain normal cells, and this ability is normally blocked by tear film components.[12,73,78] Therefore stain uptake may indicate tear film abnormalities, such as a mucin deficiency, more accurately than cell viability.[12,73,78] Rose bengal, like sodium fluorescein, is available both as an impregnated paper strip and a solution.[12,72,75] Use of the 0.5% or lower concentrations can minimize the irritation that can be associated with the 1% solution.[12] The dye has also been shown to be toxic to corneal epithelium at routine concentrations.[79] Slit-lamp biomicroscopy may be necessary for adequate visualization of rose bengal stain.

The use of rose bengal would be indicated in the horse in any of the conditions in which corneal or conjunctival ulceration is suspected, but especially when a viral or fungal cause is suspected. One report suggested that rose bengal staining is present as a result of ocular surface damage in the presence of keratomycosis.[80] Specimens obtained from horses with painful eyes should be stained with both fluorescein and rose bengal;

superficial keratitis may be negative for fluorescein but positive for rose bengal.[23,80]

ANTERIOR CHAMBER AND IRIS EXAMINATION

The intraocular portion of the ocular examination is conducted next. See Chapters 6 and 8 regarding the anatomy and diseases of the anterior chamber and uvea of the horse's eye. With a thin beam (slit) or small circular beam of light from the light source directed at a 45-degree angle to the eye, the anterior chamber depth and clarity are inspected. In a healthy horse, this will not result in any internal reflection of light from the aqueous, and the anterior chamber should appear clear (Fig. 1-44). If solids (e.g., protein, cells) are present in the aqueous, there will be a reflection of light from these particles (i.e., the Tyndall effect [see Fig. 1-44]).[19] This turbidity results in visualization of the beam of light traversing the anterior chamber and is referred to as *aqueous flare*. Aqueous flare (and other ocular lesions such as corneal edema, corneal pigment, and conjunctival redness) can be graded on a subjective scale from 1+ to 4+, with 4+ being the greatest degree of severity.

TONOMETRY

Measurement of intraocular pressure (IOP) in the horse has been revolutionized by the development of handheld portable digital tonometers. Direct tonometry via a manometer is the most accurate but invasive method for recording the IOP and is not practical for clinical use. Indirect tonometry, the

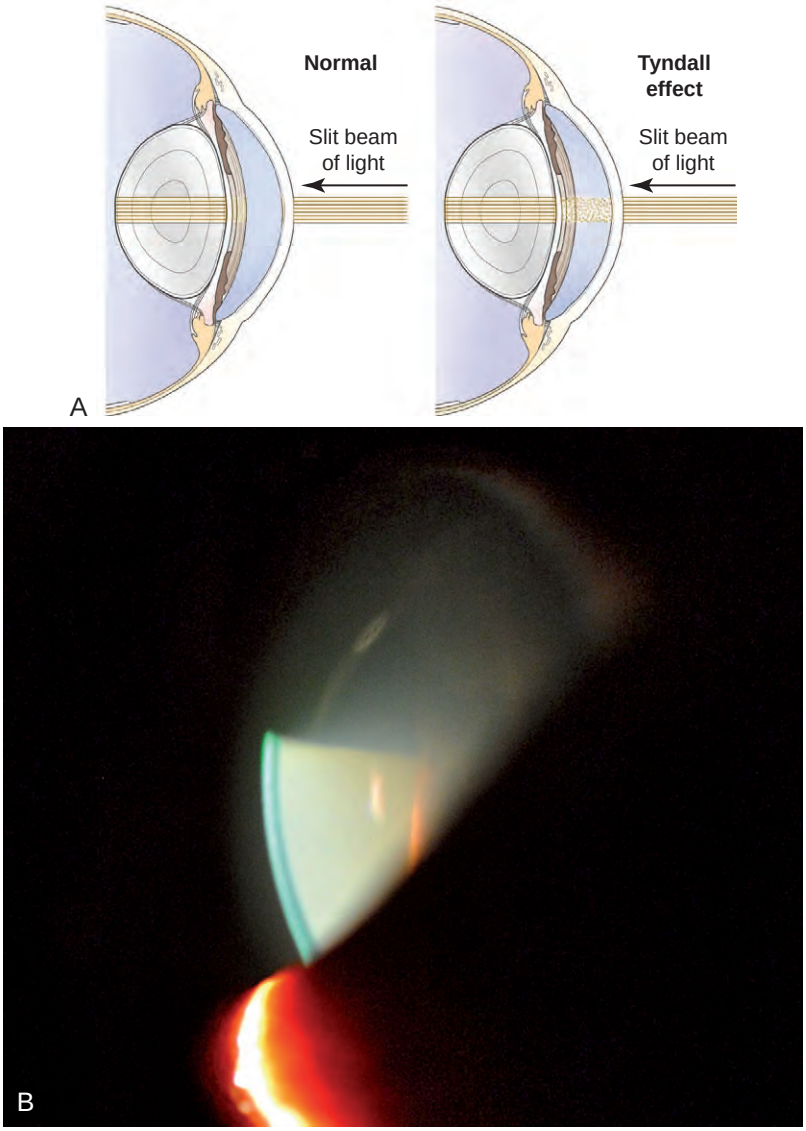


Figure 1-44. A, With a thin beam (slit) or small circular beam of light from the light source directed at a 45-degree angle to the eye, the anterior chamber depth and clarity are inspected. In a healthy horse, this will not result in any internal reflection of light from the aqueous, and the anterior chamber should appear clear. If solids (e.g., protein, cells) are present in the aqueous, there will be reflection of light from these particles (i.e., the Tyndall effect). **B,** This turbidity results in visualization of the beam of light traversing the anterior chamber and is referred to as *aqueous flare*.

measurement of corneal tension, is the technique used to determine IOP in clinical veterinary ophthalmology.[17] Digital, indentation, and applanation tonometry have all been described in the horse.[12] Digital tonometry, the estimation of IOP by digital palpation, cannot be considered accurate. Indentation tonometry, commonly performed with a Schiotz tonometer, requires general anesthesia (a lateral position) in the horse and is impractical. However, normal values have been reported for the Schiotz tonometer in the horse and are 14 to 22 mm Hg.[17] Applanation tonometry measures the amount of flattening (area of contact) of the cornea when a weight touches it.[12,17] The force it takes to flatten this portion of the cornea is an estimate of the IOP (Pressure = Force/Area). Rebound tonometry (TonoVet tonometer [ICare Finland Oy, Helsinki, Finland]) is another method to measure IOP in horses. This uses a disposable probe that is electromagnetically propelled to contact the cornea then rebound to the instrument, which then uses these rebound characteristics to estimate IOP.[81] Accurate measurement of IOP in the standing horse requires use of applanation or rebound tonometry (Fig. 1-45).[8,12] In one study involving normal horses, the TonoVet rebound tonometer correlated well to manometry IOP measurements, and IOPs obtained with the TonoVet rebound tonometer (Fig. 1-46) were higher than the TonoPen applanation tonometer (Fig. 1-47).[81]

Tonometry is indicated in horses that have focal or diffuse corneal edema, a red or painful eye, orbital trauma, a history of glaucoma in the opposite eye, or a lens luxation; it is also indicated for follow-up examinations of animals with medically controlled glaucoma.[8,12] Three separate readings with less than 5% standard error are averaged to obtain the IOP in millimeters of mercury.[12,17] If significant corneal disease is present, the most normal part of the cornea should be used to take readings.[17] A fibrotic and edematous cornea may result in a falsely elevated IOP.[17] Please see Chapter 9 for more information on the diagnosis and treatment of glaucoma.

Horses that require sedation for ocular examination may show dramatic decreases in IOP, as illustrated by one study in which xylazine decreased IOP by 23%.[82] In another report, the IOP range was 20.5 to 39.8 mm Hg and showed that both acepromazine and xylazine decreased IOP.[83] A combination of xylazine and ketamine had no effect.[84,85] It has been suggested that horses without an auriculopalpebral block will have an elevated IOP due to eyelid tension,[17,85] but this has not been supported in two other studies in normal horses.[82,86] However, horses with ocular disease such as glaucoma may be blepharospastic; therefore, auriculopalpebral blocks are recommended prior to tonometry. IOP in normal horses without an auriculo-

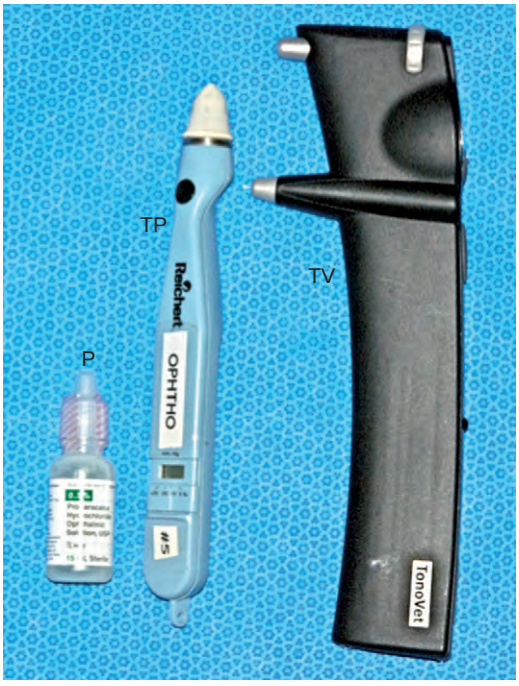


Figure 1-45. Materials needed to perform tonometry in the horse. Accurate measurement of intraocular pressure (IOP) in the standing horse requires tonometry, either using a TonoPen digital tonometer (TP) or a TonoVet rebound tonometer (TV), or similar instrument. The TonoPen tonometer requires use of a topical anesthetic, such as 0.5% proparacaine HCl (P), while the TonoVet does not.

Figure 1-46. Tonometry in the horse using a TonoVet tonometer.

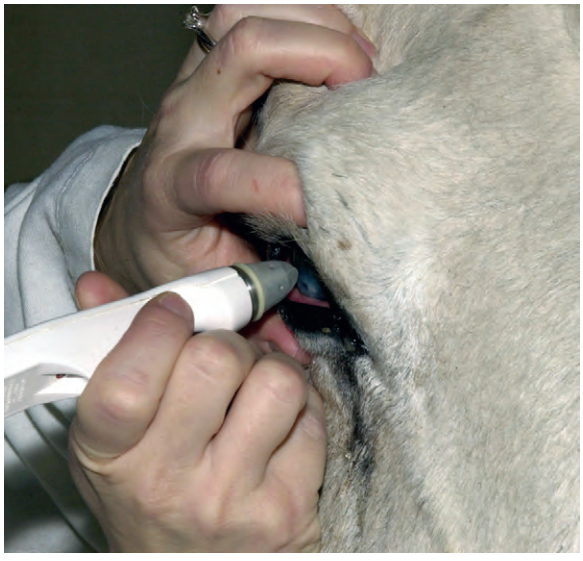


Figure 1-47. Tonometry in the horse using a TonoPen tonometer.

palpebral nerve block has been reported as ranging from 24.5 ± 4.0 mm Hg to 28.6 ± 4.8 mm Hg.[83,87] In one study of normal horses in which horses were tranquilized with detomidine and given auriculopalpebral nerve blocks, 87% of horses with their head positioned lower than their hearts had elevated IOP.[88] In another study, circadian rhythm was shown to have an influence on horses' IOP.[89] In this study, IOP was found to be low during the dark phase and high during the light phase, with a peak at the end of the light phase.[89] Evaluating the results of these studies together, it is recommended that the examiner be consistent when measuring IOPs in horses in terms of time of day, nerve blocks, and tranquilization, especially when performing repeated IOPs on the same horse. Tranquilization (always the same drug), auriculopalpebral nerve blocks, and an elevated normal head position are recommended for tonometry in horses.

Countertop electronic applanation tonometers may also still be available (e.g., MacKay-Marg [Biotronics, Redding, CA]; the Alcon pneumotonograph) and can be used to measure IOP in horses. The MacKay-Marg tonometer was shown to produce reliable results in comparison with direct tonometry in the dog, rabbit, and horse.[87,90,91] It has been used to study IOP in the horse.[82,84,86,87] IOP measured in the normal horse using the MacKay-Marg tonometer in one report was 20.6 ± 4.7 mm Hg.[82]

The Alcon pneumotonograph is an applanation tonometer-tonographer that measures IOP via a gas-suspended plunger. Measurements can be permanently recorded on heat-sensitive paper. However, pneumotonography may provide falsely elevated pressure readings in the horse.[92]

TONOGRAPHY

Tonography is the use of continuous tonometry to noninvasively estimate the pressure-sensitive facility of conventional aqueous humor outflow.[12,93] In theory, the weight of the tonographic probe on the cornea increases both IOP and rate of aqueous humor outflow without changing the rate of aqueous humor production.[12] The subsequent decline in IOP (decay curve) is measured over 2 to 4 minutes, thereby allowing an estimation of conventional outflow (corneoscleral trabecular outflow).[12] The unconventional outflow (uveoscleral) is pressure independent and thus not estimated by tonography. Uveoscleral outflow in the horse is substantial and may be the major outflow pathway, but it cannot be measured by tonography.[84] Tonography has been used in the normal horse to estimate the facility of aqueous humor outflow (C-value). A measured equine C-value of 0.88 ± 0.65 mL/min per mm Hg is substantially higher than that reported for the healthy dog and cat (0.24 to 0.27 mL/min per mm Hg).[93-95]

LENS EXAMINATION

For details on the anatomy and diseases of the lens, please see Chapter 7. Complete evaluation of the lens requires that the pupil be dilated, therefore, use of 1% tropicamide HCl is recommend prior to initiating the lens examination. The lens is initially evaluated using direct focal illumination (i.e., transillumination) and retroillumination. Transillumination of the lens is performed by directing a beam of light at a 45-degree angle into the lens and directly observing the lens using this light.[17] Retroillumination is examining the lens using light reflected by the tapetum and posterior segment structures of the eye. This done by using a direct ophthalmoscope or other focal light source (e.g., a Finnoff transilluminator) and starting about an arm's length from the horse, directing the light to obtain a bright tapetal reflex, then moving toward the animal to bring the lens structures into focus. This technique improves detection of opacities in the cornea, anterior chamber, lens, and vitreous because these opacities reflect, refract, or obstruct returning light.[17] Normal Y sutures can be visualized with transillumination but not with retroillumination.[17] With transillumination, nuclear sclerosis (i.e., the normal aging change of the lens due to increased lens density) will appear as a greater central translucence, with the cortex remaining clear (Fig. 1-48).[17] On retroillumination, the lens will appear clear with the pupil filled with the tapetal reflex, and a junction "ring" will be seen at the nuclear-cortical junction. With transillumination, the attachment of the lens zonules may be seen in a well-dilated eye immediately behind the edge of the pupil.[17] Cataracts will appear white on transillumination and black if they are not complete (i.e., light can pass around them) when observed on retroillumination (Figs. 1-49 and 1-50).[17] Direct retroillumination is performed by placing the objectives in the path of the refracted light, which causes opaque lesions to appear dark

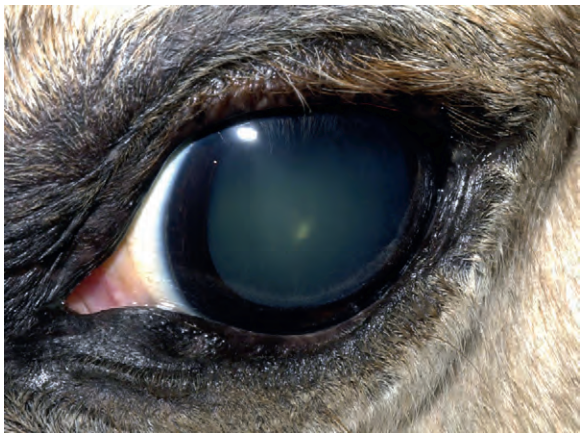


Figure 1-48. Retroillumination of nuclear sclerosis. The lens appears clear with the pupil filled with the tapetal reflex, and a junction "ring" can be visualized at the nuclear-cortical junction.

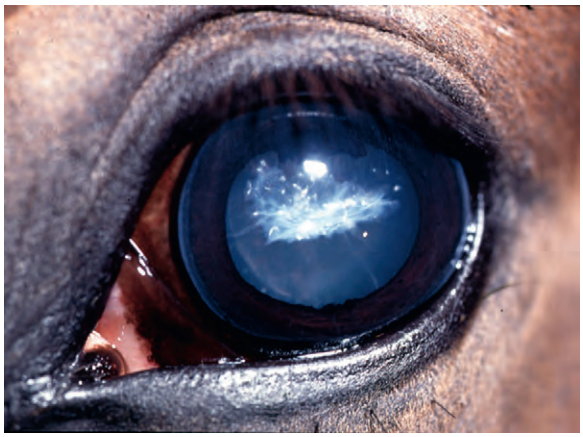


Figure 1-49. Direct transillumination of a cataract. The lesion appears white.

Figure 1-50. Retroillumination of an incomplete cataract. The lesion appears black.

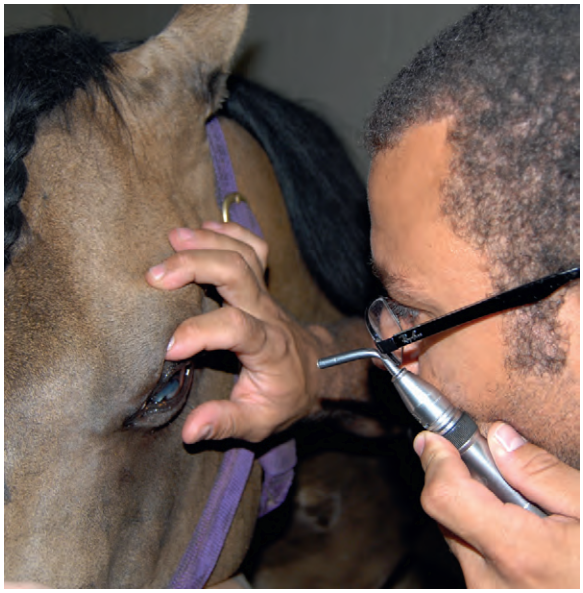


Figure 1-51. Transillumination can also be used to look directly at the ocular fundus of the horse. This is done by holding a light source against the examiner's face and directing the light into the horse's pupil.

against a light background and transparent lesions to appear clear within a dark halo.[17] Indirect retroillumination allows improved detection of transparent lesions by taking advantage of differences between their refractive indices and those of surrounding tissues.[17] Lesions are observed against a darker background because the reflected light is directed away from the objectives.[17] Any noted opacities can be further investigated with the slit-lamp biomicroscope.

BIOMICROSCOPY FOR LENS EXAM

The light beam of the biomicroscope should be angled at 20 to 45 degrees from the axis of the microscope and thus the visual plane of the observer (see Fig. 1-34). The initial examination of the lens should proceed with diffuse illumination; a wide, low-intensity slit beam should be used, and the microscope should be defocused from the light.[12] The anterior surfaces of the lens and vitreous should be inspected. The slit beam is then narrowed and intensified to reveal a two-dimensional cross-section of the lens, allowing the examiner to accurately determine lesion depth and axial positioning.[55] This is extremely important in evaluating the depth and location of lens opacities. Direct and indirect retroillumination are performed by reflecting the slit beam from deeper structures while focusing on more superficial structures.[55]

POSTERIOR SEGMENT OCULAR EXAM: VITREOUS AND RETINA

Normal anatomy and diseases of the posterior segment of the equine eye can be found in Chapter 10. Examination of the equine ocular posterior segment involves direct focal illumination (i.e., transillumination) using a focal light source as previously described in the lens section. Examination of the vitreous is performed first. Transillumination of the vitreous can reveal small posterior polar remnants of the hyaloid artery and areas of light reflection between vitreous planes.[17] Neither can be seen with retroillumination. Transillumination can also be used to look directly at the ocular fundus of the horse.[17] This is done by holding a light source against the examiner's face and directing the light into the horse's pupil (Fig. 1-51). The examiner moves forward toward the eye until the ocular fundus becomes visible. A large fundus area, approximately six times greater than that seen with an ophthalmoscope, can be visualized.[17] This is used as an initial screen for disease. Details of any observed abnormality can then be evaluated with direct or indirect ophthalmoscopy.

Ophthalmoscopy is the examination of the ocular fundus (i.e., choroid, retina, and optic nerve) and is an integral part of any ophthalmic or physical examination. There are two common methods of performing ophthalmoscopy in the horse: direct and indirect. Direct ophthalmoscopy can be performed by means of transillumination as previously described or with the use of a direct ophthalmoscope. Indirect ophthalmoscopy requires the use of a light source and a handheld lens.

Advantages of the direct ophthalmoscope are its upright image, availability of options such as slit and graticule, ability to alter the dioptric power of the ophthalmoscope, and the high magnification provided.[12,17] Disadvantages include the short working distance to the horse's head, a small field of view, lack of stereopsis, difficulty in examining the peripheral fundus, and greater distortion of the image when the visual axis is not clear.[12,17] Advantages of indirect ophthalmoscopy include a wider field of view, a safer working distance from the horse's head, potential for stereopsis (i.e., depth perception) if binocular equipment is used, greater view of the peripheral fundus, and the ability to alter the magnification by changing the diopter strength of the lens being used.[12,17] Disadvantages of indirect ophthalmoscopy include the inverted and reversed image, the expense of binocular equipment, and the initial difficulty of mastering the technique.[12,17]

The ocular fundus can be visualized without mydriasis in the horse, but a complete examination requires mydriasis. The use of a short-acting mydriatic (1% tropicamide) is recommended, as previously described, resulting in complete mydriasis within 10 to 20 minutes with a duration of 4 to 6 hours.[13] The menace response, dazzle reflex, resting pupil size, and

direct and consensual PLRs in each eye in bright and dim lighting should be evaluated before mydriasis is induced. Tonometry before pharmacologic mydriasis, indicated in small animals, is not absolutely necessary in the horse unless glaucoma is high on the list of differential diagnoses.

The normal ophthalmoscopic appearance of the ocular fundus of the horse (Fig. 1-52) is described in Chapter 10.[7,96-101] The equine ocular fundus is dominated by the tapetum fibrosum, which occupies the dorsal two-thirds of the posterior segment, and the stars of Winslow, which are end-on views of choroidal blood vessels traversing the tapetum (see Fig. 1-52). The tapetal color varies from green-yellow (most common) to aquamarine or turquoise.[8,98] Changes in tapetal color intensity from the central to peripheral tapetum have also been described.[102] The tapetum may be undeveloped in animals with albinotic or subalbinotic coat colors (Fig. 1-53).[8,103] The nontapetal area is usually dark brown, but this melanin in the retinal pigmented epithelium (RPE) may be absent, depending on coat and iris coloration. If the pigment is absent, the choroidal vessels can be visualized (see Fig. 1-53). The optic disc is horizontally oval, usually located slightly temporal and ventral in the nontapetal area, and salmon pink.[8,103] Retinal vessels radiate out only a short distance from the optic disc and are usually absent at the ventral disc border.[8,103]

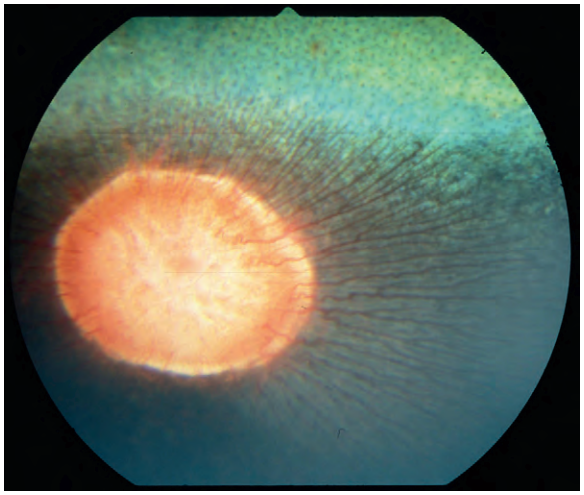


Figure 1-52. In most horses, a triangular fibrous tapetum in the dorsal choroid can be seen on ophthalmoscopic examination. End-on choroidal capillaries can be visualized as small dark dots throughout the tapetal fundus (i.e., stars of Winslow). The nontapetal area is usually dark brown.

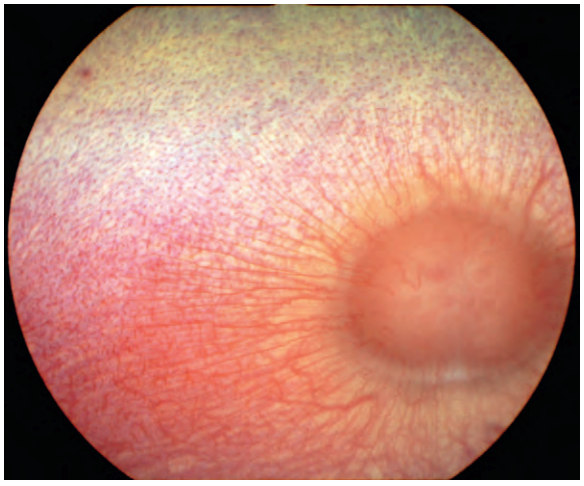


Figure 1-53. The tapetum may be undeveloped in animals with albinotic or subalbinotic coat colors. Melanin in the retinal pigment epithelium may be absent, depending on coat and iris coloration.

DIRECT OPHTHALMOSCOPY

Direct ophthalmoscopy is extremely useful for rapid ocular examination in horses, and it can be used to identify most lesions of the equine ocular fundus (Fig. 1-54).[8] In the horse, direct ophthalmoscopy can be performed with a transilluminator. The light source should be held against the examiner's face, near the eye, and directed through the horse's pupil. This provides a larger view of the fundus than can be seen with the direct ophthalmoscope, but it is not entirely in focus. This is a quick and useful method to screen for obvious signs of disease.

The direct ophthalmoscope consists of a halogen coaxial optical system and a power source.[12] A series of concave and convex lenses can be rotated through the viewing aperture by means of a dial (Fig. 1-55).[7,96,104] Green or black numbers represent convex or converging lenses, and red numbers represent concave or diverging lenses.[7,12,96,104] The size, shape, and color of the light beam can be adjusted by a second dial which produces large and small circles of light, a slit beam of light, a graticule, and two filters.[12,17] The size of the circular spot of white light should be adjusted to the patient's pupil size to minimize light reflections from the corneal surface.[12] The slit beam also aids in the detection of elevations or depressions in the ocular fundus, and distances can be estimated by changing the dioptric power of the ophthalmoscope.[12] When the retina is in focus at 0 diopter (D), the lesion is elevated if the lesion

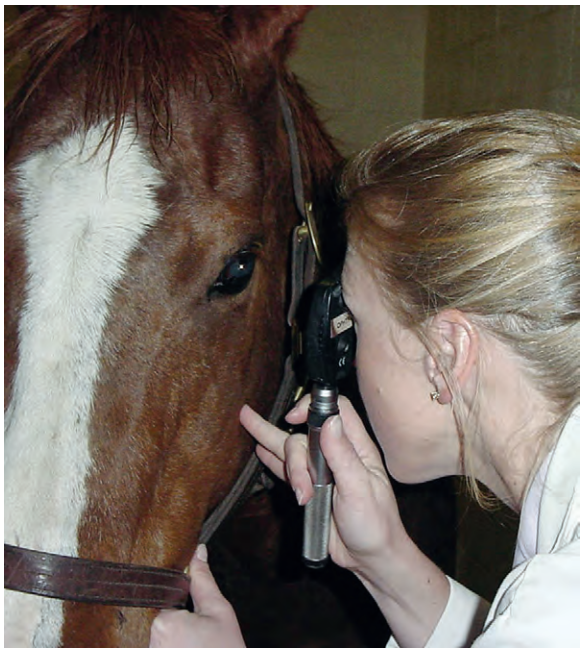


Figure 1-54. Direct ophthalmoscopy is extremely useful for rapid ocular examination in horses and can be used to identify most lesions of the equine ocular fundus. There is a short working distance to the horse's head.

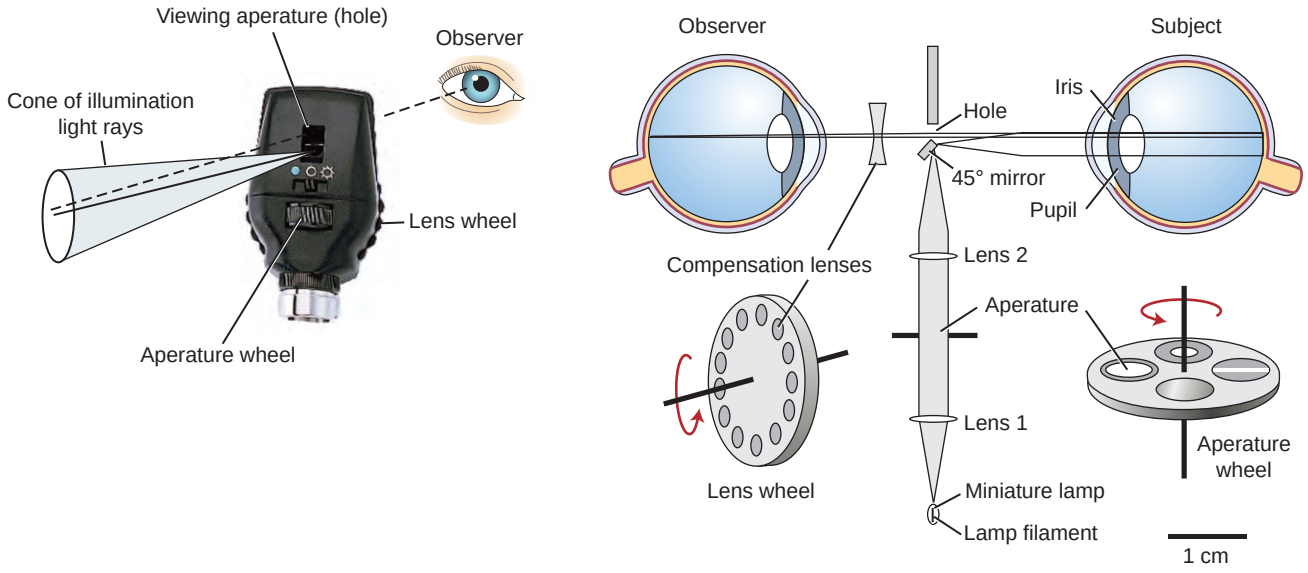


Figure 1-55. Direct ophthalmoscope schematic.

surface is in focus at a positive diopter setting (i.e., black numbers) and depressed if the lesion surface is in focus at a negative diopter setting (i.e., red numbers).[12] The graticule is a grid that can be used to size the optic disc and estimate the size of fundic lesions.[12] A red-free filter (appears green) is used to evaluate retinal vessels and differentiate hemorrhage (which appears black) from pigmented lesions (which appear brown).[12]

Most ocular fundi are in focus at 0 to −2 D if the examiner's vision is emmetropic, and therefore the ophthalmoscope should initially be set at 0 D.[12,17] The direct ophthalmoscope should be placed against the examiner's brow, and using the dominant eye, the examiner should identify the horse's fundic reflex from a distance of approximately 0.5 to 0.75 m.[12,17] Once the fundic reflex is identified, the examiner moves toward the horse to a point approximately 2 to 3 cm from the eye to visualize the fundus.[12,17] Ophthalmoscopy should then proceed to identification and examination of the optic nerve, retinal vasculature, nontapetal fundus, and tapetal fundus in quadrants. The resulting image with a direct ophthalmoscope is upright and magnified several times above normal with a millimeter equivalent per dioptric change of 1.33.[12,105] Magnification of the image varies with working distance; lesions should be compared with optic disc diameter rather than by units of measurement.[12,17]

Welch-Allyn has developed a monocular indirect ophthalmoscope (PanOptic; Welch-Allyn, Skaneateles Falls, NY) that can be used in an undilated pupil and has five times greater magnification than a routine ophthalmoscope (Fig. 1-56). The PanOptic ophthalmoscope also has a wider visual field than the direct ophthalmoscope, with an upright nonreversed image.

INDIRECT OPHTHALMOSCOPY

Monocular or binocular indirect ophthalmoscopy involves the use of a handheld converging lens held near the patient and a light source near the examiner's eye. A larger area of ocular fundus can be visualized with indirect versus direct ophthalmoscopy and may allow the examiner to more easily detect disease.

Figure 1-56. PanOptic ophthalmoscope, which has a wider visual field than the direct ophthalmoscope and an upright, nonreversed image.

In binocular indirect ophthalmoscopy, a mirror and a light source fitted onto a headband are used to direct light into the patient's eye. The handheld lens is used to magnify the reflected image, and two prisms are used to split the reflected beam so it can be directed into both the examiner's eyes, permitting stereopsis (Fig. 1-57).[12] The light intensity should be adjusted to permit adequate illumination without causing patient discomfort.[12]

In monocular indirect ophthalmoscopy, a handheld light source is used in addition to the handheld lens (Fig. 1-58). The light source should be placed near the examiner's eye and temple so that both the head and light source function as one unit. A direct ophthalmoscope can be used for indirect ophthal-

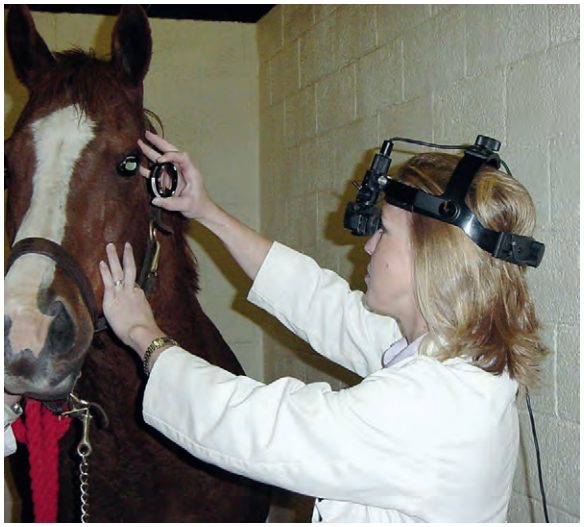


Figure 1-57. In binocular indirect ophthalmoscopy, a mirror and a light source fitted onto a headband are used to direct light into the patient's eye. The handheld lens magnifies the reflected image, and two prisms split the reflected beam so it can be directed into both the examiner's eyes, permitting stereopsis.

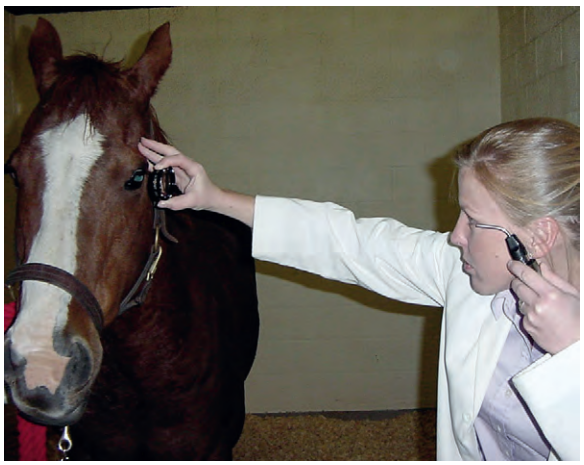


Figure 1-58. In monocular indirect ophthalmoscopy, a handheld light source is used in addition to the handheld lens. The light source should be placed near the examiner's eye near the temple so the head and light source function as one unit.

moscopy, and the dioptric power of the ophthalmoscope should be adjusted to +4 or +6 D.[12]

The handheld lens provides a virtual image (i.e., the image is inverted and reversed) of the patient's fundus. A variety of lenses are available, ranging from +14 to +90 D in strength. The +20-D and +28-D lenses are the most useful in the horse, providing a fundus view of approximately 40 degrees. The quality of the handheld converging lens affects the ease and clarity of the evaluation. The smaller the lens diopter rating, the greater the fundic magnification.[12] In the horse, lateral magnification has been reported for 14-D (1.18), 20-D (0.79), 30-D (0.51), and 40-D (0.38) lenses.[105] Axial magnification in the horse has also been reported for 14-D (0.38), 20-D (0.84), 30-D (0.35), and 40-D (0.19) lenses.[105]

The refractive error of an animal can be semiqualified during indirect ophthalmoscopy by slowly withdrawing the lens toward the examiner and further from the eye and observing any change in magnification. The fundic image will get larger (myopic) or smaller (hyperopic), or it will remain static (emmetropia).[103] For a more accurate measurement of refractive error, streak retinoscopy can be performed. This technique is described later in this chapter.

Binocular indirect ophthalmoscopes suitable for use in horses, some with battery-powered illumination, are available from Heine, Keeler, Propper, Topcon, Welch-Allyn, Zeiss, and others.

ADVANCED OPHTHALMIC PROCEDURES

RETROBULBAR NERVE BLOCK

The retrobulbar nerve block temporarily blocks the optic (CN II) and oculomotor (CN III) nerves, the abducens nerve (CN VI), trochlear nerve (CN IV), and the maxillary and ophthalmic branches of the trigeminal nerve (CN V). Retrobulbar anesthesia can be used as an adjunct to general anesthesia in horses to reduce nystagmus and enophthalmos during corneal and intraocular surgery and prevent the need to give the horse neuromuscular blocking agents.[106] It can also be used to perform standing eyelid and corneal surgeries, as well as to perform anterior or posterior chamber paracentesis for diagnostic purposes. Lastly, it can be used for the primary purpose of analgesia (e.g., during the immediate postoperative period after an enucleation). Three methods have been described for retrobulbar anesthesia in the horse: the four-point block, modified Peterson block, and direct injection into the orbital cone above or below the zygomatic arch.

The site for the retrobulbar injection above the zygomatic arch and caudal to the temporal process of the malar bone is preferred because it requires a single needle penetration, is not located near the globe, and if performed properly, avoids the direct location of the optic nerve. The orbital fossa above the dorsal orbital rim and zygomatic arch is clipped and aseptically prepped with povidone-iodine (Betadine) solution. Care must be taken to avoid getting surgical scrub (Betadine or Nolvasan) or alcohol on the ocular surface, because severe irritation and corneal ulceration may develop. Therefore these substances are avoided around the eye. A 22-gauge, 2½-inch spinal needle (BD, Franklin Lakes, NJ) is placed through the skin perpendicular to the skull, in the orbital fossa just posterior to the posterior aspect of the dorsal orbital rim (Fig. 1-59). The needle is advanced posterior to the globe until it reaches the retrobulbar orbital cone. When the needle advances to this location, the eye will have a slight dorsal movement as the needle passes through the fascia of the dorsal retrobulbar cone into the retrobulbar space. The needle is advanced until it just passes into the cone, evidenced by the sudden release of the eye back to normal position or a slight "popping" sensation. Once the needle is positioned, 10 to 12 mL of 2% lidocaine HCl is injected into the retrobulbar space. Mepivacaine (Carbocaine) can also be deposited. Before injection, aspiration should be performed to make sure the needle is not positioned within a blood vessel. During the injection, the globe is pushed externally (i.e., slight exophthalmos), indicating an accurate placement of anesthetic. Onset of anesthesia usually occurs within 5 to 10 minutes. The duration of effect is approximately 1 to 2 hours. Ocular sensation, blink reflex, and vision will be

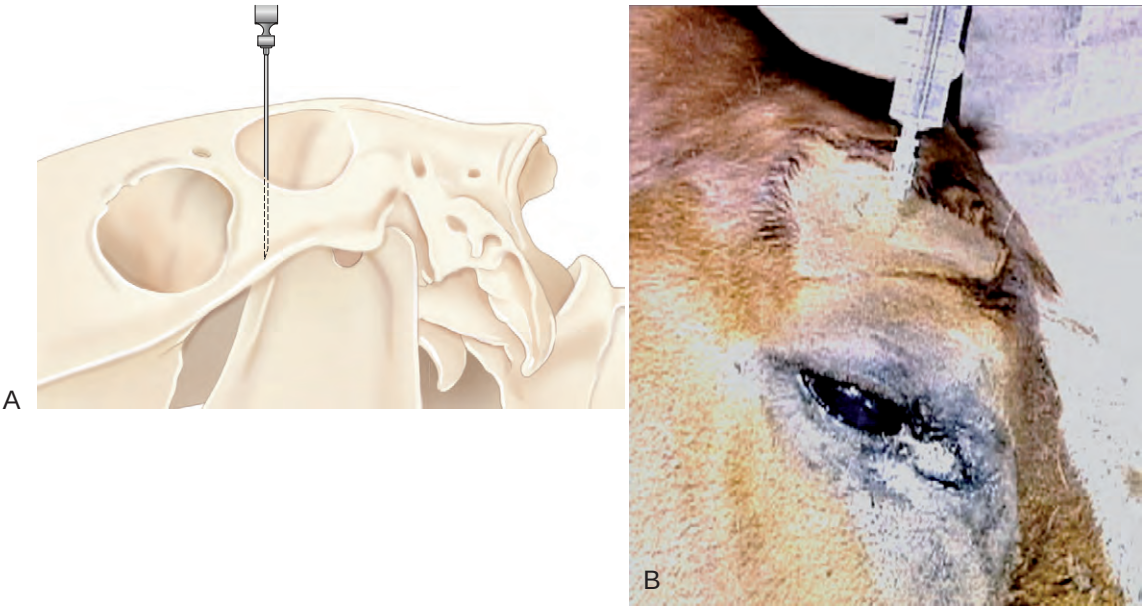


Figure 1-59. Retrobulbar block. **A,** Placement of the needle for the retrobulbar block. **B,** The orbital fossa above the dorsal orbital rim and zygomatic arch is clipped and aseptically prepped. A 22-gauge, 2½-inch spinal needle is placed through the skin perpendicular to the skull, in the orbital fossa, just posterior to the posterior aspect of the dorsal orbital rim.

compromised during this time, so stall rest and protection of the eye with lubricants or a temporary tarsorrhaphy are recommended for 2 to 4 hours after anesthesia.

Retrobulbar injections with lidocaine have been performed routinely to provide ocular anesthesia, with and without general anesthesia, for ocular surgery at the North Carolina State University College of Veterinary Medicine for over 20 years. Very few complications have been documented from the procedure. The most common complication is a hypersensitivity to lidocaine, which results in generalized formation of hives and severe retrobulbar swelling after injection. These lesions will resolve with the use of systemic nonsteroidal antiinflammatory and antihistamine medications within 3 to 5 days after the injection. Another complication is development of exposure corneal ulcers, likely caused by exposure of the cornea due to poor eyelid function and corneal desensitization. Careful monitoring of eyelid function and frequent topical lubrication until full function returns will prevent this complication. Retrobulbar block denervates the optic nerve, therefore, the horse will have decreased vision or be blind in that eye for 1 to 3 hours after injection. Therefore, it is recommended that the injection be performed unilaterally so that complete blindness does not occur after injections.

The four-point block, a local muscle block, has also been described for retrobulbar anesthesia in the horse.[17] Lidocaine or mepivacaine, 5 to 10 mL, can be deposited laterally by passing a 20-gauge, 7.5-cm (3-inch) needle through the lateral canthus skin and following the globe posteriorly. Ventrally, the needle passes through the skin or bulbar conjunctiva posteriorly. The needle should be directed slightly nasally to avoid the optic nerve. Nasally, the needle passes through the base of the elevated third eyelid and posteriorly into the orbit. Dorsally, the needle is passed through the center of the upper eyelid following the globe posteriorly. This technique should not be used when intraocular surgery is performed, because it may put pressure on the globe.[17] Failure to inject anesthetic into the muscle cone or injecting it in front of the orbital septum may cause the drug to migrate forward under the conjunctiva and cause severe chemosis.[17] There is no advantage of this technique over the single-injection retrobulbar block described earlier, therefore the four-point block is not recommended unless adequate anesthesia has not been achieved with the first block.

Use of a modified Peterson block has been described in the horse, although it would rarely have application in most types of ocular surgery and is not recommended.[17]

Although few complications have been seen after retrobulbar and eyelid nerve blocks in horses, rare problems associated with the injections can occur during or after the surgical procedure.[106] Bacteria can be deposited in the orbit by the spinal needle if the skin surgical site was not aseptically prepared. This may result in orbital abscess or cellulitis formation. Laceration of the extraocular muscles, optic nerve, sclera, or ophthalmic arteries by the needle is also possible during the injection. Traumatic injury during needle introduction could result in retrobulbar hemorrhage or optic neuritis. An isolated case of oculocardiac reflex elicitation during the block has also been reported.[107] These complications can be mostly avoided by use of appropriate tranquilization, eyelid nerve blocks, antiseptic technique, and added restraint methods to restrict movement by a standing horse. The relatively low complication rate associated with the injection techniques far outweighs the risks associated with general anesthesia in horses.

ORBITAL ASPIRATION

Aspiration of a lesion (e.g., mass, fluid) in the equine orbit can be performed for cytology, culture, and histopathologic examination.[12] An 18-gauge, 10-cm, slightly curved needle is inserted

1 cm lateral to the lateral canthus and then directed posteriorly in a line parallel to the medial canthus.[8,108] Approaching the retrobulbar space via the supraorbital fossa as described for the retrobulbar block is also possible, especially if the lesion is in the dorsal retrobulbar area. For accurate and less risky sample collection, ultrasound-guided fine-needle aspiration, versus blind aspiration, may decrease the risk of injuring orbital structures.

AQUEOUS PARACENTESIS

Aqueous humor fills the anterior segment of the eye, supplies nutrients to the avascular cornea and lens, and removes waste products from the interior of the eye. Small amounts of aqueous humor (0.2 to 0.5 mL) can be aspirated from the anterior chamber in the horse.[12,109,110] Aqueous paracentesis can be performed with the horse under general anesthesia or standing with sedation, topical anesthesia, and a retrobulbar block.[12] The site for aspiration should be the dorsal or dorsotemporal limbus to take advantage of the scleral extension beyond the iris base (Fig. 1-60).[17] The bulbar conjunctiva should be cleaned with dilute Betadine (5%) solution and sterile saline solution or eyewash.[12] Use of a topical antibiotic such as moxifloxacin (Vigamox [Alcon]) before and after paracentesis is recommended to further decrease possible bacterial contamination. The bulbar conjunctiva is grasped with thumb forceps near the site of entry, and a 27- to 30-gauge needle is directed through the limbal cornea or subconjunctival limbus (bevel up) anterior and parallel to the iris (see Fig. 1-60).[12] The needle should be tunneled for several millimeters through the limbus into the anterior chamber, which may facilitate rapid formation of a seal after the needle is withdrawn.[12] A small volume (0.2 to 0.5 mL) of aqueous humor is slowly aspirated, and the needle is withdrawn.[12] A syringe can be attached to the needle when this is first performed or after the needle is placed into the anterior chamber; or no syringe may be used, and the aqueous that fills the hub can be drawn into a capillary tube. The tip of the needle should be visualized at all times to avoid lacerating the iris or lens capsule.

Injections of therapeutics into the anterior chamber (e.g., tissue plasminogen activator, antibiotics) can also be performed using the same technique, except that injection of solution is made instead of aspiration. If an aqueous humor diagnostic sample is also required, this sample should be collected first, followed by injection of the medication.

Possible complications of aqueous paracentesis include hyphema, anterior lens capsule rupture with subsequent phacoclastic uveitis, endophthalmitis, anterior uveitis, corneal edema associated with endothelial damage, and choroidal edema and hemorrhage.[12] In an attempt to minimize development of inflammation and other complications after the procedure, the aqueous humor should be very slowly removed, and the volume removed should be 0.5 mL or less. Diagnostic procedures that can be performed with aqueous humor samples in the horse include cytology, culture and sensitivity, protein measurement, antibody titers (e.g., *Leptospira* species), and polymerase chain reaction (PCR).[111-115] See Chapters 7 and 9 for more information on the diagnostic value of aqueocentesis.

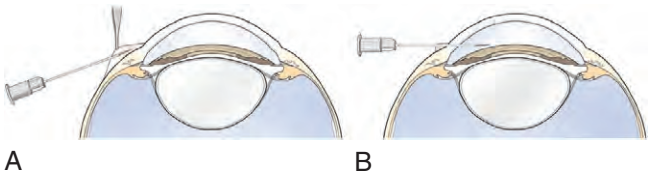


Figure 1-60. Aqueous paracentesis. **A,** The bulbar conjunctiva is grasped with thumb forceps near the site of entry. **B,** A 27- to 30-gauge needle is directed through the limbal cornea or subconjunctival limbus anterior and parallel to the iris, avoiding the lens. A drilling and tunneling motion will facilitate entry through the sclera and may facilitate rapid formation of a seal after the needle is withdrawn.

VITREOUS PARACENTESIS

The location for vitreous paracentesis is approximately 10 to 12 mm from the dorsolateral limbus. This will place the needle through the pars plana and avoid introducing the needle through the sensory retina.[116] A 23- to 25-gauge needle is inserted through the conjunctiva and sclera, with the needle directed posteriorly to avoid the lens (Fig. 1-61). As with aqueous humor, diagnostic procedures performed on vitreous humor samples include culture and sensitivity, cytology, protein measurement, antibody titers, and PCR.[12,117,118] Vitreous paracentesis can also be performed to instill therapeutic medications, such as gentamicin for ciliary body ablation in cases of glaucoma and antibiotics in cases of endophthalmitis. Complications of vitreal paracentesis include hemorrhage, retinal detachment, and endophthalmitis—risks versus benefits of this procedure have to be considered.

ADVANCED OPHTHALMIC DIAGNOSTICS

CORNEAL ESTHESIOMETRY

The corneal reflex is one of the most sensitive reflexes of the body, and its purpose is to protect the eye. Corneal sensitivity can be tested empirically by touching the cornea with a Dacron-tipped applicator and observing a corneal reflex (response of blinking, globe retraction, or avoidance), or using an esthesiometer. Corneal esthesiometers evaluate corneal sensitivity by

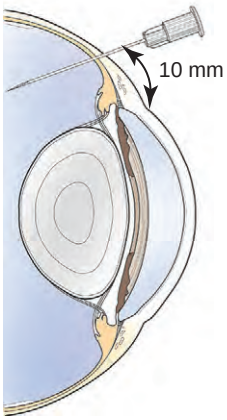


Figure 1-61. Vitreous paracentesis. The dorsal scleral overhang requires a greater distance from the limbus with a dorsal site than with a temporal site. A 23-gauge needle is inserted through the conjunctiva and sclera, with the object being to pass through the pars plana of the ciliary body. The needle should be directed toward the optic nerve to avoid the lens.

measuring the corneal touch threshold (CTT), which is the threshold of the stimulus that results in a corneal reflex.[119] Estimation of corneal sensitivity may be used to diagnose and monitor corneal diseases, evaluate progression of corneal diseases after surgery, and monitor the effects of surgery and topical medications. The Cochet-Bonnet esthesiometer (Luneau Ophthalmologie, Chartres Cedex, France) has been described to evaluate CTT in horses.[49,119] The instrument contains a nylon or platinum filament with an adjustable length and a defined diameter. The filament is applied in different lengths to the cornea until a corneal reflex is elicited with the same pressure or length of filament.[49] The length of the nylon filament estimates the applied pressure on the corneal surface and is readable on a millimeter scale. The shorter the filament, the more pressure is applied to the cornea and vice versa.

The CTT in the central area of the equine cornea, similar to that in other species, has been shown to be the most sensitive, and the dorsal region the least sensitive.[49,119] A decrease in corneal sensitivity was shown in sick neonatal foals compared with normal adults.[49] Corneas in healthy foals were slightly more sensitive than those in healthy adults.[49]

In humans, it has been shown that the CTT is influenced by age, mental status, iris color, hormone cycle, gravidity, time of day, humidity, room temperature, esthesiometric method, and investigator.[120-124] A decrease in sensitivity has been described in cats with herpes keratitis, in dogs with spontaneous chronic corneal epithelial defects, and in dogs after neodymium yttrium aluminium garnet (Nd:YAG) laser photocoagulation.[125,126] Further investigation into the effects of corneal disease, cyclophotocoagulation, and surgeries such as penetrating keratoplasty on CTT needs to be performed in the horse.

ULTRASONIC PACHYMETRY

Pachymetry is a technique that measures the corneal thickness in vivo. Ultrasonic pachymetry is an accurate and reliable in vivo method to measure corneal thickness in animals and humans.[82,127,128] Use of optical coherence tomography and confocal microscopy may be more accurate methods to measure corneal thickness,[129-131] but the cost of these modalities and the lack of portable equipment make them not as practical for use in the horse. Prior to use of ultrasonic pachymetry, corneal thickness was measured from gross postmortem specimens and histologic specimens, which overestimated corneal thickness because the cornea swells after death.[132] Ultrasonic pachymetry measures the time required for ultrasonic energy to traverse the cornea, with a preset constant for velocity of sound, and converts this to a measure of thickness.[127,128,133] A transparent cornea is required for ultrasonic pachymetry full-thickness corneal measurements.[12]

A 20-MHz ultrasonic pachymeter (DGH500 [DGH Technology Inc., Exton, PA]) has been used to study the horse. It has been used to determine corneal thickness in healthy juvenile and adult horses, Rocky Mountain horses with cornea globosa, horses that have been given an auriculopalpebral nerve block and xylazine, and healthy Miniature horses.[36,82,133,134] Corneal thickness of enucleated globes measured by a caliper was approximately 858 mm centrally, 914 to 939 mm dorsally and ventrally, and 861 to 898 mm laterally and medially.[133] With ultrasonic pachymetry, corneal thickness was reported to be 793 mm centrally, and thicker peripherally at 831 to 924 mm in vivo.[82] Three reports indicate that the dorsal and ventral portions of the cornea are thicker than the central cornea.[20,36,69] Eyelid block, sedation, age, and sex did not affect corneal thickness.[82] However, thickness of the central portion of the cornea may increase up to the age of 6 months in a healthy horse.[36] Corneal thickness in the normal Miniature horse is 785 mm centrally.[134] See Chapter 8 for more information on corneal thickness and diseases of the cornea in the horse.

SPECULAR MICROSCOPY

Specular microscopy was developed to evaluate the corneal endothelium and lens. Contact and noncontact scanning specular microscopes that allow recording a larger field of view can be used. In specular microscopy, differential focusing is used on the corneal epithelial and endothelial cell surfaces at a 45-degree angle. Noncontact specular microscopy has been used to determine corneal endothelial cell counts and corneal thickness in healthy horses (Topcon SP-2000P [Topcon America, Paramus, NJ]).[133] The average endothelial cell count was 3155 ± 765 cell/mm^2. There was not a great difference between eyes of the same horse or various quadrants of the cornea. As in dogs and humans, in the horse the endothelial cell count decreases with age.[133,135]

Corneal edema occurs when a minimal critical cell density is reached. This number has not yet been established in horses. Knowing corneal endothelial cell counts would be useful in evaluating horses with unexplained corneal edema or penetrating injury and horses that have undergone penetrating keratoplasty or phacoemulsification. Corneal endothelial cell count is also vital information in donor tissue to be used for corneal transplantation.[135-137] Confocal microscopy can be used to image the corneal endothelium and has many potential clinical uses as the technology becomes more readily available (Fig. 1-62).[131] See Chapter 8 for more information on corneal endothelium, corneal edema, and diseases of the cornea in the horse.

ELECTRORETINOGRAPHY

Electroretinography is used to determine function in the outer layers of the retina by recording the summation of electrical response when the retina is stimulated by light.[88,138,139] The electroretinogram (ERG) is the recorded total electrical response of the retina to that light. The ERG is not a measure of vision but only a measure of functional integrity of the outer portion of the retina and RPE. A blind animal (e.g., with disease of the inner retina, optic nerve, or central nervous system) can have normal ERG findings. The ganglion cells, their axons, and the optic nerve do not contribute to the ERG recording.

An ERG is indicated whenever visual problems in the outer retina are suspected. In the horse, an ERG is indicated to assess for retinal function in cases of equine recurrent uveitis (ERU), corneal or lens opacities that preclude visualization of the ocular fundus (e.g., cataracts, diffuse corneal edema), suspected congenital stationary night blindness, non–ERU-related retinitis and chorioretinitis, drug toxicity, retinal detachment, ocular trauma, and chronic glaucoma.[12,140-144] Please see Chapter 10, Diseases of the Ocular Posterior Segment, for more information on these diseases and their effect on the ERG.

The primary components of an electroretinograph are a light source (photostimulator), a high-gain amplifier, and

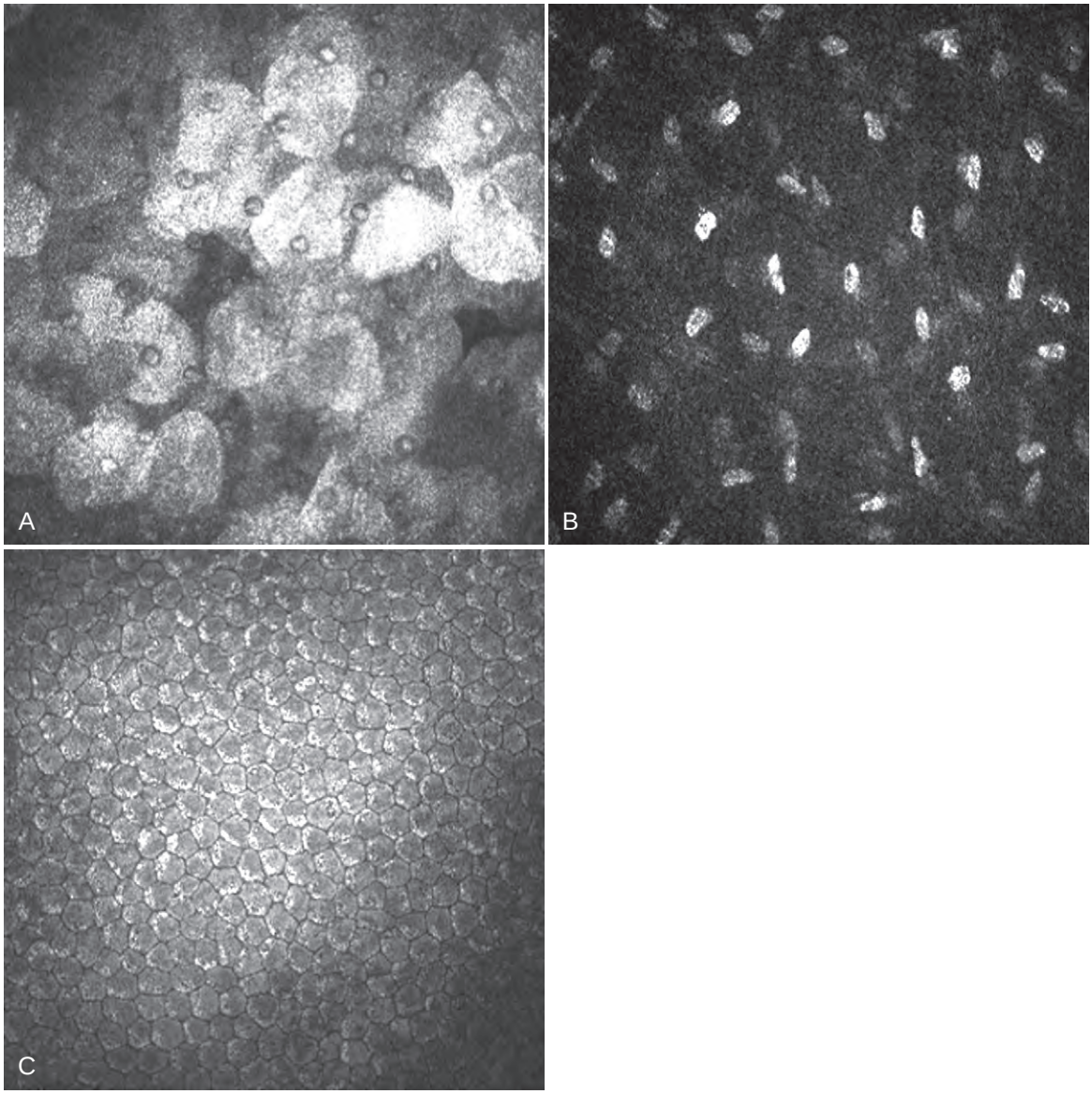


Figure 1-62. Confocal microscopy of the equine corneal epithelium **(A),** stroma **(B),** and endothelium **(C).** (Photographs courtesy Dr. Eric Ledbetter.)

a recorder.[139] Three electrodes are needed: a positive (i.e., active) corneal electrode, a negative (i.e., reference) electrode, and a ground (i.e., indifferent) electrode (Fig. 1-63, *A*).[139] The clinical ERG consists of three basic waveforms, the a-wave, b-wave, and c-wave (see Figure 1-63, *B*).[139] The a-wave is an initial negative deflection. This is followed by a positive deflection, the b-wave, which has a higher potential (amplitude) and is followed by an afternegativity. In addition to the a-wave and b-wave, there is usually a second positive deflection, the c-wave, which is more prolonged. The origin of each wave component is complex and poorly understood. Latency and implicit times, the time from onset of a stimulus to the peak of a particular response, are also important in evaluating the ERG. In a diseased eye, the amplitudes typically decrease while the implicit times increase.

One of the intrinsic factors that can affect the ERG is the eye's state of light adaptation, classified as scotopic (dark-adapted) and photopic (light-adapted).[139] The scotopic state of the eye is primarily a rod response. The photopic state of the eye is primarily a cone response. Rods are more numerous than cones in the horse, so the ERG is primarily a rod response in this species.[139] The rod and cone responses can be separated by repetitive stimuli or flickers of varying frequency, light adaptation state of the retina, and variation in the intensity of the stimulus.[139] Other intrinsic factors that may affect the ERG include age, transparency of the ocular media, retinal integrity, and retinal circulatory disturbances.[139] Amplitudes can vary according to species, state of adaptation to light, ocular movements, pupillary dilation, and pathologic state of the eye.[139]

Extrinsic factors that affect the ERG include the light stimulus used, electrodes used, and recording equipment.[139] The light stimulus may have variations in duration of flash, light intensity, frequency, and color. The positioning and type of electrode affect the level of background noise and amplitude of the

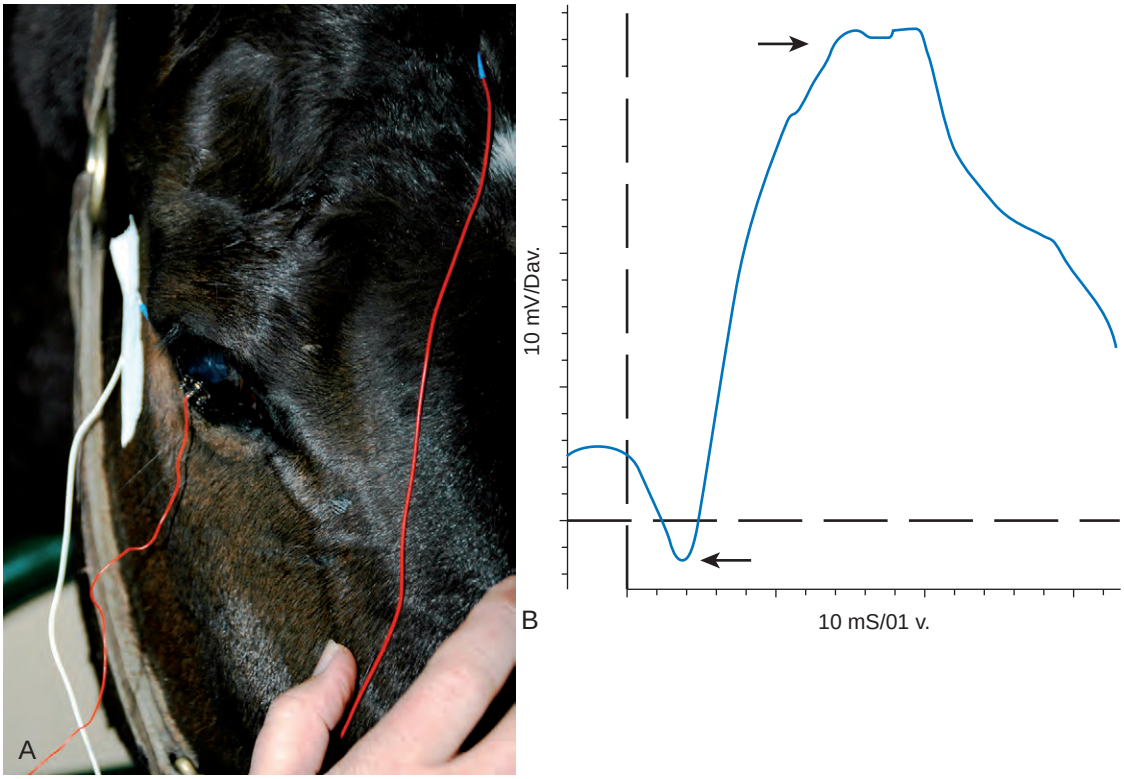


Figure 1-63. **A,** Three electrodes are in place for performance of an electroretinogram (ERG) in the standing horse. **B,** The clinical ERG consists of three basic waveforms (a-wave, b-wave, and c-wave). The a-wave, an initial negative deflection *(bottom arrow)*, and the b-wave, positive deflection, which follows the a-wave *(top arrow)*, are most prominent in the horse.

ERG. Both extrinsic and intrinsic factors can be minimized and must be monitored by establishing a protocol for evaluating the ERG in the horse.[139]

Three main techniques used in clinical veterinary ophthalmology are the flash ERG, pattern ERG, and visual evoked potentials. In contrast to the flash ERG, the pattern ERG originates in the inner retina and therefore is helpful in diagnosing diseases such as glaucoma. Limits to visual resolution can also be established by pattern ERG. Visual evoked potentials, although not ERGs, can be recorded with the same equipment and can record activity from the visual cortex. This activity has been mapped in dogs and cats but not in the horse.[145]

Flash electroretinography is the most common method for assessment of retinal function in veterinary ophthalmology.[139] Proper ERG recording requires general anesthesia in animals to prevent recording artifacts from muscle activity and to allow ideal positioning of the eyes. General anesthesia is inherently risky, expensive, and more labor intensive in the horse. Also, the inhalant anesthetics, halothane and isoflurane, have been shown to have a negative effect on the ERG amplitude and inner retinal function in other species.[139,146] Electroretinography in the standing horse can be frustrating because sedation will not eliminate the almost constant head movement. Sedated or unsedated, the horse may still shy from the closeness of the stimulator, and even small head movements can easily dislodge the other electrodes and require their replacement.[139] However, with proper restraint, auriculopalpebral nerve blocks, sedation, and patience, an adequate ERG can be recorded in the standing horse.[139]

Findings from flash ERGs in horses have been reported, and the implicit times and amplitudes were similar in the various reports.[88,139,141,143,147-149] Mean reported latencies and amplitudes of the photopic a- and b-waves are 5.19 ± 1.56 and 26.63 ± 2.26 ms and 40.89 ± 20.50 and 184.75 ± 63.26 mV, respectively.[139] Mean latencies and amplitudes of low-intensity flash (0.33 cd/m^2 with 5 minutes of dark adaptation) and high-intensity flash (4.62 cd/m^2 with 5 minutes of dark adaptation) scotopic a- and b-waves, with pseudo-Ganzfield stimulation, DTL (Dawson, Trick, and Litzkow) microfiber electrodes (Retina Technologies, Scranton, PA), and detomidine sedation in the standing horse have been reported.[139] Low-intensity flash scotopic a- and b-wave latency and amplitudes are 5.73 ± 1.88 and 36.95 ± 3.89 ms and 103.18 ± 120.72 and 409.30 ± 319.36 mV, respectively.[139] High-intensity flash scotopic a- and b-wave latency and amplitudes are 5.13 ± 1.34 and 34.75 ± 1.87 ms, and 153.68 ± 94.19 and 374.09 ± 161.93 mV, respectively.[139] ERG flicker-photometry has been used to assess the spectral sensitivities of cones in the horse,[139] but oscillatory potentials have not yet been recorded.[88,139,141,143,147-149]

FLUORESCEIN ANGIOGRAPHY

Fluorescein angiography (FA) is the dynamic recording of fluorescein dye, after IV administration, as it passes through the retinal and choroidal circulation (Fig. 1-64).[150,151] It can be used both clinically and experimentally to evaluate vascular conditions of the fundus and iris.[12] FA allows detection of lesions in the vascular wall of the retinal vessels or in tight junctions

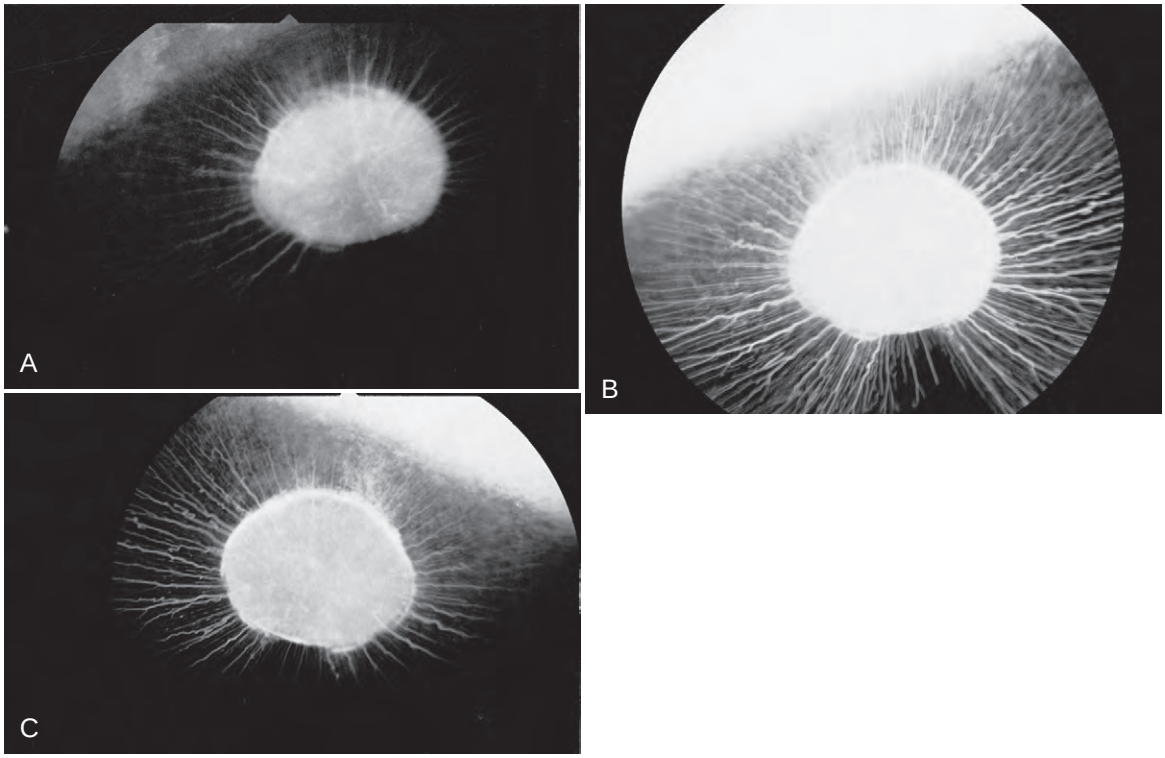


Figure 1-64. Fluorescein angiography in the horse. **A,** Filling phase. **B,** Maximum fluorescence point. **C,** Fading phase. (Images courtesy Dr. E.M. Martín-Suárez.)

between retinal pigmented epithelial cells, both of which constitute the blood-retinal barrier.[150] When given IV, 60% to 80% of the fluorescein is protein bound and does not normally cross the tight junctions between retinal pigment epithelial cells.[152] However, unbound fluorescein readily passes into the choroidal interstitium through large fenestrae after passing into the choriocapillaris.[152] So if there is any abnormality of the RPE, progressive subretinal pooling of the dye will be seen. Because of the absence of a real choroidal barrier and a choroid–optic nerve barrier, the optic nerve becomes progressively fluorescent in the late phase.[152]

Sodium fluorescein is a water-soluble, low-molecular-weight, weak, dibasic acid.[12,152] It fluoresces intensely at a blood pH of 7.4.[152] The 20% (200 mg/mL) solution was used to perform the angiogram in horses at a dose of 10 mg/kg IV.[150] The dye is excited by light with a wavelength of 465 to 490 nm (i.e., blue light) and emits light from 500 to 600 nm (yellow-green), with a maximum intensity at a wavelength of 520 to 530 nm.[12,152] Appropriate barrier filters are used to accomplish this event during the angiogram. A blue filter (Kodak Wratten 47A) in the light pathway induces maximal fluorescence, and a yellow filter (Kodak Wratten 15) in the optical pathway provides maximal contrast. The appropriate use of these filters also helps reduce much of the background fluorescence and pseudofluorescence that can make the images undiagnostic.[152] Other dyes are available for angiography, including indocyanine green, pyranine, and rhodamine, but their use has not been reported in the horse.[12]

Sedation or general anesthesia is usually required to perform an angiogram in the horse. The pupils must be pharmacologically dilated, and the ocular media must be clear. Fluorescein angiography can be performed with a direct or indirect ophthalmoscope, but a fundus camera is preferred for documentation.[12] Because of the rapid occurrence of events during the angiogram, some changes may not be seen by the examiner until the serial photographs are evaluated. Models of fundus cameras used to perform fluorescein angiography include Kowa, Topcon, and Zeiss.[12] These models can take pictures as rapidly as three times per second. If the camera is table mounted, however, its use is limited in the horse because of positioning difficulties. Kowa has marketed a handheld fundus camera that can take up to one photograph every 2 seconds.[12] Fluorescein angiography has been reported in the horse with the use of a Kowa Fundus Camera RC-2[151] and a Kowa Genesis Fundus Camera.[150] Slide film, either black and white or high-speed (400 ASA) color film, or a digital camera may be used.

The equine FA consists of four normal phases: the prefilling, choroidal, retinal vascular, and recirculation phases.[150,152] The prefilling phase occurs before injection. The choroidal phase is rapid and short and is evidenced by a brightening of the background under the RPE, centrally to peripherally, and occurs within 22 seconds[151] or 47.0 ± 9.5 seconds (although detected in only 24% of horses)[150] after injection of dye into the jugular vein (i.e., choroidal flush) in the horse (Fig. 1-65). In small animals, cilioretinal arteries also fill during this phase as fluorescein leaks into the optic nerve from the choroid through the border of Elschnig and the optic nerve begins to fluoresce, although this occurrence has not been documented in the horse.[12,153] The pure choroidal phase is difficult to capture. *Retinal vascular phase* (RVP)—which includes the filling phase, maximum fluorescence point, and fading phase—is defined as the time that elapses between the appearance of

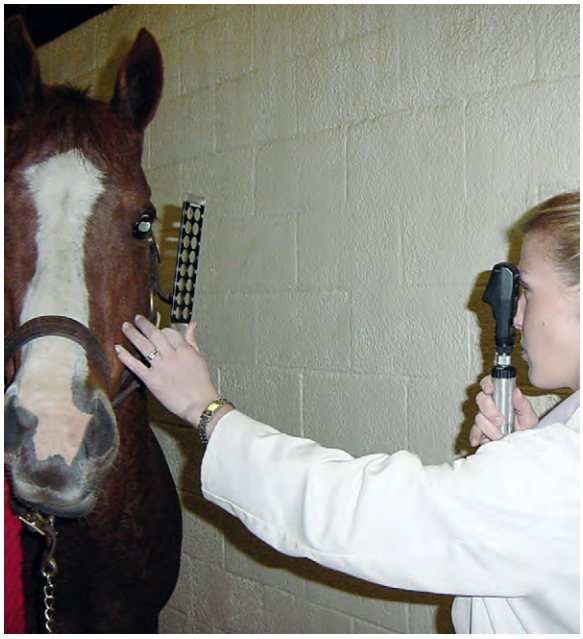


Figure 1-65. Retinoscopy with a skiascopy bar in the horse.

retinal vascular fluorescence as it exits the optic disc and the reduction of vascular fluorescence.[150] In a study of FA in horses, RVP started at 47.8 ± 10.4 seconds after fluorescein injection.[150] During the filling phase, vascular fluorescein was most visible within the nontapetum (see Fig. 1-64). Maximum fluorescence (maximum fluorescence point) occured at 60.0 ± 10.4 seconds (see Fig. 1-64). The fading phase (see Fig. 1-64) occured after the maximum fluorescence point with substantial reduction in fluorescence by 74.8 ± 9.8 seconds. The fading phase duration was 15.0 ± 7.1 seconds.[150] Recirculation phase is prolonged in horses and lasted up to 7 minutes.[150]

Fluorescein angiography will characterize but not diagnose posterior segment lesions.[152] Indications for fluorescein angiography include inflammatory conditions such as uveitis (posterior, anterior), swelling of the optic nerve (neuritis, edema), retinal lesions (with or without associated blindness), and subretinal edema. Fluorescein angiography is also used to monitor progression of disease and response to therapy.[152] Contraindications to fluorescein angiography include a known hypersensitivity to the dye, severe systemic disease, and persistent miosis.[152] Reported complications in veterinary medicine include transient nausea and vomiting in 5% to 10% of small-animal patients, urine and mucous membrane discoloration for 24 to 48 hours, and anaphylaxis.[154] Complications have not been reported in the horse, [150] but emergency cardiac and respiratory drugs (e.g., epinephrine) should be immediately available, and the angiogram should be performed in a relatively safe and open environment.

RETINOSCOPY (SKIASCOPY)

Retinoscopy, or skiascopy, is the technique used to determine the refractive error or dioptric state of the eye. Retinoscopy is the only clinical and practical method of refraction in horses. Commonly used in human ophthalmology, this technique has been used in veterinary medicine to define the normal, pathologic, and surgically induced refractive state of the eyes of the horse.[35,155-160] The instrumentation and technique used can be challenging, and the reader is referred to an article by Davidson for further information.[161]

Light rays projected onto an eye from infinity emerge from an emmetropic eye as parallel rays, from a myopic (nearsighted) eye as converging rays, and from a hyperopic (farsighted) eye as diverging rays.[161] The location at which these emergent light rays form a focal point is called the *far point*.[161] The far point is at infinity, in front of infinity, and beyond infinity for emmetropic, myopic, and hyperopic eyes, respectively.[161]

The retinoscope is either spot or streak, but streak retinoscopes are the most commonly used in veterinary medicine.[161] Both streak and spot retinoscopes are available from Copeland, Heine, Keeler, Propper, Reichert, and Welch Allyn. Plus or minus spherical lenses, available in increments of 0.25 D, are placed between the retinoscope and the horse to quantitate the refractive error of the eye.[161] A simple and inexpensive skiascopy bar or rack contains a series of plus and minus lenses in increments of 0.5 to 1.0 D.[161]

Retinoscopy is performed in a darkened room with a handler restraining the horse's head. Mydriasis is often unnecessary and can even make the technique more difficult; the limited accommodative ability of the horse makes cycloplegia less important.[161,162] The retinoscope is placed against the examiner's brow, and the examiner is positioned 0.67 m (approximately an arm's length) from the patient's eye (Fig. 1-65).[161] The streak is swept horizontally across the horse's pupil, rotated horizontally, and then swept vertically across the pupil.[161] Finally, a trial lens or skiascopy bar is placed 1 to 2 cm from the patient's cornea, and the process is repeated.[161]

As the streak is slowly swept across the pupil, the fundic reflex will move in either the same or the opposite direction, depending on the refractive error of the patient. With no refractive lens, the fundic reflex will move in the same direction as the sweep with emmetropic and hyperopic eyes (a *with* motion) and in the opposite direction of the sweep with more than 1.5-D myopic eyes (an *against* motion).[161] If a with motion is observed, plus lenses of increasing dioptric strength are placed in front of the patient's eye until an against motion is observed or neutralization is reached.[161] Neutralization is characterized by a fundic reflex that completely fills the pupil without any noticeable direction of movement.[161] If an against motion is observed, minus lenses of increasing dioptric strength are used to achieve neutrality.[161] At a working distance of 0.67 m, a +1.5-D lens is needed to achieve neutralization with an emmetropic eye; therefore the refractive error of an eye is determined by subtracting 1.5 D from the gross refraction needed to achieve neutrality.[161]

Retinoscopy may allow selection of intraocular lens implants in horses and assist with evaluation of performance problems in working animals. However, refractive error has an unknown effect on horses and is discussed further in Chapter 11 (Equine Vision). In healthy horses, refractive error has been reported to range from –3 to +3 D,[163] but most appear to be within 1 D of emmetropia.[159,164] The aphakic equine eye after cataract surgery has been reported to be hyperopic (+9.94 D)[165,166] An intraocular lens implant with a refractive power of 25 D resulted in an improvement to only +8 D hyperopia.[165,166] Astigmatism, a state of unequal refraction along the different meridians of the

eye (i.e., vertical versus horizontal), has not been reported in horses.[164] Variation in the reported refractive error in horses can be explained by the technique used, skill of the examiner, sample size, and accommodative state of the animal.

ADVANCED OCULAR IMAGING

ULTRASOUND

Ultrasonography is a rapid, safe, and practical method for examination of the intraocular and retrobulbar structures in an awake horse. Ocular ultrasonography allows examination of the globe in conditions in which opacity of the transmitting media of the eye (cornea, aqueous humor, lens, and vitreous humor) or extreme eyelid swelling otherwise prevents a complete ophthalmic examination.[134,167-171] In addition, evaluation of intraocular mass lesions, differentiation between solid and cystic structures, examination for a foreign body, axial length determination of the globe and intraocular structures, and examination of orbital structures are all indications for performing ocular ultrasonography.[170] The most common clinical indications for ocular ultrasonography in the horse are to evaluate for the presence of a retinal detachment in eyes after trauma, with uveitis, hyphema, cataract, and severe corneal opacities (e.g., edema, fibrosis), and as a preoperative cataract surgery evaluation.[144,170] Orbital evaluation is also routinely performed in instances of exophthalmos or orbital trauma. Ultrasonography can also be used to verify the stage and location of a cataract before surgical removal, as well as potential complications (e.g., posterior lenticonus) that would make phacoemulsification more challenging.[169,170] Diagnostic ultrasonography of the equine lens and posterior segment has been reported.[169] The ultrasound dimensions of the extirpated equine globe have been reported and are shorter in length than the ocular dimensions previously reported for the equine eye.[171] More thorough descriptions of the physics, equipment, techniques, and results of ultrasonography in various disease states can be found elsewhere.[134,167-169,172]

OCULAR ULTRASONOGRAPHY: GENERAL FEATURES

Ultrasound is an acoustic wave that consists of an oscillation of particles within a medium.[173] The velocity of the longitudinal wave is dependent on the medium through which it is traveling.[173] Water transmits the wave at a slower velocity than more solid media, so the wave passes more quickly through the lens than through the aqueous or vitreous.[173] Echoes are produced by acoustic interfaces created at the junction of two media with different acoustic impedances.[173] The greater the difference in the acoustic impedance of the two media that produce the interface, the stronger the reflection of the ultrasound wave (i.e., the echo).[173] So, the anterior lens capsule would produce a stronger echo when bordered by normal aqueous than when bordered by blood (hyphema). The returning echoes are affected by many factors, including the angle of sound incidence; the size, shape, and smoothness of the acoustic interface; absorption; scatter; and refraction.[173] If the sound wave strikes an interface at a perpendicular angle, all of the wave is reflected back to the transducer, and a strong echo results. If the beam is angled, some of the reflected energy is diverted away from the probe and results in a weaker echo. The smoother and straighter an interface is (e.g., retinal surface, lens capsule), the more reflected energy returns directly to the probe, resulting in a strong echo. Higher sound velocities (i.e., higher-numbered transducer probes) and greater tissue thickness increase absorption of the sound wave and weaken the echo. Refraction occurs when a sound wave is directed obliquely to an interface that demarcates two media of different sound velocities.[173] Therefore no refraction occurs when a sound wave is directed perpendicular to an interface or when the velocities of the two media are the same.[173]

Deep tissue penetration is not required for ocular ultrasonography, but high resolution is required.[170] The frequency of the ultrasonic waves emitted by the selected oscillating piezoelectric transducer determines the resolution of the image.[170,173] Transducer probes are available in a range of frequencies (e.g., 3.5, 5, 7.5, 10, 12.5, 20, 35, and 50 MHz), and the frequency is inversely proportional to the wavelength of the sound beam.[170,173] Depth of sound beam penetration is directly proportional to wavelength. Therefore a low-frequency transducer (5 MHz) provides poor near-field axial resolution but greater tissue penetration and is therefore useful for imaging more posteriorly located structures such as the orbit. A high-frequency transducer (50 MHz) provides lower tissue penetration but high near-field axial resolution and is therefore useful for imaging more anteriorly located structures.[170,173]

An optimal ophthalmic transducer for general use is a 10-MHz transducer with a focal range of 3 to 4 cm and a small scan head.[170] This probe provides adequate depth of penetration to visualize the retrobulbar structures, enhanced resolution, and ability to visualize anterior intraocular structures such as the iris, ciliary body, anterior and posterior chambers, and cornea (with the use of an offset device).[170] Alternately, a 5-MHz or 7.5-MHz transducer will also produce good ophthalmic images and have a better depth of penetration for visualization of retrobulbar structures.[170] Near-field reverberation artifacts will obscure the anterior segment of the globe unless an offset device or increased sterile coupling gel is used or the ultrasound examination is performed through closed eyelids.[170] The use of probes with frequencies of 20 to 80 MHz is referred to as *high-frequency ultrasound biomicroscopy*.[167,174-176] Ultrasound biomicroscopy allows for optimal visualization of the cornea, sclera, anterior and posterior chambers, iris, choroid, and lens and is described in the following section.

Both amplitude-mode (A-scan) and brightness-mode (B-scan) ultrasonography are useful for diagnostic purposes in ocular disease.[173] A-scan ultrasonography produces an anterior-posterior image, with peaks reflecting tissues of different identities displayed as a linear series of vertical spikes from a baseline (Fig. 1-66).[173] The time between two spikes can be converted into distance and used to measure anterior-posterior axial length of the globe, anterior chamber depth, axial lens thickness, and vitreous anterior-posterior axial length.[173] B-scan ultrasonography provides a two-dimensional real-time image of the eye and orbit and is the most common mode of ultrasound used clinically in veterinary ophthalmology (Fig. 1-67).[134,168,169]

Ultrasonographic images are described as hyperechoic, hypoechoic, and anechoic.[170,173] Four major ocular acoustic echoes (hyperechoic) are generated within a normal eye. These echoes originate from the anterior cornea, the anterior lens capsule, the posterior lens capsule, and the retina/choroid/sclera (see Fig. 1-68).[170,173] The retina, choroid, and sclera cannot be

normally differentiated from one another by ultrasonography. Additional echodensities can be generated by the iris, corpora nigra, ciliary body, optic nerve, orbital fat, muscles, and other orbital structures.[170] The optic nerve head/lamina cribrosa appears as a hyperechoic structure with the optic nerve itself seen as a hypoechoic structure extending posteriorly from the optic nerve head.[170,173] The orbital muscle cone appears as an echodensity extending posteriorly from the equatorial region of the globe and converging toward the orbital apex.[170,173] The anterior and posterior chambers, lens cortex and nucleus, and vitreous chamber are normally anechoic.[170,173]

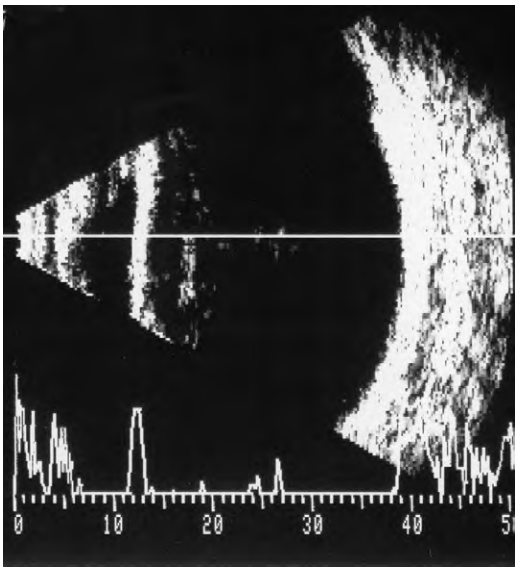


Figure 1-66. A-scan ultrasonography produces an anterior-posterior image, with peaks reflecting tissues of different identities displayed as a linear series of vertical spikes from a baseline. (Ultrasound image courtesy Dr. David Wilkie.)

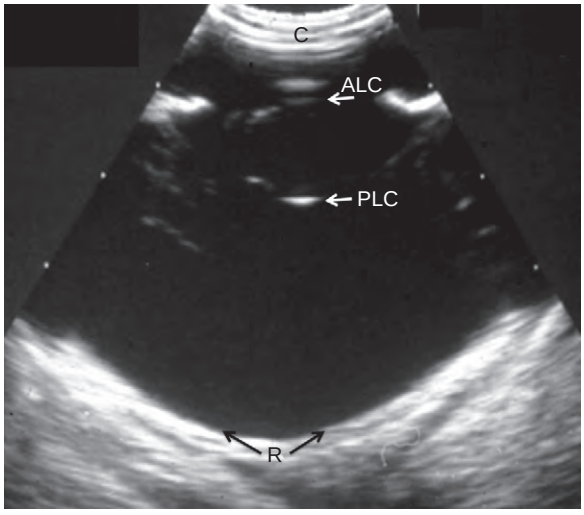


Figure 1-67. B-scan ultrasonography provides a two-dimensional real-time image of the eye and orbit and is the most common mode of ultrasound used in a clinical setting. Four major ocular acoustic echoes (hyperechoic) are generated within a normal eye. These echoes originate from the anterior cornea, the anterior lens capsule, the posterior lens capsule, and the retina/choroid/sclera. (Ultrasound image courtesy Dr. David Wilkie.)

OCULAR ULTRASONOGRAPHY TECHNIQUE

The ultrasound transducer can be placed directly on the cornea, which provides superior images of the posterior segment or orbit, or the scan may be performed through closed eyelids or with an offset device (Fig. 1-68). The transducer can be positioned to provide horizontal, vertical, and oblique scanning sections of the eye.[173] The globe should routinely be imaged in the horizontal and vertical planes through the visual axis.[170,173,177] Oblique positioning can then be performed for a complete examination.[170,173,177] The transducer can also be positioned dorsal to the zygomatic arch to scan the orbit.[170,173] Use of a small scan head diameter allows optimal placement on the cornea (Fig. 1-69).[170] When ultrasound biomicroscopy is not being performed, conducting the examination through the eyelids or with an offset device, which may require an increase in gain setting, will facilitate examination of the anterior portions of the globe.[170] A suitable tissue-equivalent offset device is available with most transducers, or alternatively, a water-filled balloon or excess coupling gel can be used (Fig. 1-70).[170]

Sedation and/or regional nerve blocks may be required, depending on globe stability and the temperament and level of discomfort of the horse. Topical anesthesia of the cornea (proparacaine 0.5% [Alcaine by Alcon]) is required for a transcor-

Figure 1-68. The ultrasound transducer can be placed directly on the cornea, which provides superior images of the posterior segment or orbit, or the scan may be performed through closed eyelids.

Figure 1-69. A small transducer head is optimal for transcorneal ultrasound examination.

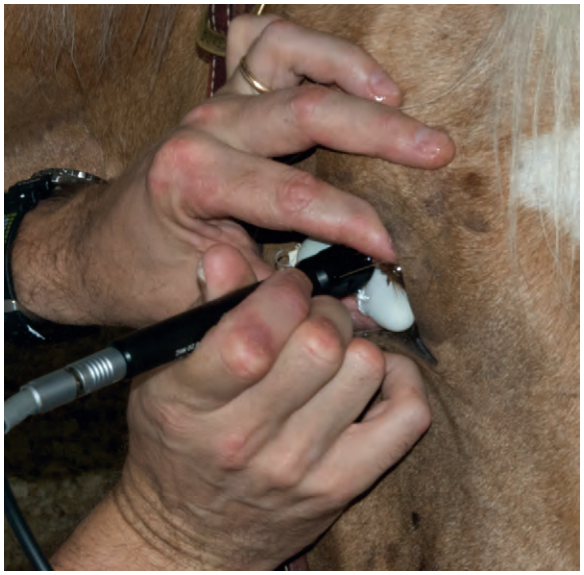


Figure 1-70. A standoff pad will facilitate examination of the anterior portions of the globe; alternatively, a water-filled balloon or excess coupling gel can be used.

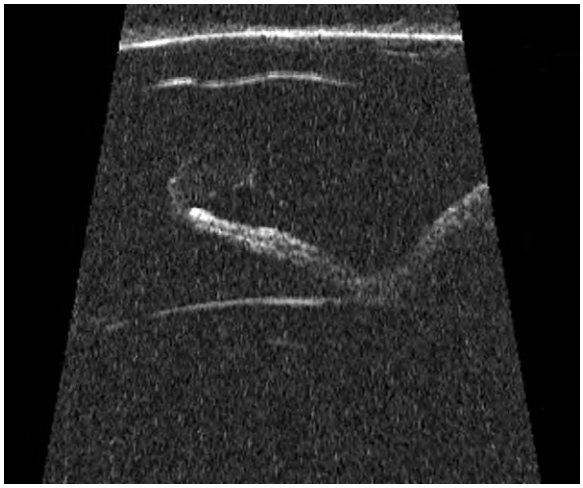


Figure 1-71. Fibrin appears as a series of disconnected echodensities throughout the anterior chamber, whereas hypopyon is most often seen ventrally and is more uniform in its echodensity. A fibrin clot is shown attached to the tip of the iris (35-MHz probe).

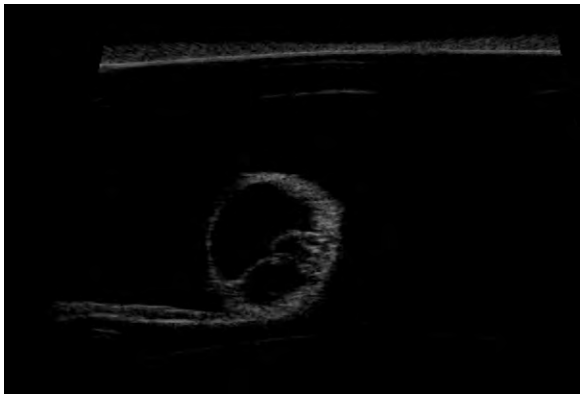


Figure 1-72. Intraocular masses consist of inflammatory, neoplastic, and cystic structures and most commonly arise from the anterior uvea (iris, ciliary body) in the horse. A corpora nigra cyst is shown with the use of a 35-MHz probe.

neal ultrasound examination. Sterile methocellulose gel, such as K-Y jelly, is recommended as the ultrasound coupling gel. It is placed on the transducer tip or on the corneal surface and should be irrigated from the eye on completion of the examination.[170] Standard ultrasound coupling gels may cause corneal irritation and should be avoided.[170]

ULTRASONIC EVALUATION OF OCULAR TRAUMA

Ocular ultrasonography is of extreme importance in the evaluation of ocular trauma in the equine patient.[170] The extent and severity of the injury, prognosis, and probable therapy can be determined in many cases through ultrasound examination.[170] In many instances, ultrasonography is the only examination method of value in an eye that is otherwise severely painful or opaque or when the eyelids cannot be opened because of swelling.[144,170] If the structural integrity of the globe is compromised, extreme care should be taken when the ultrasound examination is performed to not induce further damage to the eye.

Both blunt and penetrating trauma in the horse can result in significant intraocular changes. Penetrating trauma can result in a shallow anterior chamber; fibrin in the anterior chamber; hyphema; lens capsule rupture; lens luxation, subluxation, or expulsion; vitreous hemorrhage; retinal detachment; and possibly limbal or posterior scleral rupture.[170] In addition, hyphema, vitreous hemorrhage, cataract, lens luxation or subluxation and rupture, and retinal tear, retinal detachment, and choroidal detachment can all occur with blunt trauma.[144,170]

In instances of severe trauma, measurements of identifiable structures should be obtained for assessment of the damage.[170] For example, a reduction in the lens–posterior scleral wall axial length may indicate a posterior lens luxation, whereas an increase may indicate an anterior lens luxation or a posterior scleral wall rupture.[170] On ultrasound examination, vitreous and orbital hemorrhage can appear uniform in echodensity, blending together because they are no longer separated by the scleral fibrous tunic.[170] In addition, the normally hyperechoic posterior scleral wall is not identifiable.[170]

Hyphema and inflammatory material (e.g., fibrin, hypopyon) may accumulate in the anterior chamber as a result of trauma or anterior uveitis.[170] Fibrin appears as a series of disconnected echodensities throughout the anterior chamber, whereas hypopyon is most often seen ventrally and is more uniform in echodensity (Fig. 1-71).[170] In addition, the ciliary body and vitreous should be examined for involvement in the inflammatory process, and the lens should be examined for secondary cataract formation.[170]

ULTRASOUND EXAMINATION OF INTRAOCULAR MASSES

Intraocular masses consist of inflammatory, neoplastic, and cystic structures and most commonly arise from the anterior uvea (iris, ciliary body) in the horse (Fig. 1-72), but choroidal mass lesions can occur as well.[170] Because many of these mass

lesions arise from the anterior uvea, an offset device, extra coupling gel, scanning through closed eyelids, or ultrasound biomicroscopy is required to adequately visualize the lesion.[170] Intraocular mass lesions that are densely pigmented and cannot be transilluminated clinically can be either cysts or melanomas.[170] A cyst will have an echogenic wall but an anechoic fluid-filled center, whereas a melanoma appears homogeneous in its acoustic density.[170]

ULTRASOUND EXAMINATION OF LENS ABNORMALITIES

When findings of ocular ultrasound examination are normal, the lens appears as two distinct echodensities seen at the anterior and posterior axial lens capsules (see Fig. 1-67).[210] The anterior echo is slightly convex, and the posterior echo is slightly concave. Internally, the lens is anechoic, and peripherally, the echo is reflected away from the probe.

Abnormalities of the lens that can be detected on ultrasonography include abnormalities of lens size, cataract, luxation or subluxation, and lens rupture.[170] A cataract appears as increased internal echoes within the lens and as increased visualization of the lens periphery other than the anterior and posterior axial portions (Fig. 1-73).[170] The size and intensity of the echoes will depend on the extent and severity of the cataract (Fig. 1-74). Abnormalities of lens size, measured anterior to posterior at the axial position, include both increased and decreased lens dimensions.[170] A decrease in lens size occurs as a result of resorption of liquefied cortical material, as is seen with a hypermature cataract or microphakia (Fig. 1-75).[170] Ultrasonography can be used to evaluate the position of the lens after trauma or during inflammation when the anterior segment is opaque because of edema or hemorrhage.[170] Difficulty in obtaining a simultaneous echo of both the anterior and posterior lens capsule and changes in the anterior-posterior axial measurements of the lens or lens–posterior scleral wall may indicate a luxation or subluxation of the lens.[170]

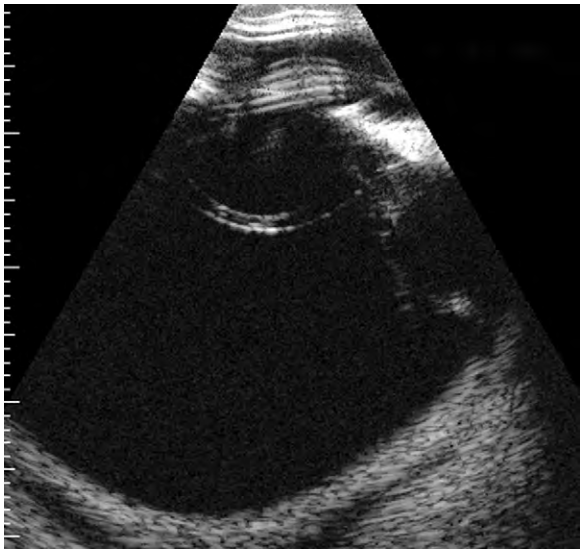


Figure 1-73. A posterior cortical cataract is apparent as a second line anterior to the posterior lens capsule (12.5-MHz probe).

ULTRASOUND EXAMINATION OF THE POSTERIOR SEGMENT

Ultrasonography is used to evaluate the posterior segment for abnormalities of the vitreous or retina in an eye with a cataract, after trauma, or in other conditions in which opacification of the transmitting media may be present (e.g., ERU).[144,169,170]

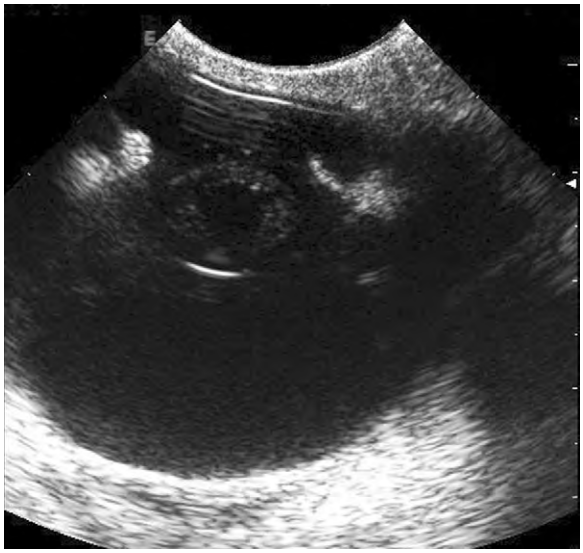


Figure 1-74. Anterior and posterior cortical cataracts.

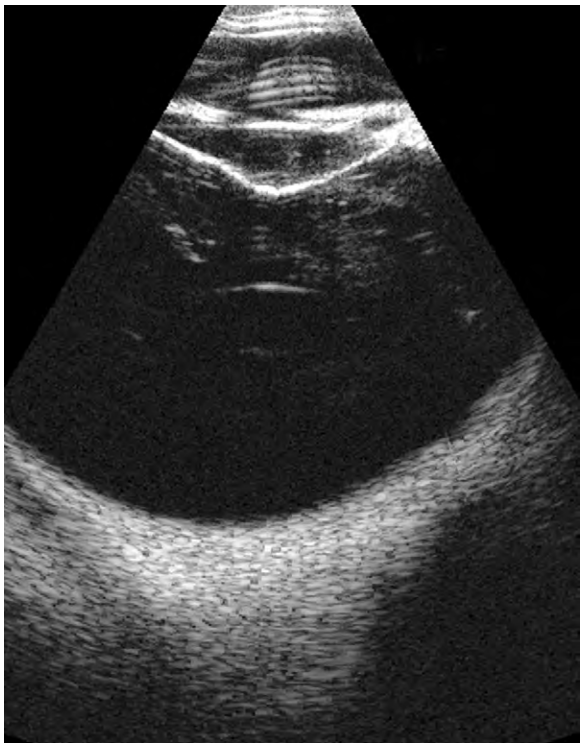


Figure 1-75. A decrease in lens size occurs as a result of resorption of liquefied cortical material as is seen with a hypermature cataract or microphakia. This hypermature cataract is smaller than normal and the fibrotic lens capsule appears hyperechoic. A reverberation artifact is also present in the vitreous (12.5-MHz probe).

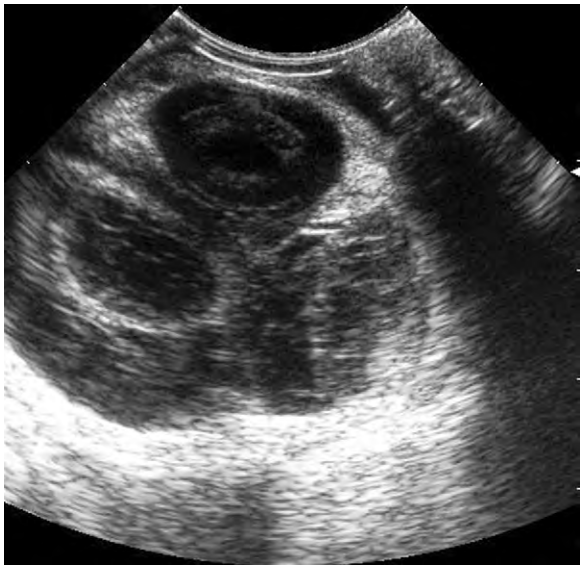


Figure 1-76. Vitreous hemorrhage appears as discrete to diffuse moderate amplitude echoes, which may demonstrate motion.

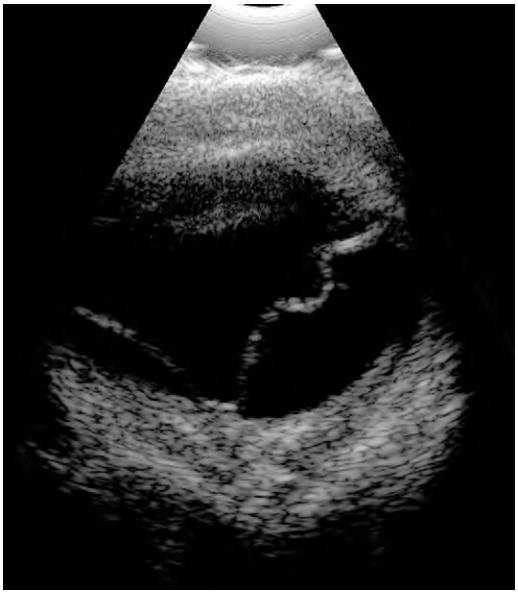


Figure 1-77. When detached, the retina appears as an echodense linear structure, most often attached at the optic disc posteriorly and the ora ciliaris retinae anteriorly, resulting in the classic funnel or gull wing–appearing detachment.

Evaluation of the posterior segment in an eye with a cataract is probably the second most common indication for ocular ultrasonography in a horse, after trauma.[169]

The vitreous cavity is normally anechoic, appearing dark or black on ultrasonography.[170] Abnormalities of the vitreous appear as echodensities and include hemorrhage, inflammation, degeneration (syneresis), asteroid hyalosis, and detachment.[170] Vitreal degeneration creates interfaces that result in ultrasonographic echodensities. These appear as multiple variable echogenic lines within the vitreous cavity and are best visualized by increasing the far-field gain setting on the ultrasound unit. Clinically, the vitreous degeneration may or may not be visible. Asteroid hyalosis appears as highly reflective, discrete, freely moving echoes that persist even as the gain setting is decreased.[170] Vitreous hemorrhage appears as discrete to diffuse moderate amplitude echoes that may demonstrate motion (Fig. 1-76). Vitreous inflammation appears as multifocal disconnected variable echodensities within the vitreous cavity.[170]

The retinal echo is indistinguishable from the underlying choroidal and scleral echo in a normal eye.[170] The retina becomes apparent as a distinct echodensity with a separation of 0.5 to 1 mm.[171] When detached, the retina appears as an echodense linear structure, most often attached at the optic disc posteriorly and the ora ciliaris retinae anteriorly, resulting in the classic funnel or gull wing–appearing detachment (Fig. 1-77).[170] A complete or only partial retinal detachment, as well as disinsertion from the ora (usually dorsally), can be present.[170] Initially, retinal detachments will be seen to undulate when viewed in real time, but with chronicity, the retina will become fixed and less mobile.[170] Examination of the subretinal space is important. An anechoic subretinal space indicates fluid such as a transudate, which may resorb. The presence of echodense material in the subretinal space may indicate hemorrhage or infiltration of neoplastic or inflammatory cells.[170] Differential diagnoses for a hyperechoic linear structure in the vitreous include choroidal detachment, vitreous hemorrhage, vitreous detachment, vitreous degeneration, traction bands, and artifacts such as reverberation from the lens.[170]

ULTRASOUND EXAMINATION OF THE ORBIT

Orbital contents include the extraocular muscles, fat, vascular tissues, glands, and the optic nerve. Exophthalmos and orbital trauma are the two most common indications for orbital ultrasound examination in the horse. Differential diagnoses for exophthalmos include orbital mass lesions (e.g., neoplasia) or hemorrhage (e.g., after trauma). An orbital mass lesion should be characterized as cystic or solid, and its location within the orbit should be determined.[170] Ultrasound-guided fine-needle aspiration or biopsy of orbital masses is useful.[170] After trauma to the orbit and associated structures, ultrasound may be used to evaluate the retrobulbar space for displaced fractures, hemorrhage, swelling, or compression of the optic nerve, and integrity of the posterior wall of the globe.[170,178]

INTERPRETATION OF OCULAR ULTRASOUND ARTIFACTS

Artifacts may be caused by inaccurate technique (e.g., insufficient amount of coupling gel or air bubbles in the water bath). Types of artifacts that can occur during the examination in the horse include Baum's bumps, absorption artifacts, and reverberation echoes (i.e., reduplication or multiple-signal echoes).[170] Entrapment of air between the transducer and the eye, resulting in the display of bright echoes across the echogram, can be avoided by ensuring that a sufficient amount of coupling gel is used.[170,171,173] Air can also be entrapped by the hair coat when a transpalpebral ultrasound examination is performed, so hair should probably be clipped.[170] Baum's bumps (Fig. 1-78) are B-scan artifacts that appear as elevations of the fundus.[170] They occur as the sound beam is refracted more quickly through the peripheral versus the central lens.[170,171,173] As a result, the posterior eye wall appears to be closer to the probe and can be seen as two discrete retinal elevations at the retinal surface.[170] The size of the elevations varies with the scan angle.[170]

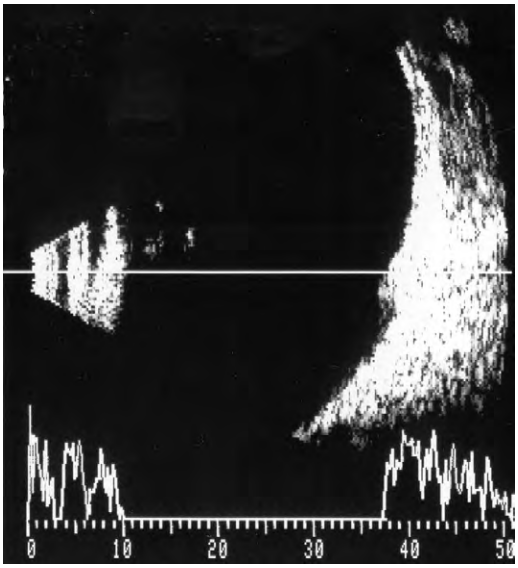


Figure 1-78. Baum's bumps occur because the normal lens refracts the sound waves from the transducer, resulting in faster passage of sound through the peripheral lens as compared with the central lens. This may result in the posterior eye wall appearing to be closer to the probe and will be seen as one or two discrete retinal elevations at the retinal surface, the size of which will vary with the scan angle. Only one bump is visible on this scan. (Ultrasound image courtesy Dr. David Wilkie.)

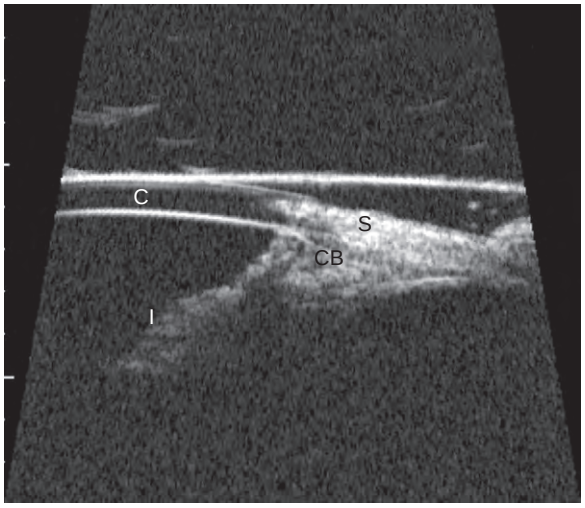


Figure 1-79. Ultrasound biomicroscopy (UBM) allows imaging of the anterior ocular segment at near-microscopic resolution in living patients. The cornea (C), sclera (S), ciliary body (CB), and iris (I) can be visualized (35-MHz probe).

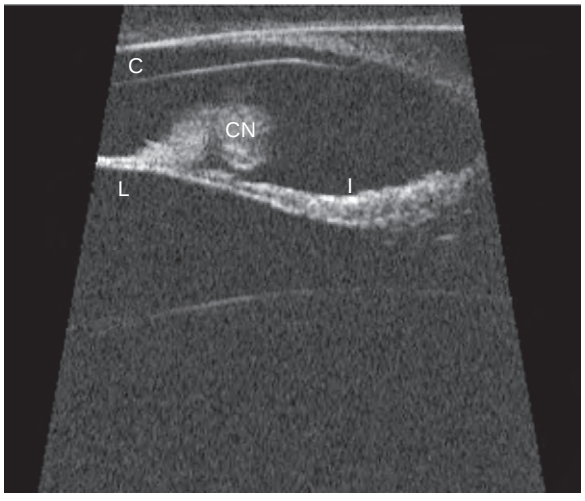


Figure 1-80. Normal appearance of the corpora nigra. Corpora nigra (CN), iris (I), cornea (C), and lens (L) can be visualized (35-MHz probe).

An absorption artifact (shadowing, attenuation) occurs when a dense structure causes sound attenuation or complete reflection of sound and produces an absence of echoes posterior to the hyperechoic structure.[170,171,173] This appears as an anechoic area that can be confused with a mass lesion.[170,171,173] Structures that can cause this "acoustic shadow" include dense cataracts and intraocular foreign bodies.[170,171,173] Refraction around the edge of an artifact can also occur. This most commonly occurs around the edges of the globe.[173] Reduplication echoes (reverberation artifacts) occur either between the probe and a highly reflective interface or between two highly reflective interfaces.[173] Because it will take longer for these echoes to reach the probe and return into the eye to be imaged, the artifacts always appear deeper in the globe than the tissue of origin.[173] Multiple signals can occur from the lens capsule, a foreign body, an air bubble, the sclera, or the orbital bone.[170,173] The typical reduplication echo occurs from the lens capsule to the transducer and back again and appears as linear hyperechodensities in the mid to posterior axial vitreous; it can be confused with vitreous hemorrhage, inflammatory debris, or degeneration.[170,171,173] The true echo and the subsequent artifacts are equidistant and decrease in strength, and the artifact may "move" with movement of the transducer.[173] Reverberation artifacts in the anterior chamber, lens, and posterior segment have been reported as a common finding in a recent study.[169]

HIGH-FREQUENCY ULTRASOUND EXAMINATION AND ULTRASOUND BIOMICROSCOPY

Ultrasound probes with frequencies ranging from 20 to 35 MHz (high-resolution ultrasound) to 50 to 80 MHz (ultrasound biomicroscopy) have been developed and allow imaging at resolutions comparable to those achieved with low-power microscopic views.[179] Routine ocular ultrasound examination with 5- to 12.5-MHz probes effectively bypasses the anterior segment of the eye. High-frequency ultrasound biomicroscopy (UBM) allows imaging of the anterior ocular segment at near-microscopic resolution in living patients and provides exceptionally detailed two-dimensional grayscale images of the conjunctiva, cornea and anterior sclera, anterior chamber, anterior chamber angle structures, uveal and ectodermal components of the ciliary body, the layers of the lens, zonules, and anterior vitreal face (Figs. 1-79, 1-80, and 1-81).[179] The important differences between UBM and conventional ultrasound examination are that the UBM transducer has a much higher frequency (20 to 100 MHz) and provides much higher image resolution.[179] However, UBM requires the use of a water bath. With early models, this necessitated heavy sedation or general anesthesia in most veterinary patients. Self-contained water bath systems

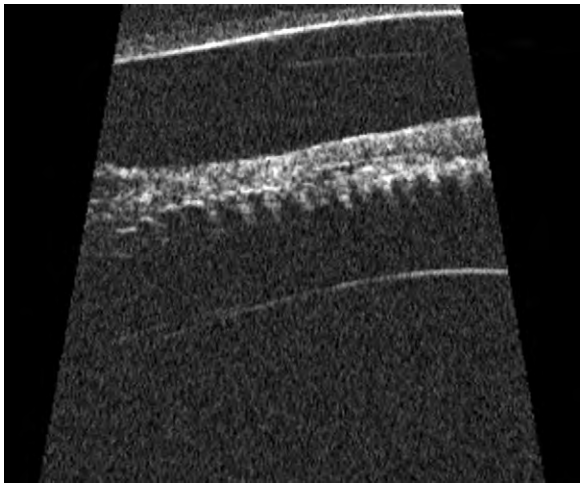


Figure 1-81. Normal appearance of the posterior surface of the iris and ciliary body (35-MHz probe).

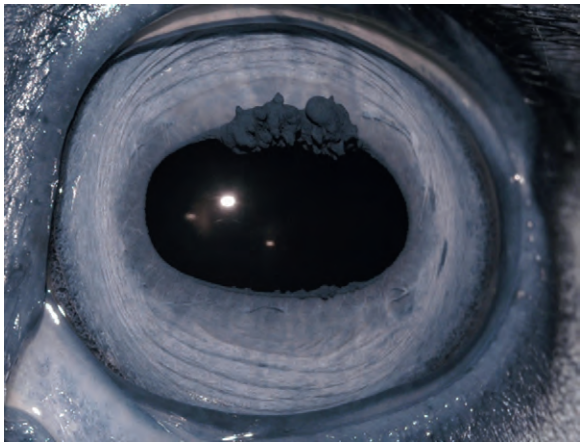


Figure 1-82. Infrared photograph of equine iris.

(i.e., within the ultrasound handpiece) that can be used in an upright position are now available and allow clinical use in veterinary patients, especially large-animal patients such as the horse.

UBM has been used extensively in human medicine and in dogs to define the dynamic mechanism of angle-closure glaucoma, evaluate the functional status of glaucoma-filtering implants, evaluate tumors of the iris and ciliary body, assess intraocular trauma, and evaluate the position of intraocular lens implants.[167,174,176,180]

In the horse, UBM can be used to evaluate depth of stromal abscesses, corneal thickness, ocular squamous cell carcinoma, uveal cysts, changes in anterior uveitis, and other anterior segment and lens changes, including trauma and cataracts (see Fig. 1-71). Scleral thickness has been measured in both fresh and formalin-fixed equine globes.[181] Caliper and UBM measurements on fresh equine tissue revealed that at all sites measured, the thickness of the sclera in fresh tissue was significantly greater than that of tissue fixed in formalin. Thickness ranged from 1.02 ± 0.19 mm at the limbus (inferior), to 0.44 ± 0.06 mm at the equator (superior), to 0.79 ± 0.12 mm at the optic nerve (nasal). There were no significant differences between measurements obtained by caliper and measurements obtained by UBM.[181]

INFRARED PHOTOGRAPHY

Infrared radiation consists of longer wavelengths of light that exist beyond the visible spectrum. Because of its longer wavelengths, infrared radiation is able to penetrate an opaque cornea, allowing better visualization of intraocular structures.[182] Infrared images are much different in appearance than black-and-white or color photographs. On infrared photography, the equine iris (Fig. 1-82) appears bluish-gray with a wide tonal range, thereby increasing image contrast. The corpora nigra, pupillary zone of the iris, and the pectinate ligament appear darker than the anterior iridal surface, and the pupil appears black.[182]

The ability of infrared wavelengths to penetrate an opaque cornea (e.g., due to edema or cellular infiltrate) makes evaluation of the uveal tract possible in diseases such as glaucoma, acute or chronic anterior uveitis, superficial punctate keratopathy, immune-mediated keratitis, chronic superficial nonhealing corneal ulcers, superficial keratomycosis, and stromal abscesses (Fig. 1-83).[182] In any case where corneal edema or fibrosis prevents visualization of the anterior chamber or iridal surface, infrared digital photography can be used to obtain an image of the pupil and provide visualization of the contents of the anterior chamber (see Fig. 1-83).[182]

RADIOLOGY

The anatomic structures in the equine head are complex and make radiographic evaluation difficult.* Radiographic techniques and exposures also vary with the area of the head being examined. Accurate radiographic interpretation becomes possible when knowledge of radiographic anatomy, radiographic signs of disease, and a basic understanding of disease processes involving the skull have been acquired.[53,184-187]

SKULL RADIOGRAPHY

Skull radiographs in the horse may be most informative if there is involvement of bone in the disease process. Radiography is a valuable diagnostic tool for diseases of the nasal cavity, paranasal sinuses, and surrounding orbital bones (Fig. 1-84).[53,184,186] Indications for skull radiography for the evaluation of ocular disease in horses include orbital and facial trauma, exophthalmos, and suspected disease of the nasolacrimal duct (e.g., chronic epiphora, dacryohemorrhea).[53,188] Trauma to the skull overlying sinuses or the nasal chambers—primarily the frontal, lacrimal, nasal and maxillary bones—usually results in depressed fractures that can impinge on the orbit or nasolacrimal duct.[188] Radiographic examination can evaluate the extent of displacement and be used to predict posthealing contour.[188] It will also aid in establishing fracture size and suitability for repair.[188] Computed tomography (CT), however, offers better imaging of the equine periorbita than standard radiography and provides three-dimensional images to better interpret orbital lesions (see Computed Tomography).

*References 1, 2, 5, 6, 53, 183, and 184.

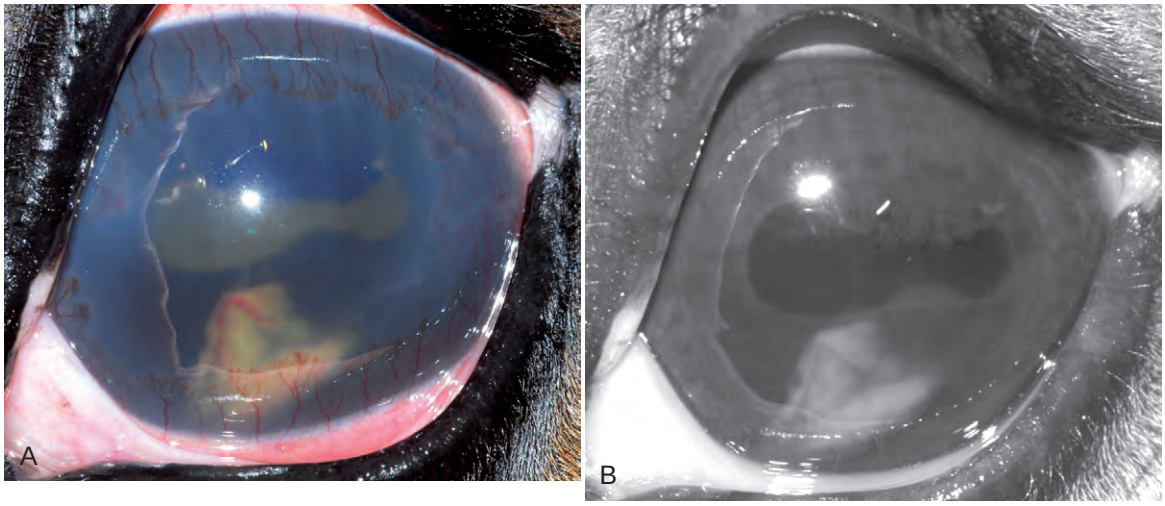


Figure 1-83. Because of the ability of infrared wavelengths to penetrate the opaque cornea, the uveal tract is less visible in a color photograph of an eye with a stroma abscess **(A)** compared to the same eye photographed with an infrared camera **(B).**

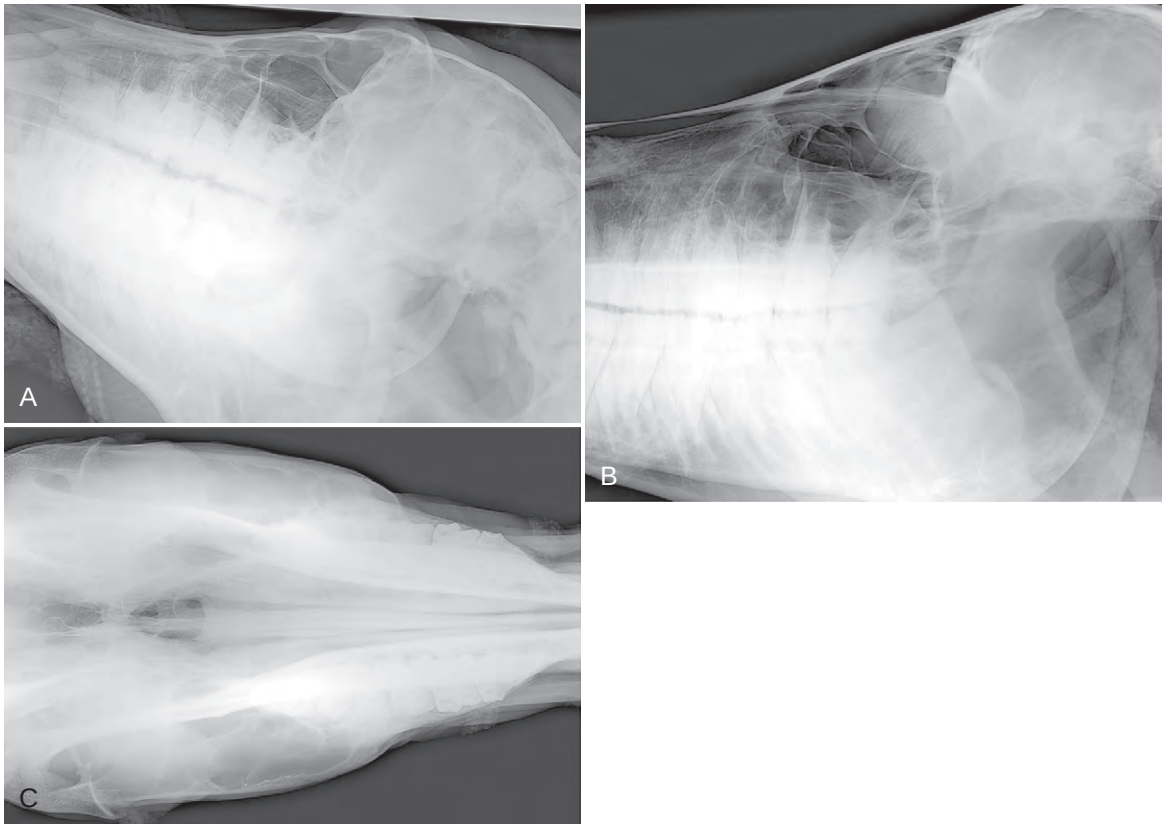


Figure 1-84. **A,** Lateral radiographic view of the equine orbit and sinuses. **B,** Oblique radiographic view of the equine orbit and nasal sinuses. **C,** Dorsal ventral radiographic view of the equine head.

CONTRAST RADIOGRAPHY

Radiographic examination of enucleated globes fixed in Zenker's solution has been described.[189] Resultant radiographs demonstrate normal and abnormal anatomy, providing a new method of studying intact globes. Contrast radiograph techniques include dacryocystorhinography, orbital angiography, orbitography, and thecography, of which only dacryocystorhinography has been described in the horse.[53,190-192]

Dacryocystorhinography

The entire nasolacrimal system can be outlined through contrast radiography (e.g., with barium or iodine), a process termed

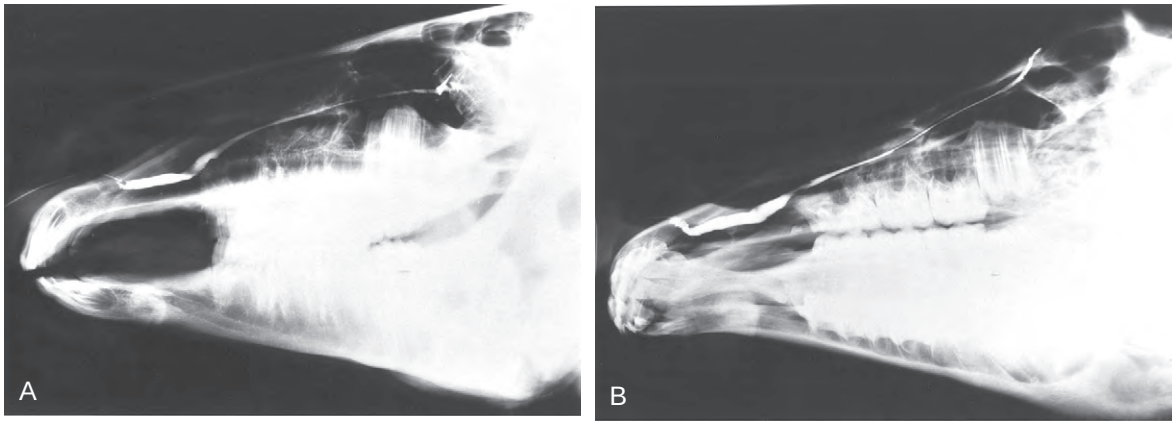


Figure 1-85. The entire nasolacrimal system can be outlined through contrast radiography (e.g., barium or iodine) and is termed *dacryocystorhinography*. **A,** Left lateral dacryocystorhinography. **B,** Right lateral, dorsal ventral, and oblique views. (Photographs courtesy Dr. Claire Latimer.)

dacryocystorhinography.[53,190-192] This technique has been used to characterize the anatomy and identify obstructive lesions of the nasolacrimal duct in horses and donkeys.[53,190,191] Dacryocystorhinography outlines the nasolacrimal system, thereby revealing obstructions, dilations, deviations, atresia, and other abnormalities. Indications for dacryocystorhinography include chronic epiphora, orbital trauma, and chronic conjunctivitis.[53,190-192]

Dacryocystorhinography can be performed in a standing, tranquilized patient after successful or unsuccessful irrigation of the duct.[53] The upper punctum (usually larger and more accessible) or the ventral punctum is cannulated, and radiopaque contrast material (3 to 5 mL) is injected into the catheter.[53] If the nasolacrimal system is patent, viscid solutions such as 37% iodized poppyseed oil (Ethiodol [Savage Laboratories, Melville, NY]) are preferred because these slowly traverse the nasolacrimal duct during radiography.[53] Use of 60% barium sulfate and iodinated contrast media such as iohexol (Omnipaque [Amersham Health, Princeton, NJ]) have also been described. Contrast is injected until it emerges from the distal punctum, external nares (unless obstruction of the duct is present), or both. After contrast injections, lateral, dorsal ventral, and oblique radiographs (Fig. 1-85) are recommended.[53,190,191] The lateral view provides a more detailed representation of the canaliculi and distal nasolacrimal duct.[53]

Computed tomography dacryocystography (CT-DCG) and magnetic resonance DCG have been used for the evaluation of chronic epiphora, nasolacrimal duct masses, and facial trauma.[193,194] CT-DCG has been described in a horse with multiple facial bone fractures for evaluation of the patency of the nasolacrimal duct.[192] The advantages of CT over skull radiography in evaluation of the nasolacrimal duct include the lack of superimposition of bones and the ability to reconstruct three-dimensional images.[192] The disadvantage is the significant increase in cost and the requirement for general anesthesia and general anesthesia's inherent risks in the horse. CT-DCG may be reserved for animals already undergoing CT for evaluation of facial and orbital bone fractures or for those cases in which routine dacryocystorhinography proves nondiagnostic. Three-dimensional color-enhanced reconstruction of the CT-DCG can assist in interpretation of the nasolacrimal duct (Fig. 1-86).

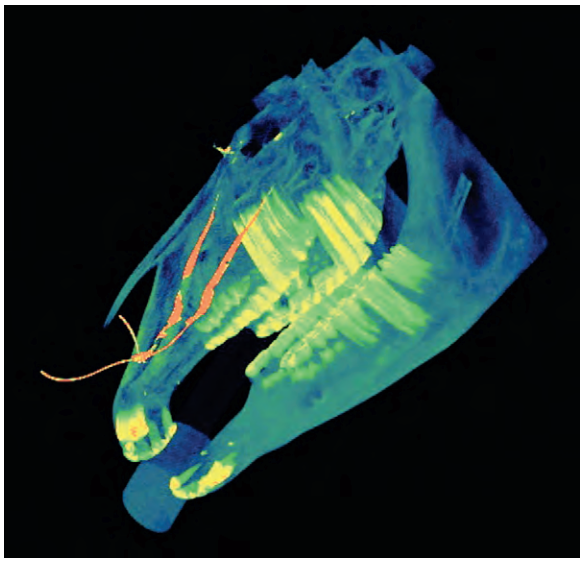


Figure 1-86. The three-dimensional color-enhanced reconstruction of computed tomography dacryocystorhinography can assist in interpretation of the nasolacrimal duct (red).

Please see Chapter 4 for more information on the diagnosis and treatment of nasolacrimal disease.

COMPUTED TOMOGRAPHY

Computed tomography (CT) is the acquisition of cross-sectional, two-dimensional slices (i.e., tomograms) of a tissue.[195] These tomograms are created by a rotating radiation source that transmits x-rays, and the degree of attenuation of the x-rays within the intervening tissue is measured by a synchronous radiation detector array.[195] Grayscale image reconstruction from the attenuation coefficients can then be digitally performed.[195] The lighter the image, the greater the absorption of x-rays through that tissue.[195] Fat is black (i.e., low density) and bone, muscle, and nerve are various shades of white (i.e., high density).[195] This provides relatively good contrast within the orbit.[195]

The use of cross-sectional CT in the equine head has been proposed to overcome the superimposition of the complex anatomic features of the equine skull that make conventional radiographic interpretation difficult.[196] References for normal transverse CT anatomy of the adult horse and the foal have been published, and the reader is referred to these articles for details.[197,198] The requirement for general anesthesia is a risk that must be calculated to gain diagnostic information.

The large amount of low-density fat in the equine orbit provides good natural contrast for differentiating the various soft-tissue structures by CT, although the primary advantage of CT over magnetic resonance imaging (MRI) is its ability to detect osseous changes (Fig. 1-87).[195,199] Disadvantages of CT over skull radiography in the horse include the need for general anesthesia and the risks associated with recovery from anesthesia, increased cost, and limited accessibility.[199] Disadvantages

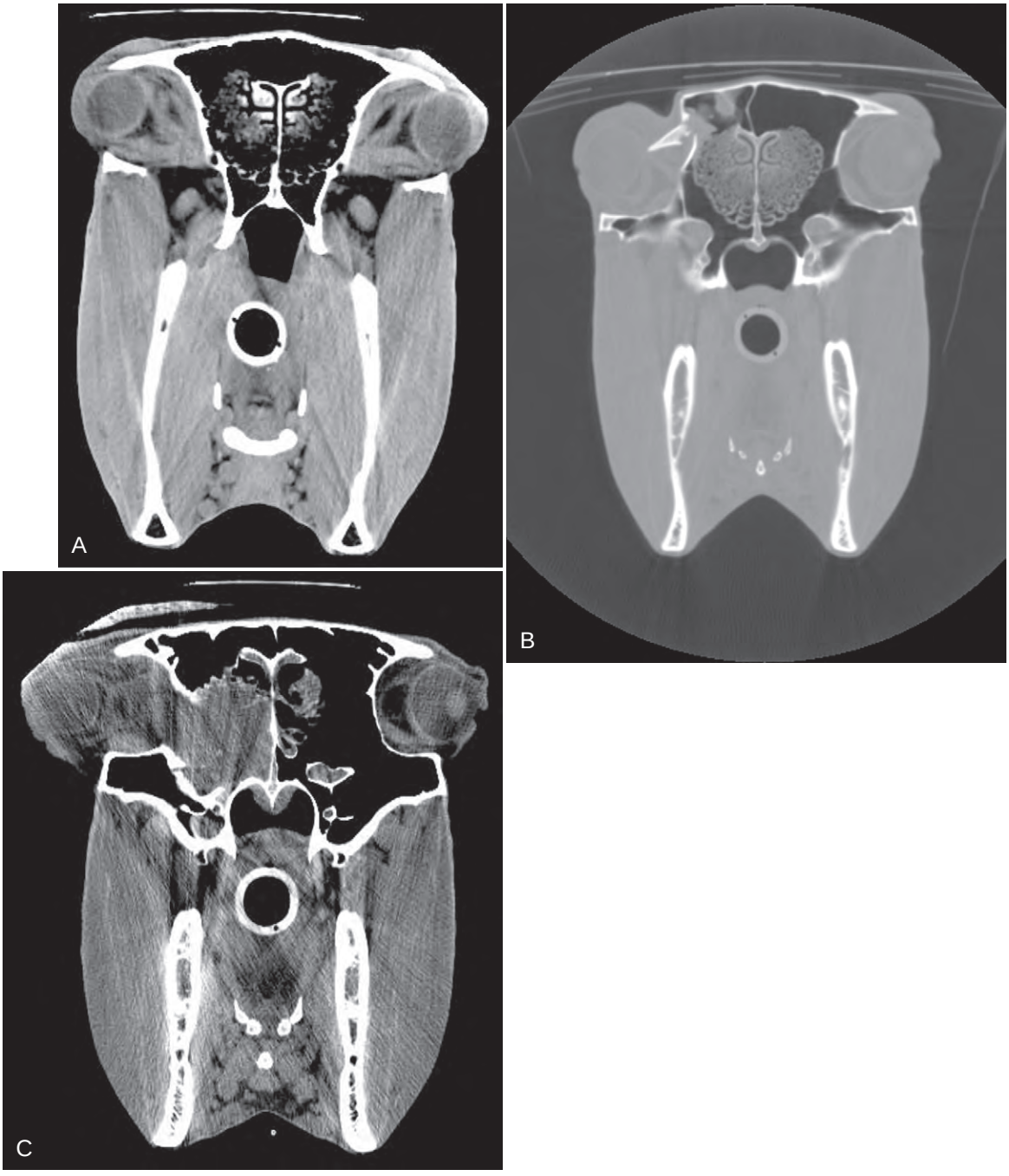


Figure 1-87. The large amount of low-density fat in the equine orbit provides good natural contrast for the differentiation of the various soft-tissue structures by computed tomography (CT), although the primary advantage of CT over magnetic resonance imaging (MRI) is its ability to detect osseous changes. **A,** Normal transverse equine CT scan. **B,** A supraorbital fracture is present on this CT scan. **C,** A nasal mass that has infiltrated the orbit is seen on this CT scan.

of CT over MRI in the horse include possible greater duration of anesthesia and the risk of irradiation of the lens.[199]

There have been few reports of CT examination of the equine orbit and nasolacrimal duct in disease. Most cases in the literature involving CT of the equine head involve evaluation of the sinuses, brain abscess, pituitary tumors, and skull fractures.[199,200-206] Very little has directly concerned the orbit (see Fig. 1-87).[178,200,206] Chapter 3 offers more information on indications for orbital imaging in the horse.

MAGNETIC RESONANCE IMAGING

MRI involves localization, quantitation, and transformation of emitted resonant energy of protons that have been magnetized.[195,199,207] Standard MRI studies of the head are typically acquired in at least three orthogonal image planes (i.e., sagittal, transverse, and dorsal) relative to the central axis of the head.[200,207] The multiplanar capacity of MRI to acquire images in any desired slice plane without repositioning the patient is an important advantage of MRI over CT.[200,207] Conventional MRI examinations of the head include three types of pulse-echo sequences: the T_1-weighted sequence (performed before and after contrast administration); proton density; and the T_2-weighted sequence.[199] Contrast enhancement with gadolinium diethylenetriaminepentaacetic acid (Magnevist [Berlex Laboratories, Cedar Knolls, NJ]) will result in a hyperintense signal in which the contrast has extravasated (e.g., as a result of breakdown of the blood-brain barrier caused by inflammation or neoplasia).[199] An IV dose of 20 mL has been reported to be adequate in the horse.[199] The longitudinal magnetic relaxation time (T_1, spin lattice relaxation time) and the transverse magnetic relaxation time (T_2, spin-spin relaxation time) are the times needed for energized protons to return from the higher energy state to reestablish alignment with the magnetic field and the rate of decrease in the signal of the excited nuclei of the protons as energy is transferred to adjacent unexcited nuclei, respectively.[199] Proton density weighted images are taken when the protons are relaxed and do not depend on time constants.[199] A T_2-weighted image can be differentiated from a T_1-weighted image by the high-intensity signal from the vitreous in a T_2-weighted image.[199]

Use of MRI to evaluate the equine orbit suffers from the same technical difficulties as CT, including the need for general anesthesia and the risks associated with recovery from anesthesia, weight limitations, and limited availability.[197,199] Normal anatomic atlases for the equine orbital structures and sinuses have been published for both T_1-weighted and T_2-weighted magnetic resonance images.[199,207-210]

The order of signal intensity for T_1-weighted images from white to black is: fat > cornea, lens capsule, iris, retina, choroid > brain > extraocular muscles, optic nerve, skin, eyelids > aqueous, vitreous humor > lens, sclera > bone, air.[207] The order of signal intensity for T_2-weighted images from white to black is: vitreous, aqueous humor > brain > extraocular muscles, optic nerve, iris, eyelids, skin > fat, bone, sclera > lens, air.[207] The oblique dorsal and oblique sagittal planes have been reported to be the most valuable for evaluating the orbit and optic pathways.[207] Equine patients less than 300 lb can be imaged by many of the existent superconductive magnets. Modification of current equipment allows for imaging the adult head.[207]

MRI advantages over CT include better resolution of retrobulbar structures, absence of ionizing radiation, direct multiplanar imaging that does not require changes in the position of the patient or gantry, enhanced anatomic detail and tissue characterization, and better assessment of both the intraorbital and extraorbital optic nerves.[195,207] Disadvantages include the requirement for general anesthesia, long data-acquisition time, increased tissue-slice thickness, poorer spatial resolution, failure to detect defects in cortical bone or soft-tissue mineralization, certain image artifacts, and the need for nonmetallic ventilation during inhalant anesthesia.[195,207] As in humans, T_1-weighted images provide the greatest spatial resolution and the best definition of normal anatomic detail of both the eye and orbit. Pathologic processes are known to predominantly affect T_2-weighted images.[207] Additional magnetic resonance studies on diseased eyes and orbits are needed to determine the value of this imaging tool in equine ophthalmology.

References

1. Budras K: Anatomy of the horse: an illustrated text. ed 3, Hannover, Germany, 2001, Schlutersche.
2. Dyce K, Sack W, Wensing C: Textbook of veterinary anatomy. ed 4, Philadelphia, 2010, Saunders (in press).
3. Kainer RA: Clinical anatomy of the equine head, Vet Clin North Am Equine Pract 9:1–23, 1993.
4. Lavach J: Large animal ophthalmology, St Louis, 1990, Mosby.
5. Prince J: Anatomy and histology of the eye and orbit in domestic animals, Springfield, IL, 1960, Charles C. Thomas, pp 128–153.
6. Samuelson D: Ophthalmic anatomy. In Gelatt K, editor: Veterinary Ophthalmology. Ames, 2007, Blackwell, pp 37–148.
7. Bistner S: Fundus examination of the horse, Vet Clin North Am Large Anim Pract 6:541–551, 1984.
8. Brooks D, Matthews A: Equine ophthalmology. In Gelatt K, editor: Veterinary ophthalmology. Ames, 2007, Blackwell Publishing pp 1165–1274.
9. Cooley PL: Normal equine ocular anatomy and eye examination, Vet Clin North Am Equine Pract 8:427–449, 1992.
10. Meredith R, Wolf E: Ophthalmic examination and therapeutic techniques in the horse, Comp Cont Ed Pract Vet 3:s426–s433, 1981.
11. Davis JL, Stewart T, Brazik E, et al: The effect of topical administration of atropine sulfate on the normal equine pupil: influence of age, breed and gender, Vet Ophthalmol 6:329–332, 2003.
12. Gelatt K: Ophthalmic examination and diagnostic procedures. In Gelatt K, editor: Veterinary ophthalmology. Ames, 2007, Blackwell Publishing pp 438–535.
13. Gelatt K, Gum G, Mackay E: Evaluation of mydriatics in horses, Vet Comp Ophthalmol 5:104–107, 1995.
14. Hacker DV, Buyukmihci NC, Franti CE, et al: Effect of topical phenylephrine on the equine pupil, Am J Vet Res 48:320–322, 1987.
15. Hahn CN, Mayhew IG: Studies on the experimental induction of ptosis in horses, Vet J 160:220–224, 2000.
16. Williams MM, Spiess BM, Pascoe PJ, et al: Systemic effects of topical and subconjunctival ophthalmic atropine in the horse, Vet Ophthalmol 3:193–199, 2000.
17. Severin G: Veterinary ophthalmology notes, ed 3, Fort Collins, CO, 1995, Colorado State University.
18. George L: Localization and differentiation of neurologic diseases. In Smith B, editors: Large animal internal medicine, St Louis: 1990, Mosby, pp 145–170.

19. Mayhew I: Large animal neurology: a handbook for veterinary clinicians, Philadelphia, 1989, Lea & Febiger.
20. Scagliotti R: Comparative neuro-ophthalmology. In Gelatt K, editor: Veterinary ophthalmology, Philadelphia, 1999, Lippincott Williams & Wilkins, pp 1307–1400,
21. Crispin SM: Developmental anomalies and abnormalities of the equine iris, Vet Ophthalmol 3:93–98, 2000.
22. Gum G, Gelatt K, Ofri R: Physiology of the eye. In Gelatt K, editor: Veterinary ophthalmology, Philadelphia, 1999, Lippincott Williams & Wilkins, pp 151–181.
23. Crispin SM: Tear-deficient and evaporative dry eye syndromes of the horse, Vet Ophthalmol 3:87–92, 2000.
24. Bacon CL, Davidson HJ, Yvorchuk K, et al: Bilateral Horner's syndrome secondary to metastatic squamous cell carcinoma in a horse, Equine Vet J 28:500–503, 1996.
25. Green SL, Cochrane SM, Smith-Maxie L: Horner's syndrome in ten horses, Can Vet J 33:330–333, 1992.
26. Neer T: Horner's syndrome: anatomy, diagnosis, and causes, Comp Contin Educ Pract Vet 6:740–746, 1984.
27. Purohit RC, McCoy MD, Bergfeld WA, 3rd: Thermographic diagnosis of Horner's syndrome in the horse, Am J Vet Res 41:1180–1182, 1980.
28. Simoens P, Lauwers H, De Muelenare C, et al: Horner's syndrome in the horse: a clinical, experimental and morphological study, Equine Vet J Suppl 62–65, 1990.
29. Smith J, Mayhew I: Horner's syndrome in large animals, Cornell Vet 67:529–542, 1977.
30. Sweeney RW, Sweeney CR: Transient Horner's syndrome following routine intravenous injections in two horses, J Am Vet Med Assoc 185:802–803, 1984.
31. Geiser D, Henton J, Held J: Tympanic bulla, petrous temporal bone, and hyoid apparatus disease in horses, Comp Contin Educ Pract Vet 10:740–754, 1988.
32. Muir W, Hubbell J: Anesthetic techniques. In Muir W, Hubbell J, editors: Equine anesthesia: monitoring and emergency therapy, St Louis, 1991, Mosby Year Book, pp 444–460.
33. Manning J, St. Clair L: Palpebral, frontal, and zygomatic nerve blocks for examination of the equine eye, Vet Med Small Anim Clin 32:187–189, 1976.
34. Rubin L: Auriculopalpebral nerve block as an adjunct to the diagnosis and treatment of ocular inflammation in the horse, J Am Vet Med Assoc 144:1387–1388, 1964.
35. Ramsey DT, Ewart SL, Render JA, et al: Congenital ocular abnormalities of Rocky Mountain horses, Vet Ophthalmol 2:47–59, 1999.
36. Ramsey DT, Hauptman JG, Petersen-Jones SM: Corneal thickness, intraocular pressure, and optical corneal diameter in Rocky Mountain horses with cornea globosa or clinically normal corneas, Am J Vet Res 60:1317–1321, 1999.
37. Beech J, Zappala RA, Smith G, et al: Schirmer tear test results in normal horses and ponies: effect of age, season, environment, sex, time of day and placement of strips, Vet Ophthalmol 6:251–254, 2003.
38. Brightman AH, 2nd, Manning JP, Benson GJ, et al: Decreased tear production associated with general anesthesia in the horse, J Am Vet Med Assoc 182:243–244, 1983.
39. Piccione G, Giannetto C, Fazio F, et al: Daily rhythm of tear production in normal horse, Vet Ophthalmol 11(Suppl 1):57–60, 2008.
40. Schwarz BC, Sallmutter T, Nell B: Keratoconjunctivitis sicca attributable to parasympathetic facial nerve dysfunction associated with hypothyroidism in a horse, J Am Vet Med Assoc 233:1761–1766, 2008.
41. Reilly L, Beech J: Bilateral keratoconjunctivitis sicca in a horse, Equine Vet J 26:171–172, 1994.
42. Collins B: Immune mediated keratoconjunctivitis sicca in a horse, Vet Comp Ophthalmol 4:61–65, 1994.
43. Spurlock SL, Spurlock GH, Wise M: Keratoconjunctivitis sicca associated with fracture of the stylohyoid bone in a horse, J Am Vet Med Assoc 194:258–259, 1989.
44. Spiess BM, Wilcock BP, Physick-Sheard PW: Eosinophilic granulomatous dacryoadenitis causing bilateral keratoconjunctivitis sicca in a horse, Equine Vet J 21:226–228, 1989.
45. Wolf E, Meredith R: Parotid duct transposition in the horse, J Equine Vet Sci 12:143–145, 1981.
46. Joyce JR, Bratton GR: Keratoconjunctivitis sicca secondary to fracture of the mandible, Vet Med Small Anim Clin 68:619–620, 1973.
47. Marts B, Bryan G, Prieur D: Schirmer tear test measurement and lysozyme concentration of equine tears, J Equine Med Surg 1:427–430, 1977.
48. Williams R, Manning J, Peiffer R: The Schirmer tear test in the equine: normal values and the contribution of the gland of the nictitating membrane, J Equine Med Surg 3:117–119, 1979.
49. Brooks DE, Clark CK, Lester GD: Cochet-Bonnet aesthesiometer-determined corneal sensitivity in neonatal foals and adult horses, Vet Ophthalmol 3:133–137, 2000.
50. Clark C, Brooks D, Lester G: Corneal sensitivity and tear production in hospitalized neonatal foals, Am Coll Vet Ophthalmol 134–136, 1996.
51. Hamor RE, Roberts SM, Severin GA, et al: Evaluation of results for Schirmer tear tests conducted with and without application of a topical anesthetic in clinically normal dogs of 5 breeds, Am J Vet Res 61:1422–1425, 2000.
52. Dziezyc J: Nasolacrimal system. In Auer J, editor: Equine surgery, Philadelphia, 1992, Saunders, pp 630–634.
53. Latimer CA, Wyman M, Diesem CD, et al: Radiographic and gross anatomy of the nasolacrimal duct of the horse, Am J Vet Res 45:451–458, 1984.
54. Cassotis NJ, Schiffman P: Calcification associated with the nasolacrimal system of a horse: case report and mineralogic composition, Vet Ophthalmol 9:187–190, 2006.
55. Berliner M: Biomicroscopy of the eye, New York, 1949, Paul B. Hoeber.
56. Martin CL: Slit lamp examination of the normal canine anterior ocular segment. III. Discussion and summary, J Small Anim Pract 10:163–169, 1969.
57. Martin CL: Slit lamp examination of the normal canine anterior ocular segment. II. Description, J Small Anim Pract 10:151–162, 1969.
58. Martin CL: Slit lamp examination of the normal canine anterior ocular segment. I. Introduction and technique, J Small Anim Pract 10:143–149, 1969.
59. Kleinfeld J, Ellis PP: Inhibition of microorganisms by topical anesthetics, Appl Microbiol 15:1296–1298, 1967.
60. Champagne E, Pickett J: The effect of topical 0.5% proparacaine HCl on corneal and conjunctival culture results, Proc Am Coll Vet Ophthalmol 144–145, 1995.
61. Collinson P, O'Rielly JL, Ficorilli N, et al: Isolation of equine herpesvirus type 2 (equine gammaherpesvirus 2) from foals with keratoconjunctivitis, J Am Vet Med Assoc 205:329–331, 1994.
62. Miller T: Herpetic keratitis in the horse, Equine Vet J 10:15–17.
63. Bauer G, Spiess B, Lutz H: Exfoliative cytology of conjunctiva and cornea in domestic animals: a comparison of four collecting techniques, Vet Comp Ophthalmol 6:181–186, 1996.
64. Lavach JD, Thrall MA, Benjamin MM, et al: Cytology of normal and inflamed conjunctivas in dogs and cats, J Am Vet Med Assoc 170:722–727, 1977.
65. Wills M: Conjunctival brush cytology: evaluation of a new cytological collection technique in dogs and cats with a comparison to conjunctival scraping, Vet Comp Ophthalmol 7:74–81, 1997.
66. Richter M, Hauser B, Kaps S, et al: Keratitis due to *Histoplasma* spp. in a horse, Vet Ophthalmol 6:99–103, 2003.
67. Forster RK, Wirta MG, Solis M, et al: Methenamine-silver-stained corneal scrapings in keratomycosis, Am J Ophthalmol 82:261–265, 1976.
68. Vengayil S, Panda A, Satpathy G, et al: Polymerase chain reaction-guided diagnosis of mycotic keratitis: a prospective evaluation of its efficacy and limitations, Invest Ophthalmol Vis Sci 50:152–156, 2009.
69. Borchers K, Ebert M, Fetsch A, et al: Prevalence of equine herpesvirus type 2 (EHV-2) DNA in ocular swabs and its cell tropism in equine conjunctiva, Vet Microbiol 118:260–266, 2006.
70. Da Silva Curiel J: Topical fluorescein dye: effects on immunofluorescent antibody test for feline herpesvirus keratoconjunctivitis, Prog Vet Comp Ophthalmol 99–104, 1991.
71. Feenstra RP, Tseng SC: What is actually stained by rose bengal? Arch Ophthalmol 110:984–993, 1992.
72. Gelatt K: Vital staining of the canine cornea and conjunctiva with rose Bengal, J Am Anim Hosp Assoc 8:17–22, 1972.
73. Kim J: The use of vital dyes in corneal disease, Curr Opin Ophthalmol 11:241–247, 2000.
74. Laroche RR, Campbell RC: Quantitative rose bengal staining technique for external ocular diseases, Ann Ophthalmol 20:274–276, 1988.
75. Slatter DH: Differential vital staining of the canine cornea and conjunctiva with fluorescein-rose bengal and alcian blue, J Small Anim Pract 14:291–296, 1973.

76. Kimura SJ: Fluorescein paper. A simple means of insuring the use of sterile fluorescein, Am J Ophthalmol 34:446–447, 1951.
77. Cello RM, Lasmanis J: Pseudomonas infection of the eye of the dog resulting from the use of contaminated fluorescein solution, J Am Vet Med Assoc 132:297–299, 1958.
78. Feenstra RP, Tseng SC: Comparison of fluorescein and rose bengal staining, Ophthalmology 99:605–617, 1992.
79. Kim J, Foulks GN: Evaluation of the effect of lissamine green and rose bengal on human corneal epithelial cells, Cornea 18:328–332, 1999.
80. Brooks DE, Andrew SE, Denis H, et al: Rose bengal positive epithelial microerosions as a manifestation of equine keratomycosis, Vet Ophthalmol 3:83–86, 2000.
81. Knollinger AM, La Croix NC, Barrett PM, et al: Evaluation of a rebound tonometer for measuring intraocular pressure in dogs and horses, J Am Vet Med Assoc 227:244–248, 2005.
82. van der Woerdt A, Gilger BC, Wilkie DA, et al: Effect of auriculopalpebral nerve block and intravenous administration of xylazine on intraocular pressure and corneal thickness in horses, Am J Vet Res 56:155–158, 1995.
83. McClure J, Gelatt K, Manning J: The effect of parenteral acepromazine and xylazine on intraocular pressure in the horse, Vet Med Small Anim Clin 1727–1730, 1976.
84. Smith PJ, Gum GG, Whitley RD, et al: Tonometric and tonographic studies in the normal pony eye, Equine Vet J Suppl 36–38, 1990.
85. Trim CM, Colbern GT, Martin CL: Effect of xylazine and ketamine on intraocular pressure in horses, Vet Rec 117:442–443, 1985.
86. Miller PE, Pickett JP, Majors LJ: Evaluation of two applanation tonometers in horses, Am J Vet Res 51:935–937, 1990.
87. Cohen CM, Reinke DA: Equine tonometry, J Am Vet Med Assoc 156:1884–1887, 1970.
88. Komaromy AM, Garg CD, Ying GS, et al: Effect of head position on intraocular pressure in horses, Am J Vet Res 67:1232–1235, 2006.
89. Bertolucci C, Giudice E, Fazio F, et al: Circadian intraocular pressure rhythms in athletic horses under different lighting regime, Chronobiol Int 26:348–358, 2009.
90. Gelatt KN, Gum GG: Evaluation of electronic tonometers in the rabbit eye, Am J Vet Res 42:1778–1781, 1981.
91. Gelatt KN, Peiffer RL, Jr, Gum GG, et al: Evaluation of applanation tonometers for the dog eye, Invest Ophthalmol Vis Sci 16:963–968, 1977.
92. Kotani T: Which are the optimal tonometers for different animal species, Anim Eye Res 12:55–61, 1993.
93. Dziezyc J, Millichamp NJ, Smith WB: Comparison of applanation tonometers in dogs and horses, J Am Vet Med Assoc 201:430–433, 1992.
94. Gelatt K, Gum G, Mackay E: Estimation of aqueous humor outflow facility by pneumatonography in normal, genetic carrier, and glaucomatous Beagles, Vet Comp Ophthalmol 6:148–151, 1996.
95. Toris CB, Yablonski ME, Wang YL, et al: Prostaglandin A2 increases uveoscleral outflow and trabecular outflow facility in the cat, Exp Eye Res 61:649–657, 1995.
96. Barnett KC: The ocular fundus of the horse, Equine Vet J 4:17–20, 1972.
97. Crispin SM, Matthews AG, Parker J: The equine fundus. I: Examination, embryology, structure and function, Equine Vet J Suppl 42–49, 1990.
98. Cutler TJ, Brooks DE, Andrew SE, et al: Disease of the equine posterior segment, Vet Ophthalmol 3:73–82, 2000.
99. Matthews AG, Crispin SM, Parker J: The equine fundus. III: Pathological variants, Equine Vet J Suppl 55–61, 1990.
100. Matthews AG, Crispin SM, Parker J: The equine fundus. II: Normal anatomical variants and colobomata, Equine Vet J Suppl 50–54, 1990.
101. Rebhun WC: Retinal and optic nerve diseases, Vet Clin North Am Equine Pract 8:587–608, 1992.
102. Cutler TJ: Ophthalmic findings in the geriatric horse, Vet Clin North Am Equine Pract 18:545–574, 2002.
103. Rubin L: Atlas of veterinary ophthalmoscopy, Philadelphia, 1974, Lea & Febiger.
104. Barnett K: Principles of ophthalmoscopy, Vet Med 62:56–57, 1967.
105. Murphy CJ, Howland HC: The optics of comparative ophthalmoscopy, Vision Res 27:599–607, 1987.
106. Raffe M: Retrobulbar block in combination with general anesthesia for equine ophthalmic surgery, Vet Surg 15:139–141, 1986.
107. Short CE, Rebhun WC: Complications caused by the oculocardiac reflex during anesthesia in a foal, J Am Vet Med Assoc 176:630–631, 1980.
108. Brooks D: Orbit. In Auer J, editor: Equine surgery, Philadelphia, 1992, WB Saunders, pp 654–666.
109. Hazel SJ, Thrall MA, Severin GA, et al: Laboratory evaluation of aqueous humor in the healthy dog, cat, horse, and cow, Am J Vet Res 46:657–659, 1985.
110. Olin DD: Examination of the aqueous humor as a diagnostic aid in anterior uveitis, J Am Vet Med Assoc 171:557–559, 1977.
111. Gilger BC, Salmon JH, Yi NY, et al: Role of bacteria in the pathogenesis of recurrent uveitis in horses from the southeastern United States, Am J Vet Res 69:1329–1335, 2008.
112. Glaze MB, McGuire TC, Schmidt GM, et al: Immunoglobulin levels in tears and aqueous humor of horses before and after diethylcarbamazine (DEC) therapy, Vet Immunol Immunopathol 7:185–198, 1984.
113. Halliwell RE, Brim TA, Hines MT, et al: Studies on equine recurrent uveitis. II: The role of infection with *Leptospira interrogans* serovar pomona, Curr Eye Res 4:1033–1040, 1985.
114. Halliwell RE, Hines MT: Studies on equine recurrent uveitis. I: Levels of immunoglobulin and albumin in the aqueous humor of horses with and without intraocular disease, Curr Eye Res 4:1023–1031, 1985.
115. Wurster U, Riese K, Hoffmann K: Enzyme activities and protein concentration in the intraocular fluids of ten mammals, Acta Ophthalmol (Copenh) 60:729–741, 1982.
116. Miller TL, Willis AM, Wilkie DA, et al: Description of ciliary body anatomy and identification of sites for transscleral cyclophotocoagulation in the equine eye, Vet Ophthalmol 4:183–190, 2001.
117. McLaughlin BG, McLaughlin PS: Equine vitreous humor chemical concentrations: correlation with serum concentrations, and postmortem changes with time and temperature, Can J Vet Res 52:476–480, 1988.
118. Wollanke B, Rohrbach BW, Gerhards H: Serum and vitreous humor antibody titers in and isolation of *Leptospira interrogans* from horses with recurrent uveitis, J Am Vet Med Assoc 219:795–800, 2001.
119. Kaps S, Richter M, Spiess BM: Corneal esthesiometry in the healthy horse, Vet Ophthalmol 6:151–155, 2003.
120. Boberg-Ans J: Experience in clinical examination of corneal sensitivity; corneal sensitivity and the naso-lacrimal reflex after retrobulbar anaesthesia, Br J Ophthalmol 39:705–726, 1955.
121. Kolstad A: Corneal sensitivity by low temperatures, Acta Ophthalmol 48:789–793, 1970.
122. Millodot M: Do blue-eyed people have more sensitive corneas than brown-eyed people? Nature 151–152, 1975.
123. Millodot M: The influence of pregnancy on the sensitivity of the cornea, Br J Ophthalmol 61:646–649, 1977.
124. Millodot M: The influence of age on the sensitivity of the cornea, Invest Ophthalmol Vis Sci 16:240–242, 1977.
125. Murphy CJ, Marfurt CF, McDermott A, et al: Spontaneous chronic corneal epithelial defects (SCCED) in dogs: clinical features, innervation, and effect of topical SP, with or without IGF-1, Invest Ophthalmol Vis Sci 42:2252–2261, 2001.
126. Weigt AK, Herring IP, Marfurt CF, et al: Effects of cyclophotocoagulation with a neodymium:yttrium-aluminum-garnet laser on corneal sensitivity, intraocular pressure, aqueous tear production, and corneal nerve morphology in eyes of dogs, Am J Vet Res 63:906–915, 2002.
127. Gilger BC, Whitley RD, McLaughlin SA, et al: Canine corneal thickness measured by ultrasonic pachymetry, Am J Vet Res 52:1570–1572, 1991.
128. Gilger BC, Wright JC, Whitley RD, et al: Corneal thickness measured by ultrasonic pachymetry in cats, Am J Vet Res 54:228–230, 1993.
129. Choi CY, Youm DJ, Kim MJ, et al: Changes in central corneal thickness of preserved corneas over time measured using anterior segment optical coherence tomography, Cornea 28:536–540, 2009.
130. Fukuda S, Kawana K, Yasuno Y, et al: Anterior ocular biometry using 3-dimensional optical coherence tomography, Ophthalmology 116:882–889, 2009.
131. Ledbetter E: In vivo confocal microscopy of the normal equine cornea and limbus (Personal Communication), 2009.
132. Ling T: Osmotically induced central and peripheral corneal swelling in the cat, Am J Optom Physiol Opt 64:674–677, 1987.
133. Andrew SE, Ramsey DT, Hauptman JG, et al: Density of corneal endothelial cells and corneal thickness in eyes of euthanatized horses, Am J Vet Res 62:479–482, 2001.

134. Plummer CE, Ramsey DT, Hauptman JG: Assessment of corneal thickness, intraocular pressure, optical corneal diameter, and axial globe dimensions in Miniature horses, Am J Vet Res 64:661–665, 2003.
135. Gwin RM, Lerner I, Warren JK, et al: Decrease in canine corneal endothelial cell density and increase in corneal thickness as functions of age, Invest Ophthalmol Vis Sci 22:267–271, 1982.
136. Bell KD, Campbell RJ, Bourne WM: Pathology of late endothelial failure: late endothelial failure of penetrating keratoplasty: study with light and electron microscopy, Cornea 19:40–46, 2000.
137. Gwin RM, Warren JK, Samuelson DA, et al: Effects of phacoemulsification and extracapsular lens removal on corneal thickness and endothelial cell density in the dog, Invest Ophthalmol Vis Sci 24:227–236, 1983.
138. Gum GG: Electrophysiology in veterinary ophthalmology, Vet Clin North Am Small Anim Pract 10:437–454, 1980.
139. Komaromy AM, Andrew SE, Sapp HL, Jr, et al: Flash electroretinography in standing horses using the DTL microfiber electrode, Vet Ophthalmol 6:27–33, 2003.
140. Gilger BC, Malok E, Stewart T, et al: Long-term effect on the equine eye of an intravitreal device used for sustained release of cyclosporine A, Vet Ophthalmol 3:105–110, 2000.
141. Nunnery C, Pickett JP, Zimmerman KL: Congenital stationary night blindness in a Thoroughbred and a Paso Fino, Vet Ophthalmol 8:415–419, 2005.
142. Riis RC, Jackson C, Rebhun W, et al: Ocular manifestations of equine motor neuron disease, Equine Vet J 31:99–110, 1999.
143. Sandmeyer LS, Breaux CB, Archer S, et al: Clinical and electroretinographic characteristics of congenital stationary night blindness in the Appaloosa and the association with the leopard complex, Vet Ophthalmol 10:368–375, 2007.
144. Strobel BW, Wilkie DA, Gilger BC: Retinal detachment in horses: 40 cases (1998-2005), Vet Ophthalmol 10:380–385, 2007.
145. Bilge M, Bingle A, Seneviratne KN, et al: A map of the visual cortex in the cat, J Physiol 191:116P–118P, 1967.
146. Yanase J, Ogawa H: Effects of halothane and sevoflurane on the electroretinogram of dogs, Am J Vet Res 58:904–909, 1997.
147. Francois J, Wouters L, Victoria-Troncoso V, et al: Morphometric and electrophysiologic study of the photoreceptors in the horse, Ophthalmologica 181:340–349, 1980.
148. Witzel DA, Smith EL, Wilson RD, et al: Congenital stationary night blindness: an animal model, Invest Ophthalmol Vis Sci 17:788–795, 1978.
149. Wouters L, de Moor A, Moens Y: Rod and cone components in the electroretinogram of the horse, Zentralbl Veterinarmed A 27:330–338, 1980.
150. Molleda JM, Cervantes I, Galan A, et al: Fluorangiographic study of the ocular fundus in normal horses, Vet Ophthalmol 11(Suppl 1): 2–7, 2008.
151. Walde I: [The fluorescence angiogram of the normal ocular fundus in the dog and horse], Tierarztl Prax 5:343–347, 1977.
152. Berkow J, Orth D, Kelley J: Fluorescein Angiography: technique and interpretation, San Francisco, 1991, American Academy of Ophthalmology.
153. Gelatt KN, Henderson JD, Jr, Steffen GR: Fluorescein angiography of the normal and diseased ocular fundi of the laboratory dog, J Am Vet Med Assoc 169:980–984, 1976.
154. Davidson M, Baty K: Anaphylaxis associated with intravenous sodium fluorescein administration in a cat, Prog Vet Comp Ophthalmol 1:127–128, 1991.
155. Farrall H, Handscombe M: Equine vision, Equine Vet J 31:354–355, 1999.
156. Farrall H, Handscombe MC: Follow-up report of a case of surgical aphakia with an analysis of equine visual function, Equine Vet J Suppl 91–93, 1990.
157. Harman AM, Moore S, Hoskins R, et al: Horse vision and an explanation for the visual behaviour originally explained by the “ramp retina”, Equine Vet J 31:384–390, 1999.
158. Knill LM, Eagleton RD, Harver E: Physical optics of the equine eye, Am J Vet Res 38:735–737, 1977.
159. Roberts SM: Equine vision and optics, Vet Clin North Am Equine Pract 8:451–457, 1992.
160. Sivak J, Allen D: An evaluation of the ramp retina in the horse eye, Vision Res 15:1353–1356, 1975.
161. Davidson M: Clinical retinoscopy for the veterinary ophthalmologist, Vet Comp Ophthalmol 7:128–137, 1997.
162. Murphy CJ, Zadnik K, Mannis MJ: Myopia and refractive error in dogs, Invest Ophthalmol Vis Sci 33:2459–2463, 1992.
163. Miller P: A limited review of feline and equine vision, Am Coll Vet Ophthalmol 1996.
164. McMullen R: Refractive state of the normal equine eye, 2009.
165. McMullen R, Davidson M, Salmon JH, et al: In vitro and in vivo evaluation of 30 D and 25 D equine intraocular lens implant, Am J Vet Res 2009, In Press.
166. Millichamp N, Dziezyc J: Cataract surgery in horses. Fort Lauderdale, FL, 1996, Association in Research and Ophthalmology, p S763.
167. Bentley E, Miller PE, Diehl KA: Use of high-resolution ultrasound as a diagnostic tool in veterinary ophthalmology, J Am Vet Med Assoc 223:1617–1622, 1599, 2003.
168. McMullen RJ, Jr, Gilger BC: Keratometry, biometry and prediction of intraocular lens power in the equine eye, Vet Ophthalmol 9:357–360, 2006.
169. Scotty NC, Cutler TJ, Brooks DE, et al: Diagnostic ultrasonography of equine lens and posterior segment abnormalities, Vet Ophthalmol 7:127–139, 2004.
170. Williams J, Wilkie D: Ultrasonography of the eye, Comp Contin Educ Pract Vet 18:667–677, 1996.
171. Rogers M, Cartee R: Evaluation of the extirpated equine eye using B-mode ultrasonography, Vet Radiol 27:24–29, 1986.
172. van der Woerdt A, Wilkie DA, Myer CW: Ultrasonographic abnormalities in the eyes of dogs with cataracts: 147 cases (1986–1992), J Am Vet Med Assoc 203:838–841, 1993.
173. Byrne S, Green R: Ultrasound of the eye and orbit, ed 2, St. Louis, 2002, Mosby.
174. Crumley W, Gionfriddo JR, Radecki SV: Relationship of the iridocorneal angle, as measured using ultrasound biomicroscopy, with post-operative increases in intraocular pressure post-phacoemulsification in dogs, Vet Ophthalmol 12:22–27, 2009.
175. Gibson TE, Roberts SM, Severin GA, et al: Comparison of gonioscopy and ultrasound biomicroscopy for evaluating the iridocorneal angle in dogs, J Am Vet Med Assoc 213:635–638, 1998.
176. Rose MD, Mattoon JS, Gemensky-Metzler AJ, et al: Ultrasound biomicroscopy of the iridocorneal angle of the eye before and after phacoemulsification and intraocular lens implantation in dogs, Am J Vet Res 69:279–288, 2008.
177. Eisenberg H: Ultrasonography of the eye and orbit, Vet Clin North Am Small Anim Pract 15:1263–1274, 1985.
178. Barnett KC, Blunden AS, Dyson SJ, et al: Blindness, optic atrophy and sinusitis in the horse, Vet Ophthalmol 11(Suppl 1):20–26, 2008.
179. Liebmann J, Ritch R, Esaki K: Ultrasound biomicroscopy, Ophthalmol Clin North Am 11:421–433, 1998.
180. Berinstein DM, Gentile RC, Sidoti PA, et al: Ultrasound biomicroscopy in anterior ocular trauma, Ophthalmic Surg Lasers 28:201–207, 1997.
181. Gilger BC, Reeves KA, Salmon JH: Ocular parameters related to drug delivery in the canine and equine eye: aqueous and vitreous humor volume and scleral surface area and thickness, Vet Ophthalmol 8:265–269, 2005.
182. McMullen R, Gilger B: Use of infrared photography in diseases of the anterior segment, Vet Ophthalmol 12:124–131, 2009.
183. Diesem C: Gross anatomic structures of equine and bovine orbit and its contents, Am J Vet Res 29:1769–1781, 1968.
184. Bertone JJ, Biller DS, Ruggles A: Diagnostic techniques for evaluation of the paranasal sinuses, Vet Clin North Am Equine Pract 9:75–91, 1993.
185. Schebitz H, Wilkens H: Atlas of radiographic anatomy of the horse, Philadelphia, 1978, WB Saunders, pp 10–15.
186. Park RD: Radiographic examination of the equine head, Vet Clin North Am Equine Pract 9:49–74, 1993.
187. Wyn-Jones G: Interpreting radiographs 6: Radiology of the equine head (Part 2), Equine Vet J 17:417–425, 1985.
188. Caron JP, Barber SM, Bailey JV, et al: Periorbital skull fractures in five horses, J Am Vet Med Assoc 188:280–284, 1986.
189. Davidson HJ, Middleton DL, Blanchard GL, et al: Radiographic examination of eyes fixed in Zenker’s solution, Vet Pathol 26:83–85, 1989.
190. Said AH, Shokry M, Saleh MA, et al: Contribution to the nasolacrimal duct of donkeys in Egypt, Anat Histol Embryol 6:347–350, 1977.
191. Latimer CA, Wyman M: Atresia of the nasolacrimal duct in three horses, J Am Vet Med Assoc 184:989–992, 1984.
192. Nykamp SG, Scrivani PV, Pease AP: Computed tomography dacryocystography evaluation of the nasolacrimal apparatus, Vet Radiol Ultrasound 45:23–28, 2004.
193. Rubin PA, Bilyk JR, Shore JW, et al: Magnetic resonance imaging of the lacrimal drainage system, Ophthalmology 101:235–243, 1994.

194. Ashenhurst M, Jaffer N, Hurwitz JJ, et al: Combined computed tomography and dacryocystography for complex lacrimal problems, Can J Ophthalmol 26:27–31, 1991.
195. Brooks D: Ocular imaging. In Gelatt K, editor: Veterinary ophthalmology, Philadelphia, 1999, Lippincott Williams & Wilkins, pp 467–482.
196. Barbee D: Computed tomography in horses, Vet Radiol Ultrasound 28:144–151, 1987.
197. Morrow KL, Park RD, Spurgeon TL, et al: Computed tomographic imaging of the equine head, Vet Radiol Ultrasound 41:491–497, 2000.
198. Smallwood JE, Wood BC, Taylor WE, et al: Anatomic reference for computed tomography of the head of the foal, Vet Radiol Ultrasound 43:99–117, 2002.
199. Tucker RL, Farrell E: Computed tomography and magnetic resonance imaging of the equine head, Vet Clin North Am Equine Pract 17:131–144, vii, 2001.
200. Boroffka S, Van Den Belt A: CT/Ultrasound diagnosis: retrobulbar hematoma in a horse, Vet Radiol 37:441–443, 1996.
201. Allen JR, Barbee DD, Boulton CR, et al: Brain abscess in a horse: diagnosis by computed tomography and successful surgical treatment, Equine Vet J 19:552–555, 1987.
202. Colbourne CM, Rosenstein DS, Steficek BA, et al: Surgical treatment of progressive ethmoidal hematoma aided by computed tomography in a foal, J Am Vet Med Assoc 211:335–338, 1997.
203. Sasaki M, Hayashi Y, Koie H, et al: CT examination of the guttural pouch (auditory tube diverticulum) in Przewalski's horse *(Equus przewalskii)*, J Vet Med Sci 61:1019–1022, 1999.
204. Tietje S, Becker M, Bockenhoff G: Computed tomographic evaluation of head diseases in the horse: 15 cases, Equine Vet J 28:98–105, 1996.
205. Wallace M: Central blindness associated with a pituitary adenoma in a horse, Equine Pract 18:8–13, 1996.
206. Davis JL, Gilger BC, Spaulding K, et al: Nasal adenocarcinoma with diffuse metastases involving the orbit, cerebrum, and multiple cranial nerves in a horse, J Am Vet Med Assoc 221:1460–1463, 1420, 2002.
207. Morgan R, Daniel G, Donnell R: Magnetic resonance imaging of the normal eye and orbit of the horse, Prog Vet Comp Ophthalmol 3:127–133, 1993.
208. Vazquez JM, Rivero M, Gil F, et al: Magnetic resonance imaging of two normal equine brains and their associated structures, Vet Rec 148:229–232, 2001.
209. Arencibia A, Vazquez JM, Jaber R, et al: Magnetic resonance imaging and cross-sectional anatomy of the normal equine sinuses and nasal passages, Vet Radiol Ultrasound 41:313–319, 2000.
210. Chaffin MK, Walker MA, McArthur NH, et al: Magnetic resonance imaging of the brain of normal neonatal foals, Vet Radiol Ultrasound 38:102–111, 1997.

Chapter 2

Practical General Field Ophthalmology

Ann E. Dwyer

FIELD OPHTHALMOLOGY BASICS

GENERAL COMMENTS

Examination of the equine eye is simplified by the fact that the adnexa, globe surface, and intraocular contents are easy to inspect and often easy to image. Thorough examination can be done in the field if the practitioner arrives at the call with functional portable diagnostic tools and all the common drugs and supplies needed for routine restraint and handling. Examination will be proficient if the practitioner takes the time to create an environment conducive to proper examination, chooses effective patient position and restraint, images observable abnormalities with a digital camera, and follows the methodical examination techniques outlined in Chapter 1.

Although some ophthalmic problems are chronic, many are presented as ophthalmic emergencies. Horse owners and clinic reception staff must be trained to regard swollen, painful, traumatized, or acutely discolored eyes as true emergencies and schedule visits for all these cases on a same-day basis. Clients who call in with a horse that is suffering an ophthalmic emergency should be instructed to keep the animal in a clean, dark stall until it is examined. A workspace that can be darkened for examination and well lit for treatment should be available. The client should be instructed to gather the materials needed for a

bale head support (4 to 6 bales of hay or shavings and a clean cover for the top bale) prior to the arrival of the clinician (Fig. 2-1). Clients should be cautioned against administration of medication in an eye that has not been examined.

Horses with acute or chronic ophthalmic problems usually require ocular diagnostic testing and imaging once examination is complete. Common tests include visual maze testing, tonometry, dye tests, culture and cytology, and biopsy. Tests applicable to the problem at hand can be done in the field using simple equipment if the practitioner follows the guidelines in this text for test completion and interpretation. Practitioners are encouraged to develop expertise in digital photography so that useful ocular images can be obtained and to practice cytologic sampling so that sample analysis can be performed in house.

Examination, imaging, and diagnostic testing must lead to a diagnosis. Ocular problems like trauma or overt neoplasia are obvious, but diagnosis of other problems can be challenging. The conditions most often misdiagnosed in the field are listed in Box 2-1; these conditions merit special study by all equine practitioners. Certain conditions, particularly diffuse nonulcerative loss of corneal transparency, glaucoma, and subclinical uveitis are not completely understood, so information on differential diagnosis is sparse. Other conditions such as stromal abscesses or fungal keratitis have diagnostic elements that may be overlooked or misinterpreted. Some problems like deep corneal infections and equine recurrent uveitis may present at a stage where multiple regions of ocular anatomy are altered, causing uncertainty as to which elements are primary issues and which elements are secondary. Improvement in diagnostic acumen is dependent on experience, constant study of new information, selection of appropriate diagnostic tests, and close surveillance of case progress and therapeutic effectiveness.

Therapy for ocular problems encompasses a wide spectrum of options and skills that are discussed throughout this text. Competence can be honed by experience with the use of medical treatment aids like subpalpebral lavage systems and frequent practice of simple field surgeries. Practitioners with special interest may pursue additional expertise in procedures like enucleation, nictitans removal, and simple corneal surgeries if they have access to a facility with stocks and/or a surgery table.

Although most routine ophthalmic problems can be diagnosed and treated by general equine practitioners, some problems need referral to specialists for optimum care. Specialty practices and universities have advanced examination equipment and offer diagnostic tests that are unavailable to practitioners. They provide surgical solutions for serious problems that may spare sight. Specialists have the broadest knowledge base for assessment of confusing presentations and can take rapid action to treat serious traumas or infections. Referral centers have sufficient support staff to provide the round-the-clock care some problems require. Practitioners must cultivate a broad enough understanding of ophthalmic surgery, pathology, and pathophysiology to recognize the problems that can benefit from specialist evaluation and refer these cases early.

Excellence in field ophthalmology is within the reach of every practitioner who makes a serious effort to study the subject and hone their ophthalmic examination, testing, imaging, and treatment skill set. This chapter outlines the basic skills and knowledge needed and presents many tips for successful practice in field conditions.

Figure 2-1. Examination, diagnostic testing, and treatment of serious eye problems in the field is aided by supporting the head of the horse with a table constructed of four to six bales of hay, shavings, or straw. Alternatively, the head may be supported by a barrel or other handy stationary object.

EQUIPPING THE AMBULATORY VEHICLE

The ambulatory practitioner must be prepared to diagnose and treat a wide variety of ophthalmic problems. Box 2-2 lists the equipment and supplies used in the diagnosis and acute treatment of common field conditions. Many common drugs that are routinely dispensed are easily obtained from veterinary distributors. However, serious or chronic ophthalmic conditions often require medication with drugs that are not carried by veterinary distributors. Box 2-3 lists drugs that usually need

Box 2-1 | Conditions Commonly Misdiagnosed in the Field

- Recurrent keratitis caused by trichiasis or eyelid foreign body
- Burdock pappus bristle keratopathy
- Stromal abscess
- Fungal keratitis
- Melting corneal ulcers
- Nonulcerative keratouveitis
- Eosinophilic keratitis
- Immune-mediated keratitis; other nonulcerative keratopathies
- Penetrating ocular injuries
- Lens luxation
- Uveitis: recurrent, insidious, posterior
- Endophthalmitis

Box 2-2 | Items for Diagnosis and Treatment of Eye Problems in the Field

- Direct ophthalmoscope (www.welchallyn.com)
- Bright focal light source: penlight or Finnoff transilluminator (www.welchallyn.com)
- 14-20 D magnifying lens (www.welchallyn.com)
- Strap-on LED head lamp
- Digital camera (4.0 megapixel camera or higher)
- (Optional) Handheld slit lamp (www.danscottandassociates.com)
- (Optional) Tono-Pen (www.danscottandassociates.com)
- Proparacaine topical anesthetic
- Eye wash
- Fluorescein dye strips
- Rose bengal dye strips
- Schirmer tear test strips
- Tropicamide (Mydriacyl)—topical agent to dilate pupils
- Proparacaine (topical anesthetic)
- Carbocaine (injectable local anesthetic)
- Small (10- to 30-mL) bottles of 1 part Betadine to 50 parts sterile saline (2% solution)
- Pour bottle of 2% Betadine for periorbital cleansing
- Sterile cotton swabs bundled 6 swabs to a pack
- Dacron polyester sterile swabs (Puritan Medical Products, 1-800-321-2313)
- Sterile 4 × 4 gauze
- Nonsterile 4 × 4 gauze, sterile gloves
- Scalpel blades packed in sterile sleeves (any size; blunt end is used)
- 2-mm biopsy punches (for "scooping" foreign bodies)
- Slide boxes with 4 microscope slides to a box (for cytology specimens)
- Formalin in small jars (for preserving biopsy specimens)
- "Write-on" plastic bags—4 × 6 inches (to dispense meds and clarify treatment schedules)
- Thioglycollate culture broth tubes or agar plates
- Portacult transport media
- Serum separator tubes (to prepare autologous serum)
- Fine suture material: 1-0 through at least 4-0 or 6-0
- Sedatives (xylazine, butorphanol tartrate, detomidine)
- Prescription pad
- Halogen light on tripod or hook (Home Depot)
- Items for subpalpebral lavage systems

Box 2-3 | Ophthalmic Medications Available from Retail, Compounding, or University Pharmacies

Topical antibiotics: tobramycin, ofloxacin, moxifloxacin, gatifloxacin, levofloxacin, erythromycin, ciprofloxacin
Topical antifungals: natamycin 5%, 1% silver sulfadiazine available commercially; 1% to 2% miconazole, voriconazole, itraconazole (compounded)
Topical antivirals: 0.5% idoxuridine ointment (compounded) or 1% trifluridine (Viroptic, King Pharmaceuticals, Bristol, TN)
Topical nonsteroidal antiinflammatory drugs (NSAIDs): diclofenac (Voltaren 0.1%), flurbiprofen (Ocufen 0.03%), suprofen (Profenal 1%), bromfenac (Xibrom 0.09%)
Topical osmotics: 5% NaCl (Muro 128)
Topical glaucoma medications: timolol maleate (Timoptic), dorzolamide hydrochloride (Trusopt), timolol maleate with dorzolamide (Cosopt)
Topical calcineurin inhibitors: 2% cyclosporine (compounded ointment or solution), 0.03% tacrolimus (compounded)

to be obtained through retail pharmacies or ordered through compounding pharmacies.

Many practitioners devote a tote box or a drawer in the ambulatory vehicle exclusively for the storage of items used in ophthalmology. The items can then be easily gathered and brought to the patient at the visit.

CREATING AN "EXAM ROOM" IN THE FIELD

Care must be taken to create a serviceable examination area in the variety of environments presented. Horse eye examinations cannot be done outdoors or in sunny sheds. Examination and care will be facilitated if:

1. An enclosed, uncluttered examination space is available that is at least 8 × 10 feet.
2. Wind disturbance is minimized.
3. The space is darkened during intraocular examination. Windows may need to be covered and barn doors closed.
4. The ocular region is well lit during diagnostic testing or treatment. The examiner may need to wear a headlight or have an assistant provide focal illumination with a strong flashlight or transilluminator.
5. The examination is performed in a quiet area without disruptions from other horses, farm animals, and human traffic.

Horses are often examined in their stalls or in barn aisles. Restraint may be provided by a trainer, groom, owner, or veterinary assistant. The handler should hold a lead rope attached to the halter. Although most horses are accustomed to having their handlers stand on their left side, equine ocular examination is facilitated if the handler stands on the side contralateral to the eye being examined and switches to the opposite side when the fellow eye is examined. Physical restraint should be minimal—attempts to fix the horse's head in a given position using physical force or lip shanks are counterproductive. Calm, nonpainful horses may be very cooperative for basic eye examination. Judicious use of a lip twitch may assist examination or treatment of skittish individuals. The examiner may need to step on a bale of hay or a stool to examine a very tall horse, or may need to sit down on a similar aid to examine a small pony or Miniature horse. It is important that the examiner not stand directly in front of the horse and be aware of the position of the horse's feet at all times.

WORKING ON PAINFUL OR FRACTIOUS ANIMALS

Flighty or very painful animals will require sedation for examination. Sedation will also be required on horses undergoing invasive or painful diagnostic or surgical procedures. Two drugs are commonly used for chemical restraint: xylazine (0.5 to 1 mg/kg) and detomidine hydrochloride (Dormosedan, 0.02 to 0.04 mg/kg). Detomidine produces more profound sedation than xylazine. Both take effect very quickly after intravenous

(IV) administration. The exact dosage of drug and duration of sedation depends on the disposition of the animal, the existing level of pain, and the length of time and manipulation involved in any anticipated procedures. Variations exist among horse breeds in sedation effects: Draft breeds like Belgians and Percherons typically exhibit profound sedation at the lower end of the dosage spectrum, while high strung breeds like Arabians and Thoroughbreds may require higher doses. Please see Chapter 1 for more information on use of sedation for ophthalmic examinations.

Sedation can be minimized if the practitioner has assembled all the supplies, drugs, and examination aids needed for the situation at hand so the ocular examination can quickly be followed by any appropriate diagnostic tests, imaging, and therapy. It is better to err on the low side and add additional sedation as needed than to give so much sedative the animal collapses or becomes very ataxic. Butorphanol tartrate (Torbugesic, 0.01 to 0.02 mg/kg) is a sedative less frequently used in equine ophthalmology because effective doses are often accompanied by troublesome head tremors. However, in combination with detomidine, this drug may provide the profound sedation needed for fractious animals undergoing painful procedures.

LOCAL AND REGIONAL ANESTHESIA

General examination of a comfortable eye in a cooperative horse does not require nerve blocks. However, motor and/or sensory denervation may be necessary for examination, diagnostic testing, and initial field therapy for eyes that are painful from keratitis, uveitis, or other serious conditions. Nerve blocks are essential for handling any eye in danger of rupture due to tectonic instability.

All practitioners should be skilled at performing auriculopalpebral and supraorbital nerve blocks as described in Chapter 1. Please see Chapter 1 for more information on performance of these nerve blocks.

Corneal or conjunctival topical anesthesia is necessary for many examinations and diagnostic tests. Short-term tissue desensitization is achieved by applying proparacaine onto the target surface. A dose of 0.5 mL per eye should be drawn up out of the dropper bottle into a small syringe using a 25-gauge needle. The needle should then be broken off and discarded and the anesthetic sprayed or dripped onto the corneal surface through the remaining hub. Topical anesthesia of focal areas on the conjunctiva or nictitans can be enhanced by briefly holding a sterile Dacron or cotton-tipped swab soaked in topical anesthetic against the target area. Duration of corneal desensitization may be brief in very painful conditions, so the examiner should be prepared to reapply anesthetic as needed.[1]

PERFORMING EXAMINATIONS IN FIELD SETTINGS

Routine eye examination in the field by general practitioners involves inspection of a standing animal with simple, inexpensive equipment. Most examiners start by using a bright light source such as a penlight or (ideally) Finnoff transilluminator to inspect the head, adnexa, and ocular surfaces. The same instrument is then used for transillumination, retroillumination, and direct inspection of intraocular structures. The bright light survey is then followed by direct ophthalmoscopy, which is done both from a distance to retroilluminate focal densities against the tapetal reflection, and close to the eye to view detail directly. Many practitioners get additional information through magnification aids such as head loupes (Optivisor [Donegan Optical Co. Inc., Lenexa, KS]), handheld lenses, and digital images that have been magnified on a camera viewfinder or cropped on a viewing computer.

Detailed specifics of the ocular examination are described in Chapter 1. Several tips that may be helpful in field situations:

1. A full history and physical examination is appropriate to check for concurrent issues in other systems.
2. Hygiene is important. Carry a spray or pour bottle of 2 to 5 mL Betadine diluted with 100 mL of saline as a cleanser, and apply this solution with gauze to clean the periorbit. Methicillin-resistant *Staphylococcus aureus* (MRSA) infections are being increasingly documented in equine veterinary practice, so use of examination gloves is prudent (Fig. 2-2).
3. A systematic anatomic examination of both eyes should always be performed, even if a problem is obvious. Inspection must include the periorbit, adnexa, conjunctiva, sclera, cornea, anterior chamber, iris, lens, vitreous, and ocular fundus.
4. Pupillary light responses are most vigorous if the beam is directed towards the visual streak in a direction that is temporal (lateral) and slightly dorsal to the optic disc.
5. The direct ophthalmoscope must be fully charged to provide sufficient illumination. If the charge becomes drained on the road, the handle battery can be charged in the vehicle using a DC transformer that plugs into the vehicle outlet.

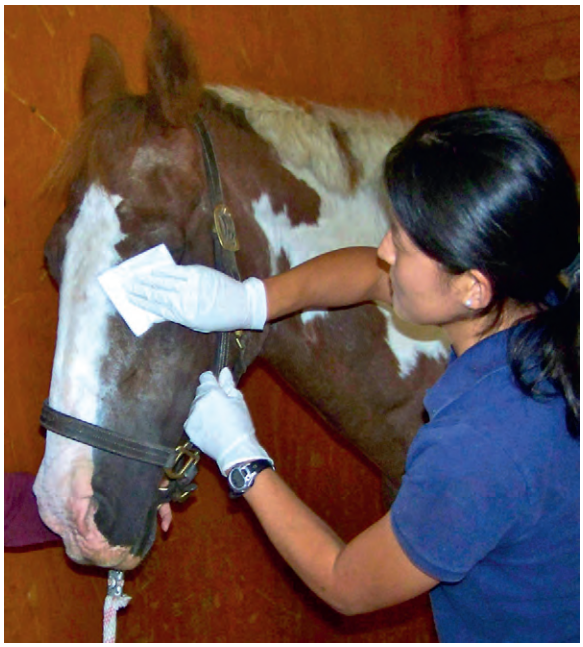


Figure 2-2. Hygiene is an important consideration in the field. The periocular region should be cleansed with a solution of 2% Betadine prior to any diagnostic or therapeutic procedure.

6. An otoscope lens attached to the direct ophthalmoscope handle provides useful low-level magnification of the anterior segment. Alternatively, an inexpensive head loupe can be used in the field (Optivisor).
7. Medical records should thoroughly document all findings, even incidental ones. Many practitioners use forms with anatomic diagrams of the cornea, iris, lens, and fundus.

LIFE STAGE ISSUES

Practitioners are responsible for the health of their patients throughout their lifespans. Surveillance for ophthalmic problems should begin shortly after birth. Ideally, ophthalmic exams should be performed regularly throughout the horse's life. Equine practitioners should be familiar with the ocular problems commonly encountered during the various life stages listed in Box 2-4.

Most healthy foals are seen between 12 and 36 hours of age for their neonatal physical examination. During the visit, the mare is checked for postfoaling problems, and the foal is scrutinized for adequacy of colostral transfer, adjustment problems, infections, and congenital conditions. Neonatal ophthalmic examination is a very important part of the process. It should be done in a consistent, thorough manner using a focal light source and a direct ophthalmoscope.

Patient cooperation is optimized if one person holds the mare and another person holds the foal near the mare's head. If two assistants are not available, most mares can be turned loose and will usually behave well as long as they can see the foal directly in front of them. Excessive foal restraint is inappropriate—eye examinations are best performed with the foal simply cradled by an assistant (Fig. 2-3). Rambunctious foals can be restrained with a firm arm around the chest and a tail hold. Sometimes it is helpful to position the foal in a corner or

Figure 2-3. Neonatal ophthalmic examination is best done with an assistant cradling the foal's chest and tail and the examiner steadying the head. The foal should be positioned towards the mare's head to minimize her anxiety.

Box 2-4 | **Equine Life Stage Ophthalmic Issues**

Neonatal—Congenital at Birth

- Microphthalmos
- Lacrimal puncta agenesis or duct atresia
- Strabismus
- Dermoids
- Aniridia
- PPMs (persistent pupillary membranes)
- Anterior segment dysgenesis (may not be noticed till maturity)
- Cataracts
- Coloboma
- Persistent hyaloid artery
- Congenital glaucoma or retinal detachment (rare)

Neonatal—Acquired in First Days or Through Birth Process

- Entropion
- Subconjunctival hemorrhage
- Retinal hemorrhage
- Uveitis secondary to septicemia
- Jaundice secondary to neonatal isoerythrolysis
- Various manifestations of hypoxic ischemic encephalopathy (HIE)
- Ulcers: uncomplicated, melting, infected, persistent erosions
- Secondary manifestations of adenovirus, botulism

Pediatric

- Blunt head trauma—concussive during pasture roughhousing or training accidents—can cause acute blindness
- Blunt globe trauma—as above
- Sharp facial or lid trauma
- Uveitis secondary to Rhodococcus equi or strangles
- Corneal ulcers
- Vitiligo

Young Mature Horses

- Trauma: blunt and sharp
- Corneal ulcers
- Uveitis
- Squamous cell carcinoma
- Sarcoid

Geriatric Horses

- Sinus disease with ocular manifestations
- Periocular neoplasia
- Indolent ulcers
- Cataract
- Glaucoma
- Insidious or subclinical uveitis
- Vitreal syneresis
- Asteroid hyalosis/synchesis scintillans
- Senile retinopathy
- Proliferative optic neuropathy

against the stall wall. The foal's ventral mandible can be cradled with one hand while the other is used to hold the light source.

Most newborn foals are remarkably tolerant of a direct ophthalmoscope fundic exam. If the holder is calm and the examiner holds the head steady with the nonexamining hand, foals often "freeze" their head movements when the light beam engages the optic disc region.

The neonatal pupil is somewhat round in contour. The globe has a mild ventromedial orientation at birth that gives neonates a slight downward gaze. The pupil acquires a horizontal elliptical shape and becomes parallel to the lower lid over the first month of life. Pupillary light response may be sluggish in the first few days of life but should be brisk after a few days. The color of the neonatal iris may be a little grayer than the rich chocolate color commonly seen in adults (Fig. 2-4). Lens suture lines may be very prominent and should not be mistaken for cataracts. Tapetal color is variable and is correlated with coat color. The optic disc is round to oval in shape and whitish pink to salmon in color. Light gray streaks, representing bundles of axons traveling to the optic nerve, may be seen in the peripapillary area.

Common findings in neonatal foals include episcleral or retinal hemorrhage, a persistent remnant of the hyaloid artery, and entropion of one or both lids. Some problems, like entropion or corneal ulcers, may necessitate immediate therapy. If the foal is a member of a breed that is at risk for eye problems (e.g., Appaloosa, Rocky Mountain horse) the neonatal examination provides an opportunity to educate the owner about known risks that might require screening later in life. If any congenital anomalies have been observed in the foal, the mare should get a thorough eye examination to see if she has similar problems.

Immature horses are at increased risk for ocular trauma due to herd interactions, training accidents, and exuberant behavior. Young mature horses, particularly Warmbloods, Appaloosas, or draft horses, may develop recurrent or insidious uveitis associated with an inherent genetic susceptibility to this immune-mediated syndrome. Pastured mature horses in temperate climates like the Northeast are susceptible to uveitis associated with acquired leptospiral infections. Horses living in tropical climates like the Southeast are prone to fungal keratitis. Mature horses living in sunny climates or high altitudes are at risk for development of actinic blepharitis or squamous cell carcinoma of the adnexa or globe, particularly draft horses, Appaloosas, and color-dilute breeds like Paints. Horses of all ages frequently present for adnexal or corneal trauma, and many practitioners report an increased incidence of ocular trauma in the late summer or fall months.

Mature horses frequently develop nuclear sclerosis as they age. This can give the lens a faint blue appearance that may be opaque on transillumination (Fig. 2-5). Geriatric horses often present with degenerative or age-related conditions of the eyes: cataracts, vitreal syneresis, asteroid hyalosis, senile retinopathy, supraorbital fat atrophy, or proliferative optic neuropathy. Horses older than 15 years are at increased risk for many kinds of neoplasia. Aged gray horses are at increased risk for melanoma and will occasionally present with ophthalmic forms of this disease.

Geriatric horses may have ocular manifestations secondary to chronic conditions such as dental disease, sinus infections, and Cushing's syndrome. Diagnosis and management of equine geriatric ophthalmic problems have been reviewed,[2] and more information on ocular manifestations of systemic disease can be found in Chapter 13.

OPHTHALMIC TESTS IN THE FIELD

FIELD TIPS FOR VISION TESTING

A rough assessment of vision can often be made with maze testing. This test involves the use of blinkers or a large towel to cover first one eye and then the other, observing how the horse navigates a short obstacle course with only one eye receiving visual data. The maze tests should be done under dim and normal light conditions.

Barn aisles that have been cleared of hazards are good stages for maze testing. An obstacle course is created using overturned buckets or other smooth, solid objects that are easily rearranged and safe if the horse runs into them. Stall doors and barn door openings and other paths that exit the maze area should be closed off for safety concerns.

Handlers and observers should be instructed to stay away from the maze line and avoid giving the horse any verbal cues

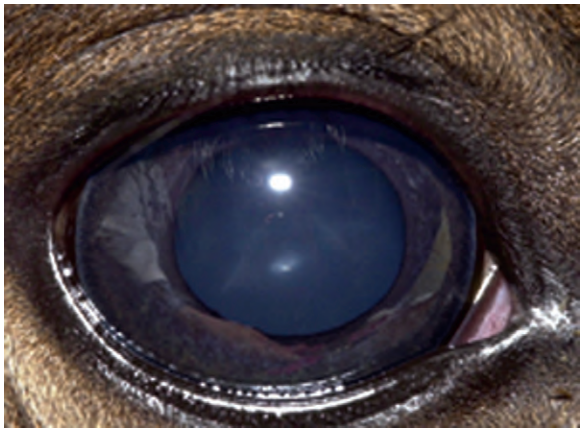


Figure 2-4. The appearance of the neonatal iris often has a grayish brown tint. The pupil is somewhat round in contour. Lens suture lines may be prominent.

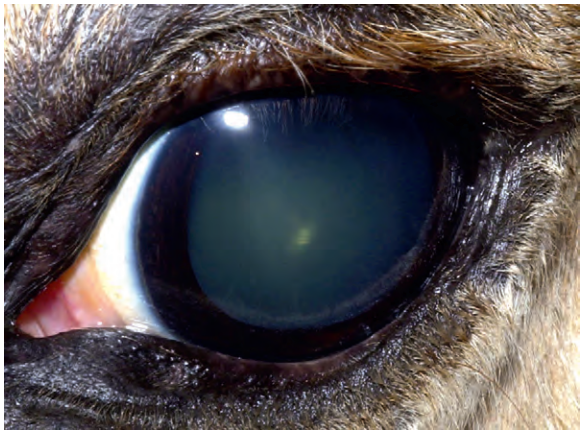


Figure 2-5. Nuclear sclerosis gives this lens in an aged horse a faint blue appearance.

to orientation. The horse being tested should be turned loose in the aisle. One person should stand at the end of the maze path and coax the horse to navigate the obstacles by shaking a bucket filled with grain (Fig. 2-6). Fractious horses may have to be restrained on a long lead, but the handler must avoid giving any positional cues to the horse.

Horses that are visual in the uncovered eye will usually walk towards the food bucket with confidence and show head and body movements that acknowledge the obstacles in the path. Horses that are blind in the uncovered eye will show a dramatic difference in their maze behavior. They will either stand still and refuse to move or walk very tentatively forward, often running into the ground obstacles.

Maze testing is very useful in instructing owners and trainers. People who work with the animal every day may not "believe" that a damaged eye is blind until they observe the asymmetric behavior in the maze.

TIPS FOR TONOMETRY

Tonometry is discussed in Chapter 1. The two instruments most commonly used in the field are the Tono-Pen Vet applanation

Figure 2-6. Maze testing is useful in providing a rough assessment of unilateral vision and instructing an owner of a patient's visual status. The horse is blindfolded first on one side **(A)** and then on the other and is coaxed to navigate an obstacle course of harmless obstacles **(B)** to reach a food reward **(C).** Most barn aisles can be set up as suitable stages for maze testing. All doors and paths that exit the maze path should be closed off.

tonometer (Reichert Inc., Depew, NY <http://tonopen.com/>) and the TonoVet rebound tonometer (Icare Finland OY, Helsinki, Finland <http://www.icaretonometer.com/index.php?page=tonovet-for-animals>).

Obtaining consistent readings with either instrument can be challenging in the field. Spurious readings that are very high or very low may occur during the sampling process. Horses with substantial corneal edema may show altered applanation tonometry readings as the instrument calculations may be affected by the edema within the cornea.

Consistent technique is important for sequential readings done on different days. In general, horses should undergo light sedation, auriculopalpebral nerve blocks, topical anesthesia, and assume a consistent, normal head position for each intraocular-pressure (IOP) testing session. Ideally, each exam should be done at the same time of day.

The Tono-Pen Vet should be calibrated every day it is used. The instrument head should be cleaned often with alcohol and blown free of particulate matter with a can of compressed air. The Tono-Pen Vet will not operate well in very cold weather and should not be left in the ambulatory vehicle in cold months.

FIELD TIPS FOR OPHTHALMIC DYE TESTS

Ophthalmic dye testing procedures are discussed in Chapter 1. All eyes undergoing examination for a problem should undergo fluorescein dye staining. If eyewash is not available to mix with a test strip, sterile saline can be mixed with the torn-off paper dye strip in a syringe and sprayed onto the cornea.

A cobalt blue light is useful in assessing fluorescein dye tests. A direct ophthalmoscope can have a lens that is rarely used retrofitted with a cobalt blue filter (http://www.welchallyn.com/). Alternatively, an inexpensive cobalt blue filter that covers a standard penlight can be ordered from a human ophthalmic supply catalog (Bernell: 1-800-348-2225; Item ALPENF <www.bernell.com/product/140/2>).

Many practitioners do not appreciate the diagnostic potential of rose bengal staining of the cornea. This dye test is indicated in any suspected corneal ulceration or abrasion; it may suggest defects in the ocular tear film or the presence of viral or fungal pathogens. As with fluorescein, rose bengal test strips (Akorn Inc., Lake Forest, IL) can be mixed in a syringe barrel with saline or eyewash in advance of corneal application. Spare dye strips of both types can be stored in the ophthalmoscope case for ready access.

PERFORMING CULTURE AND CYTOLOGY IN THE FIELD

The most common indication for ocular culture and cytology in equine practice is a corneal ulcer that is obviously infected, unresponsive to therapy, or melting. Such cases are often critical, requiring urgent analysis for therapeutic decision making. Practitioners can process and analyze ocular samples in-house to make rapid therapeutic decisions. Additional samples may be sent to reference laboratories as appropriate.

Supplies for culture and cytology should be packed in the ambulatory vehicle at all times (Box 2-5). The sample collection process can be paired with all the other procedures that are appropriate to the case, including digital imaging, dye tests, more extensive débridement of the lesion, and instillation of a subpalpebral lavage (SPL) system. Good planning of the sequence of sampling, imaging, and treatment will allow all procedures to be done quickly with minimal sedation.

Figure 2-7. All supplies needed for culture, cytology, and any planned débridement or imaging should be assembled and set on a nearby table prior to diagnostic sampling of a corneal lesion.

Box 2-5 | Supplies Used for Corneal Culture and Cytology in the Field

- Topical 2% Betadine and gauze for periocular cleansing
- Xylazine and detomidine for sedation
- Proparacaine for topical anesthesia
- Lidocaine or mepivacaine for regional anesthesia
- 1-, 3-, and 12-mL syringes
- 25-gauge needles
- Sterile gloves
- Sterile scalpel blades wrapped in autoclaved sterile sleeve
- Sterile cotton-tipped swabs wrapped in autoclaved sterile sleeve
- Sterile Dacron-tipped or calcium alginate–tipped swabs
- Thioglycollate broth in glass tubes with screw tops
- Mueller-Hinton and blood agar culture plates
- Kirby-Bauer antibiotic sensitivity wheel dedicated to eye cultures
- Incubator
- Microscope slides
- Slotted plastic slide boxes
- Diff-Quik stain kit
- Gram stain kit
- Microscope with ×100 lens
- Immersion oil

PREPARATION FOR DIAGNOSTIC SAMPLING IN THE FIELD

1. Assemble all the supplies needed for culture, cytology, and any planned débridement or imaging. Set them on a nearby table or elevated surface (Fig. 2-7).
2. Minimize wind disturbance and traffic of people or other animals.
3. Build a “bale table” for support of the head by stacking hay or straw bales to a height of about 4 feet, and cover the surface of the table with a sheet or towel.

4. Assure ample illumination by using available overhead lights, a headband light, and/or focal illumination from a light held by an assistant.
5. Position the horse in front of the bale head stand, and administer sedation of choice until the horse rests its head on the homemade table.
6. Put on a pair of examination gloves, and use gauze 4 × 4s to clean the periorbital skin with 2% Betadine.
7. Administer local nerve blocks if needed, including any skin blocks anticipated for an SPL system.
8. Obtain presampling images.

CULTURE SAMPLING AND HANDLING

If possible, obtain the culture without topical anesthetic. If the horse will not tolerate this, apply 0.5 to 1 mL of 1% proparacaine onto the cornea for desensitization.

1. Use the blunt end of a sterile scalpel blade (using the foil wrapper as a handle) or a Dacron-tipped swab premoistened in thioglycollate broth as a sterile surface to obtain the sample. Apply the sampling tool onto the surface of the lesion, taking care to avoid touching other areas of the eye (Fig. 2-8).
2. If the collection is done on the road, drop the entire sample blade into a screw-topped tube of thioglycollate broth, or snap off the tip of the swab into the tube in a sterile fashion (Fig. 2-9). Place in a cooler for transport. If the collection is done in the clinic, the sample can be directly plated on agar (blood agar, eosin methylene blue [EMB] agar, Sabouraud agar).

On return to the clinic, the culture sample should be placed in an incubator. Samples sitting in broth or plated on agar should be checked daily for turbidity or colony growth. If bacterial growth is seen in either medium, a smear should be prepared and Gram stained to determine morphology and staining characteristics (cocci or rods, gram-positive or gram-negative bacteria). Characterization of these bacterial properties will dictate the best type of agar plate to use for antibiotic sensitivity testing (Mueller-Hinton plain agar versus Mueller-Hinton agar with blood).

Antibiotic sensitivity testing can be referred to a reference lab or performed in-house using the Kirby-Bauer disk diffusion method of applying antibiotic impregnated disks to agar that has been plated with diluted colonies of bacteria. A sensitivity wheel should be designated for ophthalmic testing and filled with disks impregnated with the antibiotics commonly used to treat corneal infections (Fig. 2-10).

Samples plated on Sabouraud agar should be checked daily for fungal colony growth. Plates with growth can be sent off to a reference laboratory for sensitivity analysis but results may not be received in time to influence therapy choice. Please see Chapter 5 for more information on choice of therapy based on culture results.

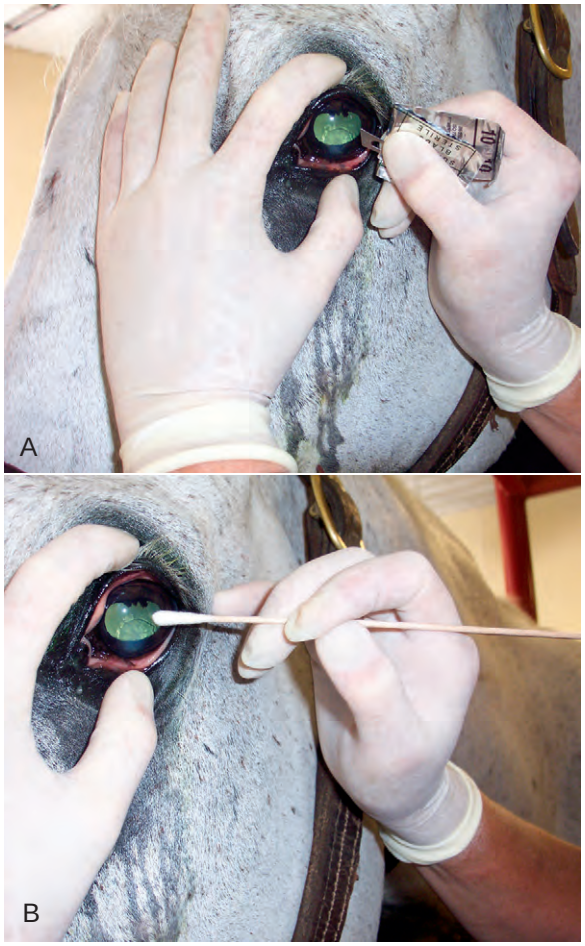


Figure 2-8. **A,** The blunt end of a sterile scalpel blade can be used to obtain a corneal culture sample. After the sample is obtained, the blunt end of a second sterile scalpel blade can be used to obtain cytology samples. **B,** Alternatively, a Dacron swab can be used to obtain the sample. Care should be taken to touch just the target surface with the sampling tool.

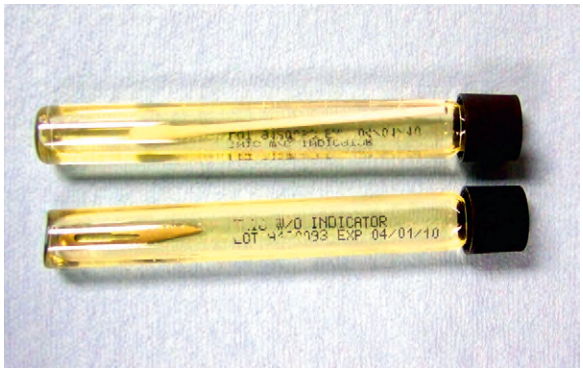


Figure 2-9. The sampling blade or swab used for culture is then dropped into a screw-topped tube of thioglycollate broth for transport.

CYTOLOGY SAMPLING AND HANDLING

All cytology sampling will require topical anesthetic, and a topical dose should be applied if it was not done prior to culture.

1. Use a sterile Kimura spatula or the blunt end of a new sterile scalpel blade (again, using the foil wrapper as a handle) to scrape the margin of the ulcer with a firm but sensitive stroke. Create enough local pressure to dislodge visible cellular elements onto the blunt metal blade, but take care not to jeopardize integrity of the globe.
2. Use the metal blade to spread the scraping sample thinly onto three or four dry glass microscope slides. Label with

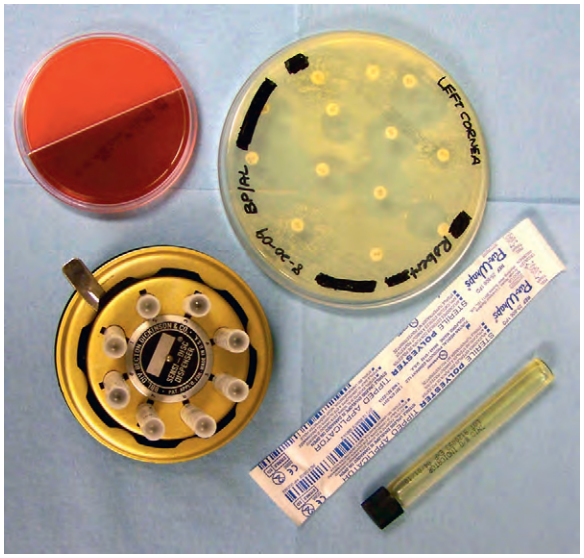


Figure 2-10. If ocular cultures are processed in-house, a Kirby-Bauer antibiotic sensitivity wheel should be stocked with antibiotic-impregnated discs that represent the spectrum of drugs commonly used to treat ocular bacterial infections.

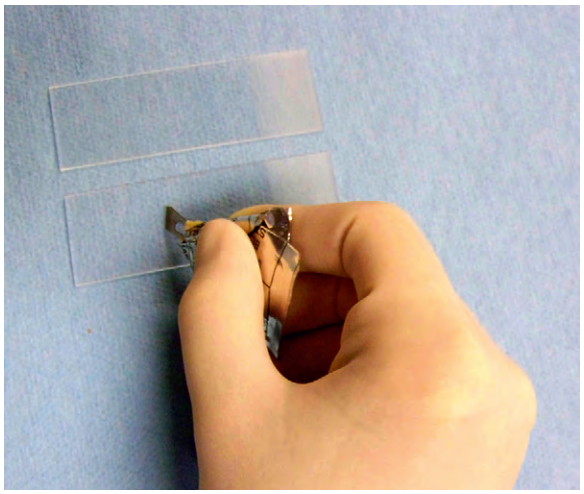


Figure 2-11. Cytology samples should be spread thinly onto three or four dry glass microscope slides. They should be placed in a slotted plastic transport box without any fixative.

patient and owner names and date of sample. Store the slides in a slotted plastic slide transport box (Fig. 2-11). (Five-slide-capacity plastic mailer boxes available through the Animal Health Diagnostic Center, Cornell University, 607-253-3935, email: ahdlshipping@cornell.edu.)

3. Perform additional débridement, imaging, and treatment as appropriate.

The cytology samples can be stained with Diff-Quik stain as soon as they are air dried (Fig. 2-12). They do not need any fixative or other prestaining preparation. Diff-Quik stain is a Romanovsky stain that yields excellent detail of cellular elements and is effective for staining cocci, most large and small rods, some bipolar rods, and most fungal hyphae.

Samples that show bacteria on initial screening should be Gram stained. Extra slides should be saved in case submission

Figure 2-12. Cytology samples should be stained with Diff-Quik stain and Gram stain. These stains can easily be performed in a practice setting, and the slides can be read on the same day the samples were taken.

to reference laboratories is needed. Reference laboratories can provide further analysis using other Romanovsky-type stains (Wright-Giemsa) or special stains like periodic acid-Schiff (IPAS), Gomori methenamine silver (GMS), or Cellufluor (Calcofluor white) to identify acid-fast bacteria or fungal elements.

INTERPRETING OCULAR CYTOLOGY SAMPLES

The goals of analyzing a corneal sample are simple: Assess the cells native to the sampling site, the cellular response to the condition, and the noncellular elements that are present.

Only a limited number of cell types will be found in corneal samples, and the list of "other elements" commonly present in cytology samples from ulcers is short. With a little practice, typical findings can be easily discerned by equine practitioners and veterinary technicians (Fig. 2-13).

Slides should be examined first under low-power magnification. Areas of interest should be scanned under high dry power, then viewed under the oil-immersion lens. A cytology report should be drafted that describes numbers, types, and staining characteristics of native corneal cells, infiltrating nonresident cells, and noncellular elements.

Scrapings of healthy cornea should contain nothing but sheets of epithelial cells (Fig. 2-14). Cells from the superficial layers are flattened with large amounts of blue cytoplasm and central basophilic nuclei. Cells from intermediate layers are more polyhedral, while cells from basal layers are more cylindrical and round and stain more darkly, showing less cytoplasm. Normal corneal cells do not contain bacteria and are exfoliated in sheets. Individual cells that are flat in contour may

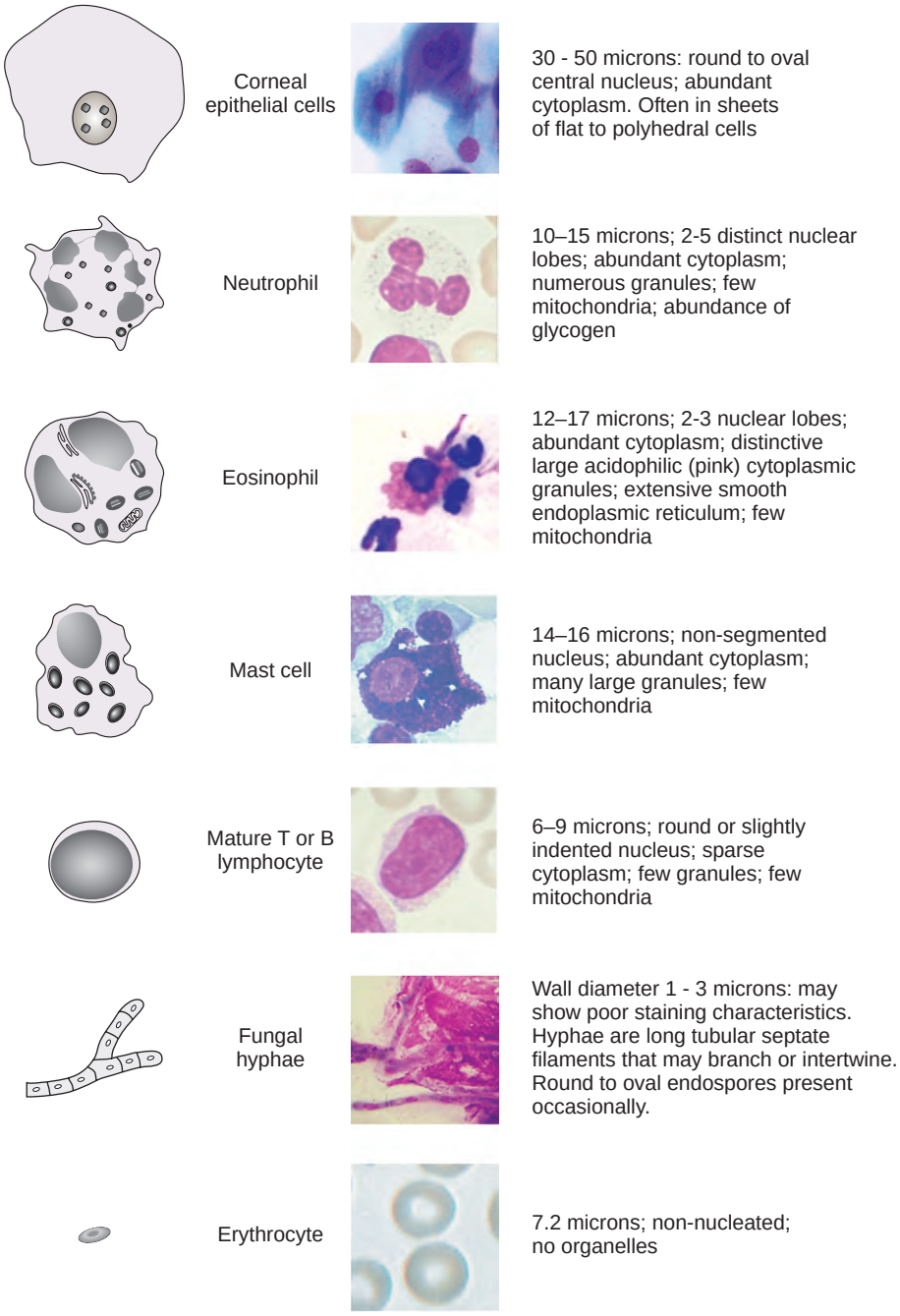


Figure 2-13. Drawing of common cellular elements.

roll up into tight scrolls on the slide and must not be mistaken for hyphae or foreign bodies.

Scrapings from corneas with a cellular inflammatory response will show an infiltrate. The most common finding is a suppurative infiltrate, where neutrophils with or without toxic changes dominate the response (Figs. 2-15 and 2-16). A small number of lymphocytes, monocytes, or plasma cells may also be present. Although a suppurative infiltrate is not pathognomonic for infection, it is highly suggestive of it. Occasionally a corneal sample will show an eosinophilic infiltrate. Presence of eosinophils or basophils is abnormal and suggests either acute allergic hypersensitivity or eosinophilic keratitis (Fig. 2-17). Some fungal infections incite a granulomatous infiltrate consisting of epithelioid macrophages and giant cells. If hemorrhage has occurred due to the disease process or sampling trauma, red blood cells will be present in large numbers.

The most common noncellular elements found in corneal scrapings are infectious agents. Bacteria commonly seen include cocci, large rods, small rods, and bipolar rods. Most cocci are gram positive in their staining patterns, and most rods are gram negative, but some small rods may have gram-positive stain patterns. Intracellular bacteria are highly correlated with infection.

The presence of even a few fungal hyphae in a cytology sample is indicative of mycotic keratitis. Hyphae are slender, septate, branching, or linear structures. Most fungal hyphae stain well with Romanovsky stains and can be seen as a tangle

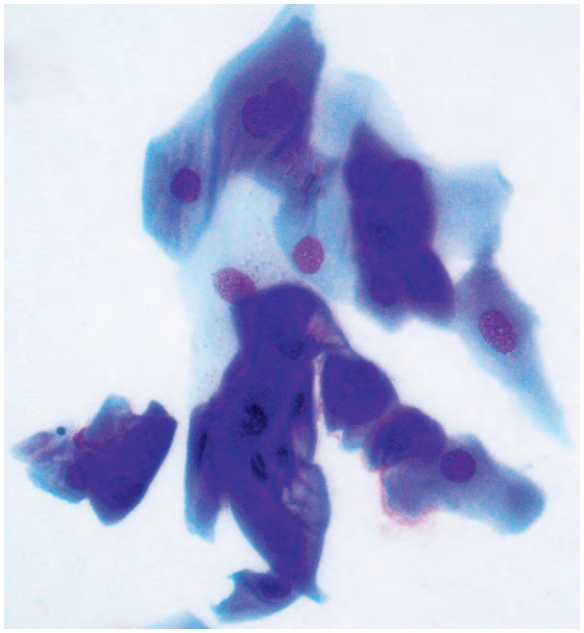


Figure 2-14. Photomicrograph of healthy corneal epithelium. Normal corneal epithelial cells do not contain bacteria and are exfoliated in sheets (Diff-Quik stain ×100).

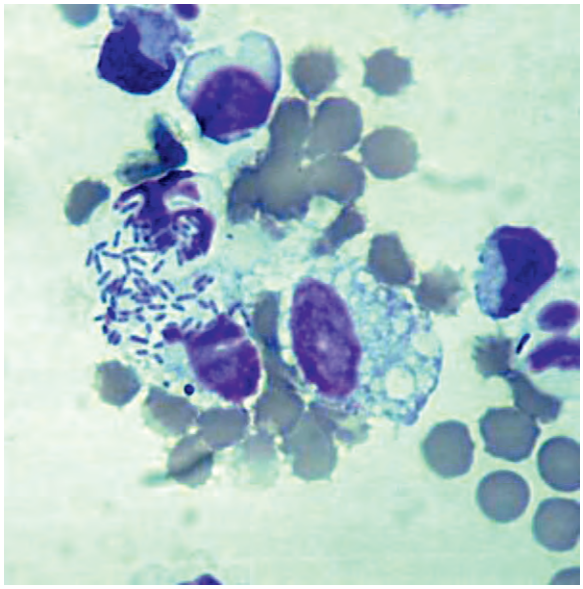


Figure 2-16. Photomicrograph of corneal cytology showing a suppurative cellular response (neutrophils) and intracellular rods indicating bacterial infection.

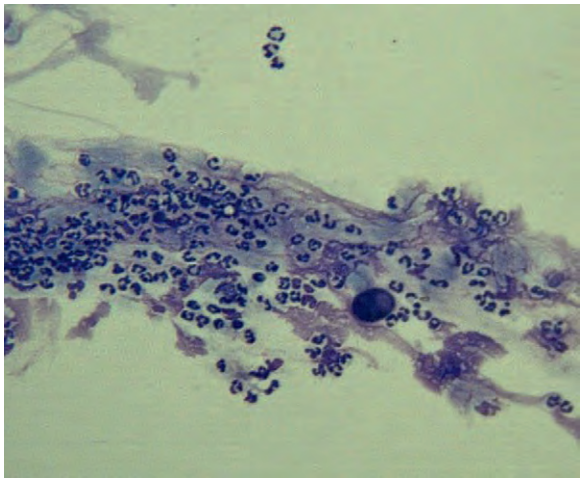


Figure 2-15. Photomicrograph of corneal cytology showing a suppurative cellular response (numerous neutrophils) and intracellular cocci indicating bacterial infection.

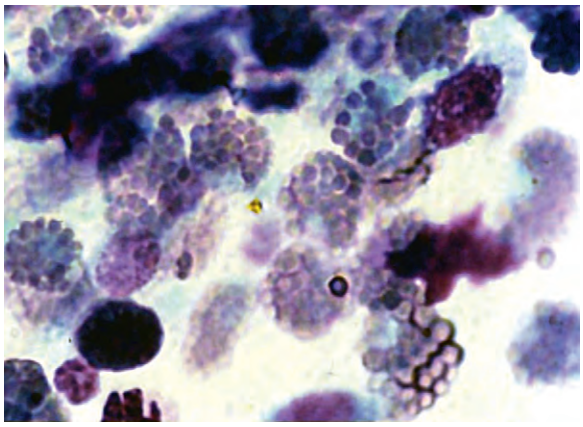


Figure 2-17. Photomicrograph of corneal cytology showing eosinophils interspersed with a few epithelial cells indicating eosinophilic keratitis.

of spaghetti-like densities interspersed with native epithelial cells (Fig. 2-18). Care must be taken to differentiate "scrolled" epithelial cells and long, thin strands of necrotic cellular debris from fungal hyphae (Fig. 2-19). The presence of fungal elements is always significant in ulcer samples, but the absence of hyphae does not rule out infection; hyphae may be present in corneal layers deep to the sampling site.

Occasionally, filamentous rod-shaped organisms may be present in cytology samples. These organisms (as well as some fungal species) do not stain with Diff-Quik stains, and their elements may be seen as "negative images"—transparent structures interspersed among stained structures. Special stains available through reference labs may be needed for analysis of these samples.

Other noncellular elements that may be seen on corneal cytology include intracytoplasmic melanin granules (dark green to black granules found in cells scraped from the limbal region or from pigmented areas [Fig. 2-20]), vegetative foreign bodies (Fig. 2-21), and mineralized crystals. The latter may stain light blue with Diff-Quik and may correlate with deposits of calcium in the subepithelial layers of horses with stromal keratopathies.[3]

TREATMENT CHOICES BASED ON CORNEAL CYTOLOGY

Rational therapeutic choices will follow as the cytology results are correlated with the clinical conditions described in Chapter 5 and the dominant infectious agents are identified. Most of the time, cytology will aid in choosing antiinfective, antiinflammatory, and antiprotease therapy, but in cases of suspected indo-

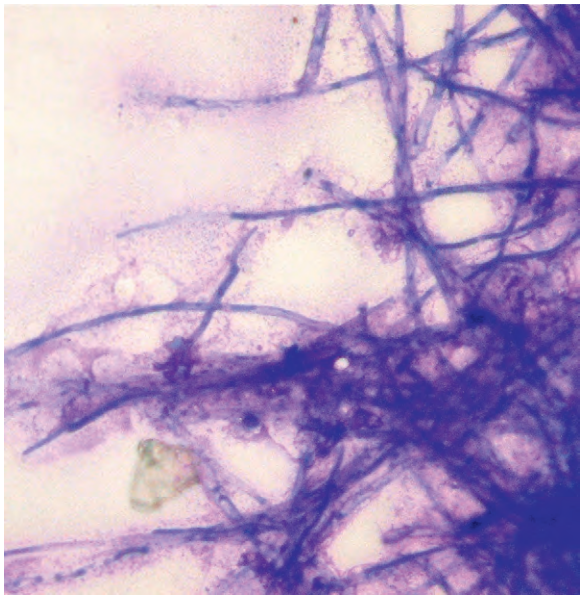


Figure 2-18. Photomicrograph of corneal cytology showing fungal hyphae. Fungal hyphae can be positively identified by their branching morphology and parallel walls (Diff-Quik stain ×100).

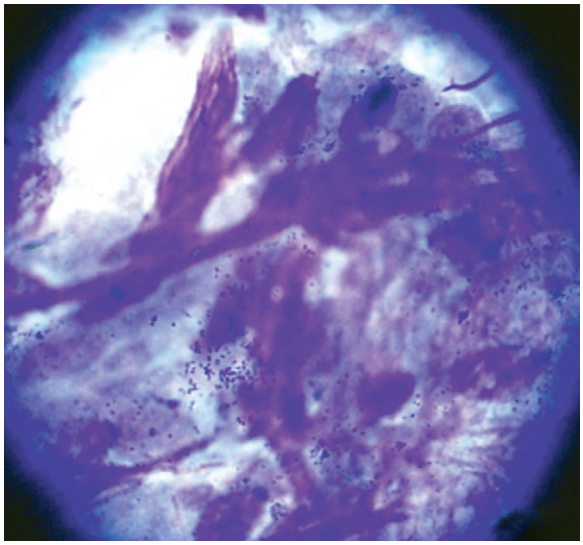


Figure 2-20. Photomicrograph of corneal cytology showing epithelial cells removed from paralimbal region of the cornea. The cells contain pigmented melanin granules. These normal cytoplastic elements should not be confused with intracellular bacteria.

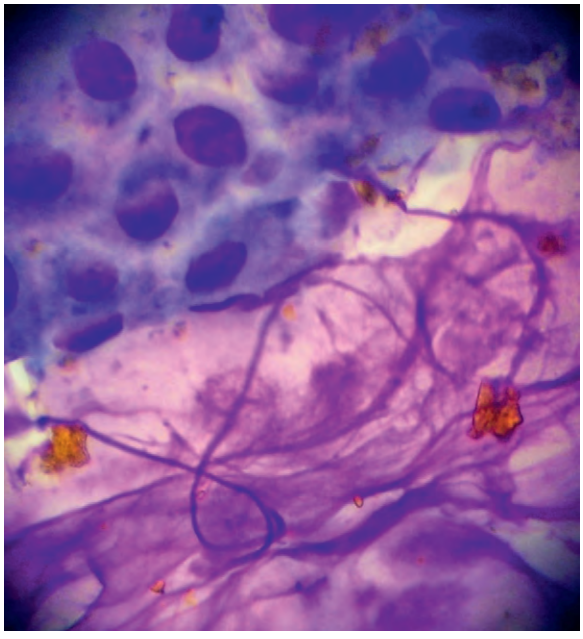


Figure 2-19. Photomicrograph of corneal cytology of corneal epithelial cells *(upper left)* showing necrotic cellular debris *(lower right)* that can easily be confused with fungal hyphae. Necrotic cellular debris does not present in a branching morphology, and the walls of the strands of degenerative cytoplasm are of variable thickness (Diff-Quik stain).

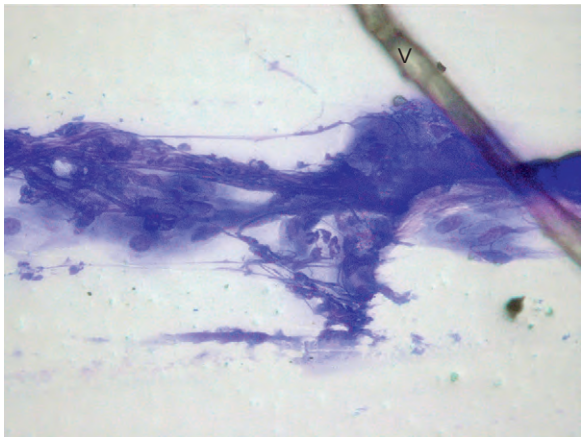


Figure 2-21. Photomicrograph of corneal cytology from a horse showing vegetative foreign material (V). This material should not be confused with fungal hyphae or other forms of infectious keratitis (Diff-Quik Stain, ×40).

lent ulcers, verification of the absence of cellular reaction or infectious elements is a critical step that must precede deeper débridement of a chronic lesion.

OTHER OCULAR CYTOLOGY INDICATIONS

Cytology may also be indicated in tissues other than cornea. Samples can be taken from bulbar, palpebral, or nictitans conjunctiva that is inflamed, infected, or abnormal in appearance and analyzed as described earlier. Conjunctival samples may contain goblet cells in addition to the cellular and noncellular findings described in cornea. These cells have eccentric nuclei and pale blue cytoplasm (Fig. 2-22). A lymphocytic or eosinophilic infiltrate may be apparent in cases with allergic inflammation. Material can be collected from the tarsal margin to analyze cases of chalazion or meibomianitis.

Lesions that are suspect for adnexal or corneal neoplasia can be analyzed by cytology samples of cells débrided from the surface, cells from impression smears, and cells from fine-needle aspirates. It is beyond the scope of the practice laboratory to analyze these specimens. They should be submitted to a reference laboratory. Most lesions suspicious for neoplasia should also be biopsied and fixed tissue samples submitted for histopathology (Fig. 2-23). Reports from clinical pathologists

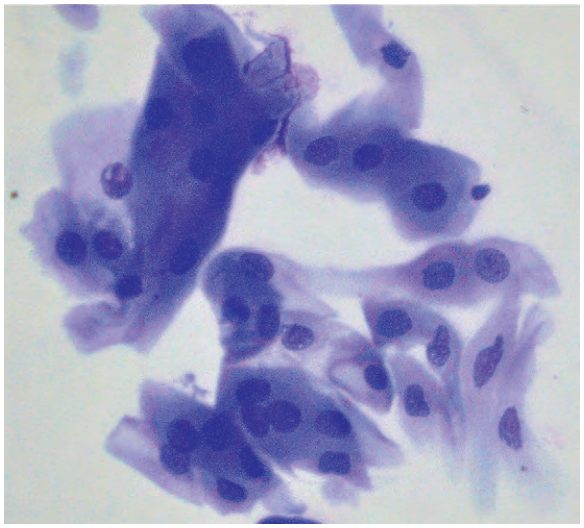


Figure 2-22. Photomicrograph of normal conjunctival cytology (Diff-Quik Stain, ×100).

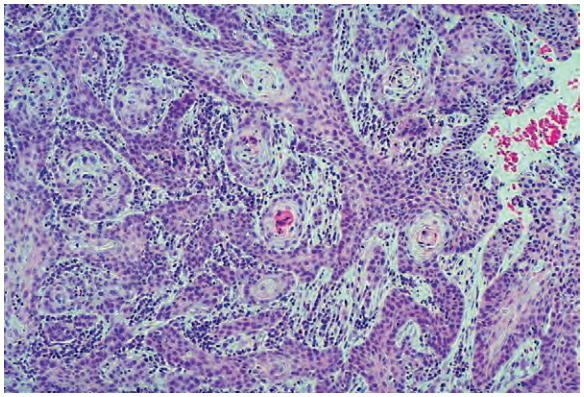


Figure 2-23. Photomicrograph of a histologic section of a horse with a corneal squamous cell carcinoma. There is a proliferation of neoplastic epithelial cells and formation of a keratin pearl, suggesting that this tumor is well differentiated. Diagnosis of ocular surface neoplasia is beyond the scope of the practice laboratory—these specimens should be sent off to a reference laboratory for evaluation.

focus on several criteria when assessing dysplastic, anaplastic, or metaplastic cells for malignant potential[3]:

1. Cell type: epithelial, mesenchymal (spindle cell), or discrete round cell
2. Exfoliative tendencies
3. Cellular size and shape (malignant cells may have wide variations in size, shape, and cellularity within the tissue)
4. Nuclear size and shape (nuclei of malignant cells may have wide variations in size, shape, and number and pattern of mitotic figures)
5. Cytoplasm and chromatin staining patterns

The report will list the cell type(s) found and give a presumptive or definitive diagnosis. Treatment or referral choices can then be made using information on the specific condition as outlined within this text.

IMAGING IN THE FIELD

DIGITAL PHOTOGRAPHY

Inexpensive, high-quality digital cameras have made imaging of ophthalmic problems simple and accessible to all practitioners. Just as radiography and ultrasound are widely used to image the axial skeleton, body cavities, and reproductive tract, digital photography is appropriate for imaging the anterior segment of the eye. A digital image provides accurate documentation of the observable problems, permits further study of the lesions as they relate to surrounding anatomy, and provides a baseline for monitoring subsequent progression or resolution of said lesions.

Digital cameras use a series of lenses to focus light onto a semiconductor device. The device records the light electronically, and a computer in the camera translates each tiny piece of electrical data into digital data called a *pixel*. The summation of the pixel data becomes the image. The camera software allows the image to be displayed and magnified on the liquid crystal display (LCD) screen on the back of the camera after it is captured. Images can be easily transferred to a computer for viewing where photo-editing software can be used to crop and frame the area of interest with resultant digital magnification. Images can also be downloaded to a variety of digital storage devices, transferred to the electronic medical record of the patient, or emailed to the owner or consulting veterinarian.

Digital imaging of equine eyes is simplified by understanding the sophisticated autofocus system present in cameras with electrical viewfinders (EV). The EV is activated when the shutter release on the camera is depressed halfway. This action causes an infrared signal to be emitted from the camera. The infrared signal bounces off objects in the field of view of the camera and is reflected back and received by an automatic microprocessor. The microprocessor processes the information from both the infrared signal and the internal light meter in the camera. It activates motors that adjust the lenses and aperture for sharp focus and appropriate lighting when the camera is in the automatic mode of operation. Once this is complete, the LCD screen on the back of the camera displays a bracket on the screen that frames the area of sharpest focus. It is important to understand that the EV system cannot focus on objects that are less than 10 to 12 cm away from the lens surface. Photographs taken at very close distances will thus be blurred.

POINT-AND-SHOOT (ELECTRONIC VIEWFINDER) CAMERA SELECTION FOR FIELD USE

General equine ambulatory practitioners should invest in a good point-and-shoot camera equipped with an active autofocus system and electronic viewfinder. These cameras can focus on objects located anywhere from about 12 cm in front of the lens to several yards away and thus perform well for all general clinical imaging. They are affordable, easy to use, rugged, and relatively light.

Higher-cost cameras are not necessary to obtain adequate field images of the equine eye. High levels of resolution (higher megapixel specifications) or advanced zoom features do not automatically improve the camera field capabilities for ocular imaging. Some simple guidelines and specifications (Box 2-6)

Box 2-6 | Essential Specifications for a Point-and-Shoot Field Camera

- At least 4 megapixels of resolution
- Automatic flash
- Active automatic focus that is easy to use
- Macro lens setting
- Large LCD screen for reviewing images
- Digital zoom for reviewing images in magnified form

will help the practitioner narrow down a short list of cost-effective cameras for ocular and general imaging in ambulatory practice. Final camera selection is a matter of taste and budget. Selection will be simplified if a few simple guidelines are followed:

1. The camera should be user friendly. Try out a few full-featured point-and-shoot models on real horses. Be sure that the menu, controls, and flash are easy to use and that the camera feels good in your hand.
2. Make sure the camera is rugged and free of features like extra light flashes or odd shutter noises that may startle the horse. Many of these functions can be manually disabled, so be sure to read through the user's manual.
3. Take a number of images of normal horse eyes to test operation in field conditions. Pay particular attention to the ease of using the autofocus system.
4. Look for a model with a large LCD screen where images can be reviewed and magnified with digital zoom. This feature allows selection of the sharpest images and will be invaluable for stallside client education.
5. Download test images of horse eyes to a viewing computer to compare sharpness, color, and contrast.
6. Choose a model with good battery life that is also easy to recharge. Investing in a second battery is relatively inexpensive and will help ensure you are never without a camera in time of need.
7. Invest in additional digital storage media (SD or MMC card) and a rugged case that is well padded. An external card reader allows quick and easy downloading of images to a computer without having to connect the camera.

PROCEDURE FOR OCULAR IMAGING

Horses become restless if the operator spends too much time setting up a photograph, and subsequent head movement can cause the resulting image quality to suffer. You will need to learn to photograph the equine eye taking this behavior into account. Practitioners will realize the best results if they learn to stage the camera quickly and determine the instant the autofocus system is ready. Quick shutter action will assure that the focus stays true before the horse has time to move or blink. An external light source, such as a Finnoff transilluminator or other bright white focal light source, can be used to acclimatize the horse to the flash, which increases the chance of the horse keeping its eye open while the photograph is being taken. Recommended automatic camera settings are listed in Box 2-7. Simple instructions for taking useful photographs in the field:

1. A flash should always be utilized to allow for proper illumination of the subject (eye, adnexal structures, etc.).

Box 2-7 | Point-and-Shoot Camera Settings for Ocular Imaging

1. Set the camera on PROGRAM mode. This allows full access to menu options, but the camera automatically sets the shutter speed and aperture based on the available lighting.
2. Select the MACRO option for close-up focusing. The icon is a flower symbol.
3. Enable the AUTOFLASH or FLASH FILL option.
4. Set the autofocus on "SPOT" or "CENTER" to assure that the camera focuses on the object closest to the center of the framed image (not needed in every camera).
5. Set the zoom button to "WIDE ANGLE" mode. Neither the digital or optical zoom functions are used when obtaining eye images.

2. Stand the horse in a relatively dark area. Make sure there are no windows, doors, or bright objects on the opposite side of the horse or behind the photographer, because images of these objects will be reflected on the glossy surface of the cornea or interfere with the lighting around the eye.
3. Instruct the handler to stand on the opposite side of the horse, holding it calmly with a lead rope attached to the halter.
4. Set the camera lens to the MACRO setting (flower icon). Aim the camera at the globe from a distance of about 15 to 25 cm. Experience will dictate the best focal distance range for a particular camera model. Focus on the cornea, concentrating on obtaining sharp, well-defined corneal reflections. This will increase the likelihood of the anterior segment being in focus.
5. Activate the autofocus system by pushing the shutter button halfway down. Depress the shutter, and take the image as soon as the focus system is ready, without moving the camera at all.
6. Take several photographs of the desired angle in rapid succession, repeating the autofocus process for each one.
7. Review the images on the LCD screen, and delete images that are out of sharp focus. Repeat steps 1 to 5 if useful images have not been obtained.

The author obtains high-quality images using a point-and-shoot camera that has an autofocus mode that produces a soft audible chime when the camera lens is focused on a central object (Kodak EasyShare Z712IS). The chime lets the operator know exactly when the autofocus system is engaged. If the camera is held too close to the subject, the electronic viewfinder will not work properly, and the chime will not sound (Figs. 2-24 and 2-25). This feature allows the operator to manipulate the camera without looking through the viewfinder. It also simplifies one-handed operation of the camera, freeing the other hand for opening the eyelids or steadying the horse's head. The author does not routinely use the LCD screen for framing photograph composition; instead, camera aim is directed by shining the focusing light that accompanies the initial shutter depression on the region of interest. However, while developing the skills necessary to repeatedly obtain high-quality digital images, you should consider using the LCD screen to frame your shots. This will ensure that the camera is focusing on what you want it to, and it will also allow you to

Figure 2-24. A, The autofocus (AF) system of a point-and-shoot digital camera is dependent on an infrared beam that is emitted from the camera when the shutter button is pushed partway down. The system can only operate when the camera lens is 12 to 20 cm away from the object of focus. Here the camera is positioned too close to the horse's eye, and the AF system cannot engage. The resultant photograph will be out of focus. **B,** The camera is positioned within the operating range of the autofocus system. This photograph will be in sharp focus as long as neither the operator nor the horse moves after the autofocus system is engaged.

Figure 2-25. The LCD screen of the point-and-shoot camera can be used to view and magnify the image immediately. Application of the digital zoom function to the image under review, combined with use of the positional controls to center the area of interest on the screen, will create a magnified image that can be studied and later inserted into the patient medical record.

quickly learn the capabilities and limitations of your camera. The horse is watched to assure the target eye is held open for a good photograph. Additional tips for good ophthalmic photography are listed in Box 2-8.

The images can be viewed immediately on the LCD screen while the owner is present. The digital zoom can be used to magnify the image on the screen and shift the center of the image to the anatomy of concern (Fig. 2-26). It is much easier to demonstrate lesions on the screen than on a live horse. Owners gain a deeper understanding of the problem at hand if they can see an image of it during the farm call (Fig. 2-27).

Follow-up images can be paired with originals and emailed to the owner so that progressive findings are well understood. Treatment and referral decisions are thus simplified, and compliance with home therapy advice is enhanced.

ADVANCED PHOTOGRAPHY: DIGITAL SINGLE LENS REFLEX IMAGING AND INFRARED IMAGING

Most ophthalmic specialists image the equine eye using digital single lens reflex (DSLR) cameras. The major advantage of these cameras is that the viewing and metering are done through the lens, allowing accurate composition and exposure. They produce very sharp images and great depth of field. DSLR cameras perform well in a variety of ambient light conditions and allow the operator to vary the lens or flash used. However, these cameras are expensive, relatively heavy, and require some fundamental understanding of the principals of photography in order to obtain the best results. DSLR cameras may be a good choice for practitioners with a special interest in photography.

Infrared imaging of the equine eye[4] is a specialized imaging mode that is useful for specialists and practitioners with an interest in advanced equine ophthalmology. Infrared images provide enhanced detail of iris and corpora nigrans surface features and sharp detail of any abnormal mass or fluid in the anterior chamber, such as melanomas, iris cysts, or hyphema. Corneal opacities such as edema and corneal fibrosis that obscure the examiner's view of intraocular detail in conven-

Figure 2-26. The magnified image on the LCD screen can be used to educate the owner about the condition at hand. This practice increases understanding of the problem and reinforces the need for compliance with any prescribed therapy. The best images can later be sent to the owner electronically and posted in the medical record.

Box 2-8 | Tips for Great Field Photography

- Excessive ocular discharge or periorbital dirt should be cleaned off prior to imaging.
- Head stability may be aided by resting the horse's head on a bale table.
- With practice, the operator can hold the camera and take the photo with the dominant hand and spread the eyelids with the other hand. However, this will leave a reflection on the corneal surface.
- If possible, the operator should lift one lid and have an assistant open the other to avoid a palmar reflection on the corneal surface.
- Operators should avoid wearing white or red clothing—these will produce a reflection on the cornea.
- Mild tranquilization and/or auriculopalpebral nerve block will aid photography of a painful eye.
- Exposure of the sclera and limbus will be aided by rotation of the horse's head. Rotating the head so that the ears roll away from the photographer will aid exposure of the dorsal region of the globe, and rotating the head so that the ears roll towards the photographer will aid exposure of the ventral region of the globe.
- A sterile cotton-tipped swab can be inserted in the fornix or lid to retropulse, expose, or evert areas of interest.
- Short-term mydriasis with the topical application of a few drops of tropicamide (Mydriacyl) will aid photography of most cataracts.
- A small, white image artifact on the cornea from the flash is inevitable. If this obscures any desirable detail, additional photos can be taken from slightly different angles so the flash artifact is superimposed over less important regions.
- A dry Schirmer tear test strip has a small ruler that serves as an easily photographed measuring device.
- Standard photographs of the globe taken from a directly lateral viewpoint can be supplemented with photographs taken from the nasal or temporal angle that demonstrate the corneal curvature and anterior chamber.

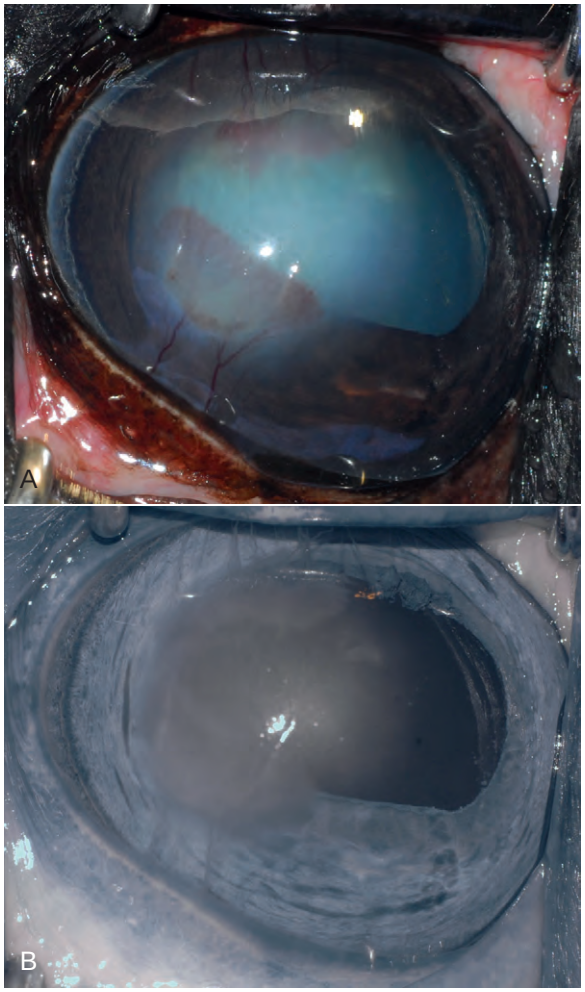


Figure 2-27. **A,** Photograph of immune-mediated keratitis (IMMK) taken with a Nikon D200 DSLR camera and a 35-105 zoom Nikkor lens. Use of a high f-stop allows excellent depth of field. Specialists or practitioners with an interest in photography may want to invest in this equipment to be able to take excellent ocular photographs. **B,** Photograph of the same ocular lesion as in **A,** taken with a Nikon D70 converted to an infrared camera. Infrared photography provides excellent uveal detail, which is especially useful when there are corneal opacities. (Photographs courtesy Dr. Richard McMullen.)

tional photography become more transparent with infrared imaging, because the long infrared wavelengths penetrate an opaque cornea much better than those wavelengths of light within the visible spectrum. The longer infrared wavelengths of light are much less susceptible to scatter than those wavelengths in the visible spectrum. Corneal vessels become more easily visible within areas of corneal fibrosis or edema, inasmuch as they are more solid structures and will remain visible. Cataractous changes of the lens are also enhanced and readily visible when viewed by infrared imaging. Several companies provide conversion services for many DSLR cameras and selected electronic viewfinder (point-and-shoot) camera models (www.lifepixel.com, www.maxmax.com). See Chapter 1 for more information on infrared photography of the eye (Figs. 2-28 and 2-29).

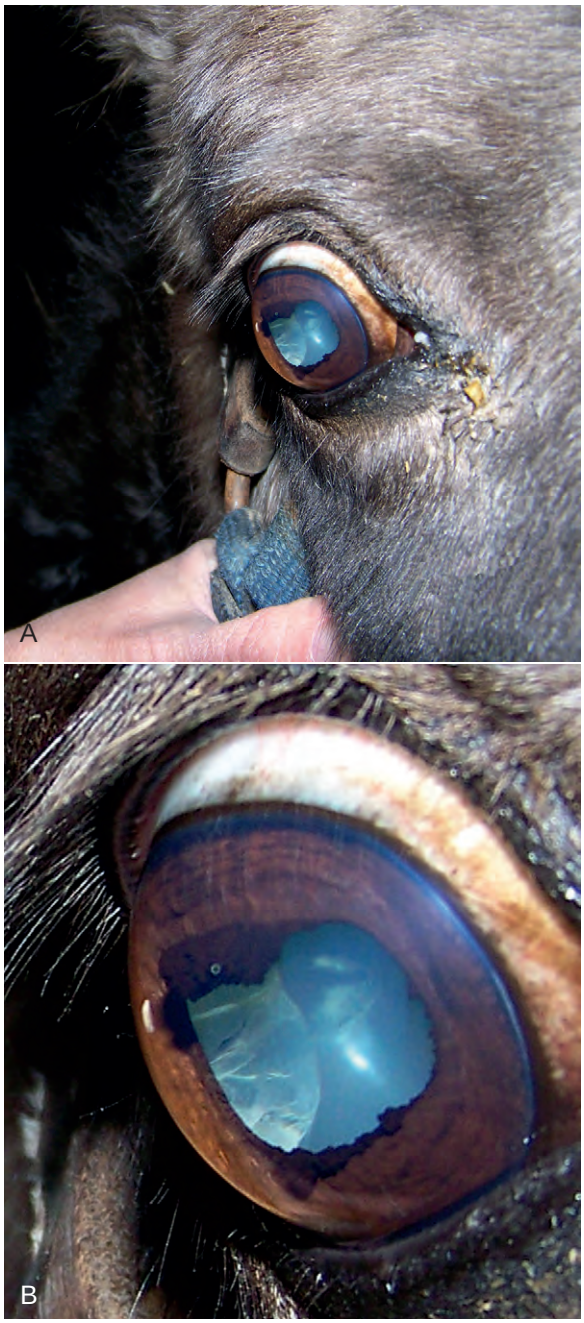


Figure 2-28. **A,** Images obtained in the field should be cropped to remove superfluous detail. This photograph shows the entire image captured by a digital camera focused about 20 cm away from the patient. **B,** Photograph showing the cropped image with excellent final detail and magnification of the ciliary body cyst present on the targeted globe. Cropping was performed using Apple iPhoto software. Original image was photographed using a Kodak Z712IS point-and-shoot digital camera costing less than $300.

IMAGE MANIPULATION

Images are downloaded from the camera onto a viewing computer on return to the clinic or office. The image is cropped to magnify the area of interest and eliminate superfluous detail using a standard photo-editing program (Apple iPhoto or Aperture, Adobe Photoshop, Microsoft Photo Editor, etc.). This editing process is essentially a "digital zoom." Cameras with high megapixel resolution will produce large files (over 1 MB) for every full-screen image. Often as much as 75% of the area of the original image is removed in the cropping process, but the remaining detailed remnant is useful as long as the original image was sharply focused on the area of interest (Figs. 2-30 and 2-31). The cropped file will still be fairly large, but standard compression programs can be used to reduce the file size for email or presentation purposes, without the loss of a lot of detail.

Figure 2-29. Ultrasound imaging of the equine globe can easily be performed in the field using equipment that is also suitable for orthopedic soft-tissue imaging. Here a 7.5 curvilinear microconvex probe attached to an Aloka 900 machine is used to obtain transpalpebral images of the right globe.

ULTRASOUND OF THE EQUINE OCULAR REGION IN THE FIELD

There are many clinical situations involving the eye or orbit in equine practice that can be aided by simple field ultrasound examination. Please see Chapter 1 for more information on ocular ultrasonography. The most common indications for ocular ultrasonography are:

1. Imaging of the rim of the orbit and adjacent skull to screen for fractures or foreign bodies
2. Imaging of a grossly swollen eyelid or periorbital enlargement to check for abscess, masses, or foreign body
3. Imaging of the globe to obtain detail on intraocular masses and cataracts or to check for lens luxation, retinal detachment, or vitreal densities
4. Imaging of the globe and retrobulbar region to assess buphthalmos or exophthalmos

Ultrasound equipment used for normal ambulatory reproductive or orthopedic imaging is generally serviceable for imaging the eye. A 7.5- to 10-MHz probe will yield the highest-quality images, but a 5-MHz probe is satisfactory for basic screening. Convex or microconvex scanning probes produce the best images, but linear probes can also be used.

Figure 2-30. Radiographic imaging of the periorbital region is appropriate for selected conditions. Digital radiography is superior to conventional imaging in this region. Practice tips include the use of a gauze "halter" for restraint and securing radiodense markers (BB pellets) to identifiable landmarks with tape.

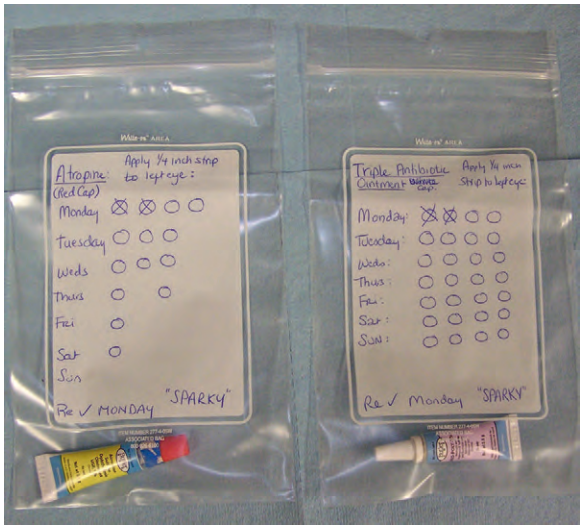


Figure 2-31. Ophthalmic ointments can be dispensed in small plastic "Write-on" bags (Associated Bag Company, Memphis, TN). The therapy schedule can be outlined on the bag label and treatments checked off as they are completed.

The ultrasound machine, attached probes, and any printing accessories should be set up on a nearby table or a stack of hay bales. Hair on the skin area in question may need to be clipped if a heavy winter coat is present. The horse should be sedated and the target skin cleaned and moistened with water prior to applying the ultrasonic transmission gel.

Imaging of the orbit, periorbit, or lids is done through the skin over the target area (see Fig. 2-29). Orbital fractures will produce a discontinuous bright echo as the probe is advanced along the bone of the orbital rim. Abscesses will be imaged as round or ovoid echolucent structures within the surrounding stroma.

Imaging of the globe and retrobulbar region can be done through the skin of the upper eyelid. It can also be done through a transcorneal approach if the cornea is desensitized with topical anesthetic. The ultrasound probe is covered with a sterile watertight covering (e.g., surgical glove), and sterile packs of transmission gel are used to promote sound-wave conduction. A normal globe will produce distinct echoes that represent the corneal surface, the iris and corpora nigrans, the anterior and posterior capsule of the lens, and the inner surface of the globe containing retina, choroid, and sclera. The ciliary body may be visible as an echogenic bulge behind the base of the iris. The anterior chamber, lens cortex, and vitreous are echolucent if normal. Both eyes should be imaged to compare any findings that appear abnormal. See Chapter 1 for more information on the technique of ocular ultrasound and the normal appearance of the equine eye on ultrasound.

Field interpretation of ocular ultrasound is aided by comparing images of the abnormal eye with the normal fellow eye. Echolucencies or echodensities that are not artifacts should be absent in the normal eye. A globe that is enlarged can be distinguished from a globe that is made abnormally prominent by extraocular tissue (orbital compression or retrobulbar mass) by measuring the axial length of the abnormal globe and comparing it to the normal eye.

RADIOGRAPHIC IMAGING OF THE EQUINE OCULAR REGION IN THE FIELD

There are fewer indications for radiographic imaging than ultrasound imaging in equine field ophthalmology, but radiographic assessment is helpful in cases of blunt trauma to the periorbit, sinus disease, or unexplained globe deviation. Radiographic imaging is also useful to check for radiodense foreign bodies or bony changes associated with periocular neoplasms.

Computed or digital radiology systems provide images that are far superior to conventional radiography. Creative oblique angulation of the beam and imaging plate may be required to obtain the most useful orbital images, since standard lateral and dorsoventral projections will position the orbit superimposed over deeper structures. Contrast radiology may be helpful in the case of open sinus fractures.[5]

Positioning for periocular radiography is aided by supporting the head of the horse on a bale table. It may help to elevate the ventral mandible on a small wooden riser on top of the bales so the imaging plate can rest lower than the base of the head. The imaging plate is usually held by an assistant. Sedation is important for optimal positioning and image quality.

Interpretation of images that are taken of various angles of the complex periorbital region is aided by securing a radiodense marker to a known landmark on the skull near the area of interest. Useful markers include surgical staples placed in the skin or BB pellets taped to the skin (see Fig. 2-30). Conversely, hardware from the horse's halter may obscure important radiographic detail, so the halter should be removed. Horses can be restrained for radiographic imaging by making a positioning halter out of a gauze roll that is tied around the head in a halter configuration, with a length of gauze acting as a lead rope to the head. Tension on the gauze "strap" can be used to steady the head in the desired position. Additional information on ocular radiography is detailed in Chapter 1.

TREATMENT OF OCULAR PROBLEMS IN THE FIELD

GENERAL COMMENTS

Treatment in the field is generally a combination of stallside therapeutics and home care. Excellence in standing surgical and medical procedures is within the grasp of every equine practitioner. Practitioners who stock their vehicles as described in Box 2-1, take time to prepare the "field treatment room" to optimize restraint and ocular stability, and exercise good judgment in administering sedation and regional anesthesia should be able to diagnose and initiate effective therapy for many common equine infectious, inflammatory, traumatic, or neoplastic ocular problems.

Ongoing medical therapy in ambulatory practices is usually delivered on the farm. Skills in applying medication vary widely among caretakers, especially when the underlying condition is painful. Compliance with an ideal treatment schedule may be poor if caretakers are unable to medicate a patient more than a few times a day. Therapeutic aids such as SPL systems (described later) may help with the mechanics of administering treatment, but treatment may still be suboptimal due to inevitable caretaker "burnout" from the sustained effort required to treat severe problems. Home treatment compliance is a major challenge for the ambulatory practitioner. Referral to a hospital environment should be encouraged if the owners are unable to treat appropriately. If the owners are not willing to hospitalize the horse, experience will dictate whether catastrophic consequences such as a progression of infection to perforation or endophthalmitis might result; owners should be counseled as to the potential outcome.

Ocular problems, particularly those involving infection or inflammation, require frequent veterinary monitoring to assess progress, perform serial diagnostic tests, administer additional intervention, and decide if therapy should be changed or stopped. Acute infections require multiple visits in a short interval (days to weeks). Inflammatory problems like uveitis, glaucoma, and nonulcerative keratopathies require multiple visits over longer periods, often for the life of the patient. Neoplastic problems may recur or require multiple visits to effect the appropriate adjunctive therapy.

Compliance with appropriate visits to monitor acute or chronic ocular problems is another major challenge for the ambulatory practitioner. Candid counseling is extremely important because the expense and effort involved are significant.

Owners must be educated as to the consequences that can result if they opt to make medication decisions without an examination. A common challenge is the horse that has been treated in the past for uveitis. After several recurrences, owners may be tempted to use old steroid eye ointments every time the horse presents with a painful eye, foregoing a veterinary call. Data collected by the author has shown that 25% of horses with uveitis suffer corneal ulcers at some time after an initial diagnosis with uveitis (see Chapter 8), and steroid therapy in these cases can potentiate very serious infections. Another challenge is the owner who "has some eye ointments on hand" (commonly mydriatics, antibiotics, or steroids) and uses them indiscriminately on painful eyes. This practice may delay appropriate diagnosis of infections or inflammations and may harm the welfare of the patient. Practitioners must constantly educate their clients about the signs of ocular pain in horses, the need for examination, and the importance of evidence-based therapy.

Ongoing therapy decisions are another challenge for the practitioner, particularly in the management of corneal trauma and infection. Topical mydriatic, antibacterial, antifungal, and anticollagenase therapy combined with systemic antiinflammatory therapy is usually appropriate in severe cases. As many medication options are available, practitioners often add additional medications to the treatment schedule if the horse is not improving. The polypharmacy approach, while justified, helps only if the chosen medications are effective against the specific infectious agents and adverse host factors involved. Practitioners must always implement serial diagnostic testing to obtain case evidence to support their treatment decisions.

Decisions on the number of times treatment should be given in a day and when to stop treatment are difficult. Frequent monitoring is advised, and the medical record should carefully detail favorable developments (reduced size of lesions, decreased pain, increased clarity of normally transparent structures, etc.) as well as unfavorable developments (increased size of lesions, increased pain, increased opacity, melting stroma, etc.). Generally, therapy should be continued until the defect is healed and the patient has shown good comfort for several days in a row. Uveitis flare-ups are usually treated with decreasing doses of antiinflammatory medications for about 1 month. Horses with glaucoma often require daily therapy aimed at lowering intraocular pressure for life. Horses with nonulcerative keratopathies respond variably to treatment. Some show improvement with several weeks of treatment and just require therapy for recurrences, whereas others must be managed with topical medication on a constant basis.

Often clinicians encounter severe cases they want to refer but cannot because of economics or lack of a referral facility. These cases are challenging but often can be resolved with diligence and patience. Generally, if vision is present and the lesion has not progressed to severe melting, perforation, or endophthalmitis, it is worth instituting aggressive home therapy for several weeks. In these cases, clinical treatment should focus on (1) controlling pain and secondary uveitis from the insult and (2) instituting aggressive antiprotease, antiinfective, and mydriatic therapy while monitoring progress of blood vessels growing towards the defect. Practitioners should never underestimate the ability of corneal vessels to heal defects that have not epithelialized. Deep or extensive defects that have been present many weeks often heal quickly once corneal vessels reach their margins.

Finally, a minority of cases will fail to respond to therapy. Traumas may be irreparable, corneal infections may progress to perforation or endophthalmitis, neoplasias may recur, and horses with uveitis or glaucoma may become chronically painful or develop untreatable secondary complications. These cases are some of the toughest that equine practitioners face, especially if a significant amount of time and expense has been invested in trying to help the horse. They also are great disappointments for the owner. It is a fact of veterinary practice that some horses become blind in one or both eyes and some require enucleation. Fortunately these individuals often do very well and remain valued companions once their pain from the ocular problem is resolved. More information on management of blind and enucleated horses can be found in Chapter 14.

MEDICAL PROBLEMS

The majority of medical ocular problems seen by ambulatory practitioners will be treated with topical and oral medications. A minority will require subconjunctival injections, subpalpebral lavage tubes, and/or injectable systemic or local medication.

The simplest cases require topical application of ophthalmic medication in ointment form. To improve successful medication application and good owner compliance, the following practice tips are recommended:

1. Dispense the medication in plastic "Write-on" bags (Associated Bag Company, Memphis, TN [800-688-3796]). Mark circles on the bags to create a daily treatment schedule, and direct the client to mark treatments off as completed (see Fig. 2-31).
2. Instruct the client to store medication at room temperature and protect it from extreme heat or cold. Some products may need to be refrigerated (e.g., serum, cefazolin) or kept out of light (e.g., miconazole).
3. Coach the owner on effective techniques for ointment application. Useful tips include having the owner touch the crease in the upper lid and then feel the orbital rim. The finger that lifts the eyelid for medication access can apply light pressure to the lid crease and slide this tissue up until the lifting finger rests underneath the rim of the orbit. The palpebral fissure then opens just wide enough to apply the medication along the tarsal margin but not so wide to produce troublesome reflex blepharospasm. The ointment can be applied directly out of the tube or transferred off the tip of the caretaker's clean or gloved finger onto the tarsal margin. The owner should aim to apply a ¼-inch strip, or a "match-tip" volume of ointment (Fig. 2-32).
4. Another technique that has been used successfully by one ophthalmic specialist is to dispense a box of tuberculin syringes for therapy, and have the farm manager infuse a small quantity of each prescribed medication into the same syringe, effectively mixing the mydriatic with antiinfectives and other ointments. The tuberculin syringe then serves as a clean single-use applicator for medication.[6]
5. Horses may tolerate lengthy courses of treatment if they are given small treats (peppermints, carrots, etc.) right after the medication is applied.

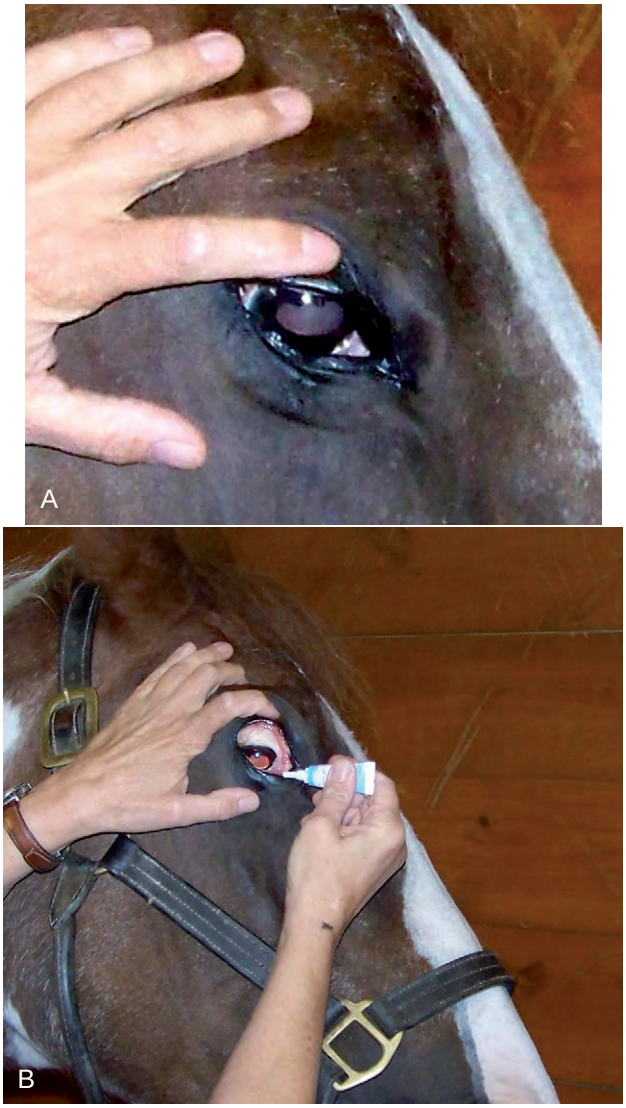


Figure 2-32. **A,** Owners appreciate learning tips for medication application. A useful technique involves teaching the client to feel the rim of the orbit and explaining that it can be used as a "ledge" to support the finger that is used to lift the upper eyelid. **B,** The client is then instructed to touch the crease of the eyelid lightly with the index finger and lift the lid up until the lifting finger rests against the orbital rim. Ointment can then be spread in a quarter-inch strip along the inner palpebral margin of the lower lid.

SUBCONJUNCTIVAL INJECTIONS

Subconjunctival injections are sometimes indicated to supply a concentrated dose of a therapeutic agent to the cornea or globe.

Horses requiring subconjunctival injections should be sedated. The procedure will be safest if the ventral mandible of the horse is supported on a bale table. The periocular region should be cleaned with 2% Betadine, and topical anesthetic should be applied to the cornea and sclera. A sterile cotton-tipped applicator is used to apply additional topical anesthetic to the area chosen for injection (usually a patch of the bulbar conjunctiva over the dorsotemporal sclera). Access to the dorsal bulbar conjunctiva is facilitated by having the handler (who is standing on the opposite side of the horse) grasp the ear contralateral to the treated eye and pull it gently. This action rolls the top of the head away from the clinician. The resultant oculovestibular motion rolls the target globe ventrally, exposing the dorsal sclera.

Subconjunctival injections are delivered in a volume that does not exceed 1 mL and are best administered with a ⅝-inch, 25- or 27-gauge needle attached to a tuberculin syringe. Prior to injection, a pair of Bishop-Harmon forceps is used to lift the target conjunctiva to test topical anesthesia and sedation. If no reaction occurs, the needle is then inserted under the conjunctival surface with the bevel up, and the solution is injected (Fig. 2-33). A proper subconjunctival injection slips the drug underneath Tenon's capsule just above the sclera, raising a bubble of conjunctiva containing the injected medication. Hemorrhage from the needle puncture is common, especially if the conjunc-

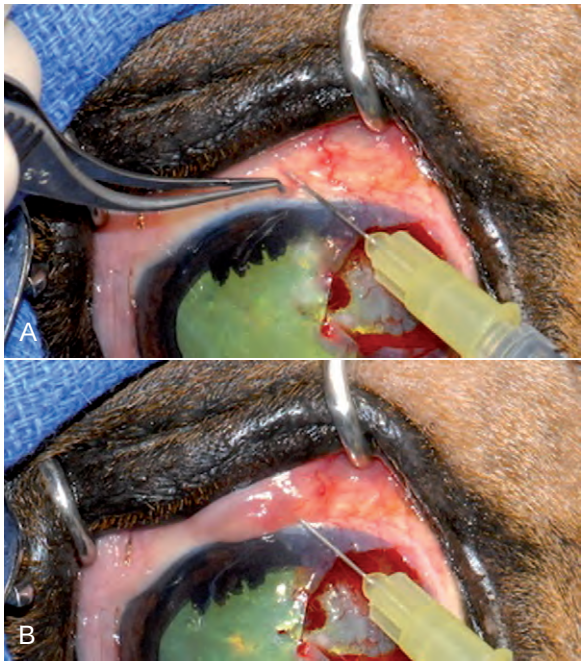


Figure 2-33. Subconjunctival injection in a horse after a superficial keratectomy. **A,** A 27-gauge needle is inserted under the dorsolateral bulbar conjunctiva. **B,** Up to 0.25 mL of fluid can be injected in one area, resulting in a balloon-like appearance to the bulbar conjunctiva.

tiva is inflamed. This complication (which can alarm observers) can be minimized by applying a sterile swab soaked with a few drops of 1:1000 epinephrine or 2.5% phenylephrine to the target conjunctiva prior to the injection.

SUBPALPEBRAL LAVAGE TUBE SYSTEMS

Corneal lacerations, deep ulcers, melting ulcers, ulcers with keratomalacia and cases of severe uveitis are conditions that require intense topical therapy. SPL systems are specialized ophthalmic catheters that allow the administration of liquid medication through the lumen of a long tube that runs from the withers into the eyelid and discharges the drug through a special footplate that sits in the conjunctiva of the upper or lower fornix. The injected solution(s) then mix with the tear film to medicate the cornea.

SPL systems are often a necessary treatment tool for several reasons:

- Horses with painful eye conditions may be fractious to handle and difficult to treat.
- Severely traumatized globes are at risk for rupture and may not tolerate close handling for topical treatment.
- Many topical medications are only available in liquid format, and it is difficult to administer a precise dosage into the tear film of horses without an SPL.
- The amount of effort required to treat serious cases round the clock is intense, and SPL systems make the therapy as easy as possible for the caretakers.

SPL systems with a sharp 12-gauge trocar swaged onto the tubing are sold by Mila International, Florence, KY (www.milaint.com or 1-888-645-2468) and Jorgensen Laboratories, Loveland, CO. The kits with swaged on trocars are easiest and safest to insert. The Mila kits are sold in two different lengths (36 inches and 60 inches) with a single diameter (5 Fr) of silicone tubing. The longer tubes are most appropriate for large horses with long necks, and the shorter ones are sufficient for foals, ponies, and small horses.

SPL systems that require passage of the silicon tubing through the lumen of a 12-gauge, 3-inch needle that is placed in the fornix are also available (Jorgensen Laboratories <http://www.jorvet.com/>).

Figure 2-34. When a subpalpebral lavage system is planned, all items listed in Box 2-9 should be gathered and placed on a raised surface.

Box 2-9 | Items Needed for Subpalpebral Lavage System Placement

- Subpalpebral lavage kits
- Wash solution of 2% Betadine
- Dry gauze
- Adhesive tape roll
- Local anesthetic and topical anesthetic
- Tuberculin and 3-mL syringes
- 25-gauge and/or 23-gauge needles
- Nonabsorbable 2-0 or 1-0 suture, cutting needle
- Head lamp
- 20-gauge, 1-inch catheters
- Male catheter caps
- Tongue depressors
- Rubber bands for mane braids
- Bale table for head support

INSERTION OF THE SUBPALPEBRAL LAVAGE SYSTEM IN THE STANDING HORSE

The items listed in Box 2-9 are assembled (Fig. 2-34). The forelock and the mane on the horse's neck are braided in 5 to 10 long braids secured with rubber bands or tape prior to insertion. The SPL tubing will be threaded through the braids to prevent it from catching on obstacles. If the patient is a young foal or horse with a sparse mane, a number of tufts of mane can be gathered into short "pigtails" and secured with tightly wound rubber bands or short sections of adhesive tape.

Horses are heavily sedated with IV detomidine for tube insertion. Very young or fractious foals may require short-term general anesthesia for safe insertion. The process of inserting and securing the system will be facilitated in the standing horse with head support and administration of auriculopalpebral and supraorbital nerve blocks. SPL tubes can be inserted into the

fornix of the upper lid or cul-de-sac of the lower lid, depending on clinician preference, patient temperament, and the location of the lesion being treated (Fig. 2-35).

The periorbital region is cleaned with a solution of 2% Betadine. The skin over the intended target site in the lid fornix is infiltrated with local anesthetic. Several drops of topical anesthetic are instilled onto the corneal surface. Tolerance of lid manipulation should be tested by inserting a gloved finger towards the chosen exit site in the fornix and applying pressure on the skin over the fingertip with a finger of the opposite hand. If sedation appears adequate, the SPL trocar is guided into the desired site by reinserting the finger to the test site, this time with the trocar lying in the space between the gloved digit and the lid but not projecting beyond the tip of the digit. The trocar is then carefully advanced to the conjunctiva adjacent to the orbital rim and then pushed completely through the lid skin (Fig. 2-36). The trocar and attached long tubing are then pulled through the lid. Care is taken to assure that the slanted treatment footplate is oriented parallel and snug with the oblique angle of the eyelid fornix (Fig. 2-37).

White adhesive tape is used to construct two or three "butterfly wings" that adhere to the outside of the tubing and secure it to the face at one site directly above the fornix exit and in one or two additional sites more proximal to the ipsilateral ear. Each half of the adhesive tape wing is affixed to the skin with nonabsorbable suture of 2-0 or 1-0 diameter. The tubing may also be laced through the plastic U-shaped guides provided with the catheter kit, and the guides then sutured to the skin in similar sites (Fig. 2-38).

The trocar remains attached to the SPL tubing until the tubing has been threaded through the braids or mane tufts. The best pattern for tubing security is to weave the needle under the braid/tuft, thread it through the center of the section adjacent to the neck crest, then pass the tubing over the remainder of the braid/tuft before going "under" the next braid/tuft down the neck. The tubing is woven all the way to the base of the neck near the withers (Fig. 2-39). The trocar is cut away and discarded.

A 20-gauge, 1-inch IV catheter is carefully fed into the open tubing that has been cut off the trocar, and the system should be closed by threading a standard male catheter injection cap into the catheter. The injection assembly (tubing, 20-gauge catheter, and catheter cap) are taped to a short section of tongue depressor with adhesive tape and secured to one of the braids or tufts of mane. The combined "handle" of the braid, tongue

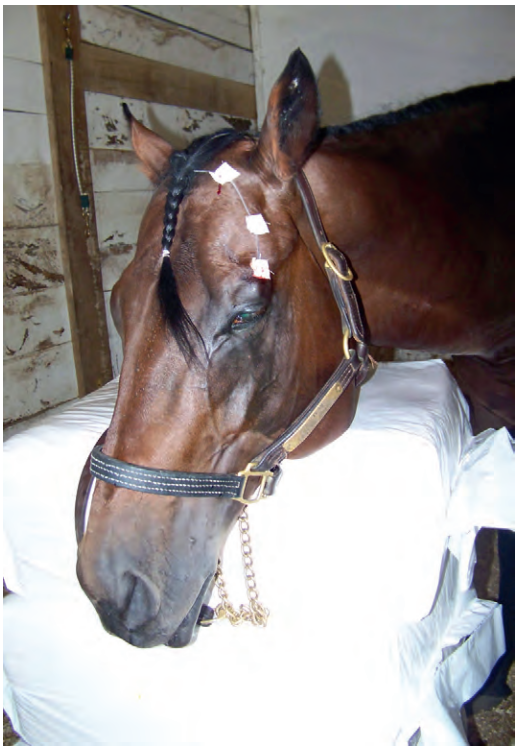


Figure 2-35. Subpalpebral lavage system placement is facilitated by head support, heavy sedation, topical anesthesia, and administration of auriculopalpebral and supraorbital nerve blocks. The system can be placed in the fornix of the upper lid or the cul-de-sac of the lower lid, depending on clinician preference, patient temperament, and location of the lesion being treated.

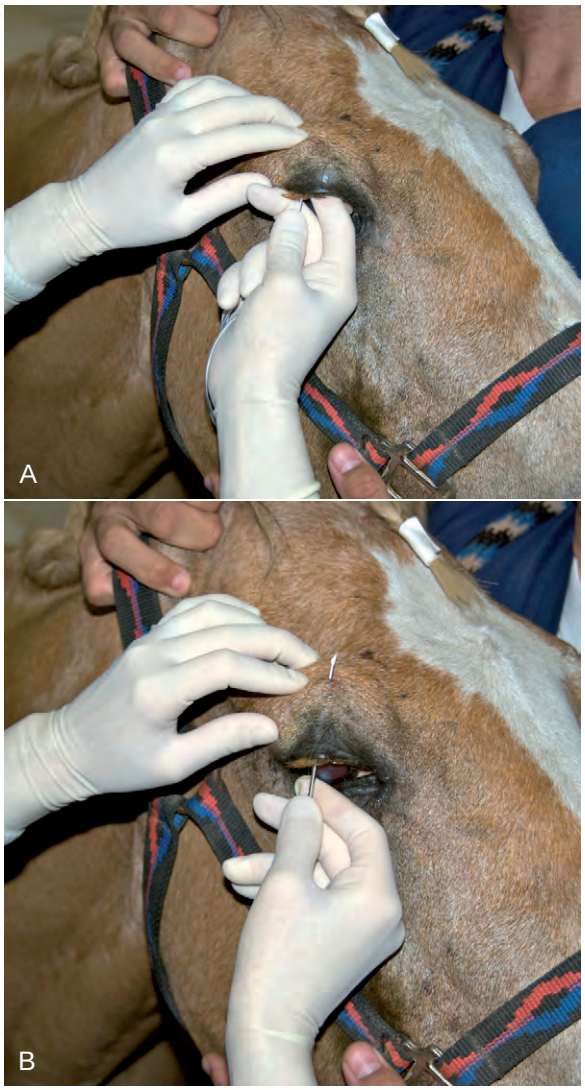


Figure 2-36. A, The lid is pierced with the trocar of the subpalpebral lavage system as deep into the fornix as possible. Prior to the skin piercing, the trocar is advanced to the intended exit site, with the surgeon using a gloved finger as a guide for the trocar to prevent damage to the globe or lids. **B,** The trocar is advanced to pierce the skin.

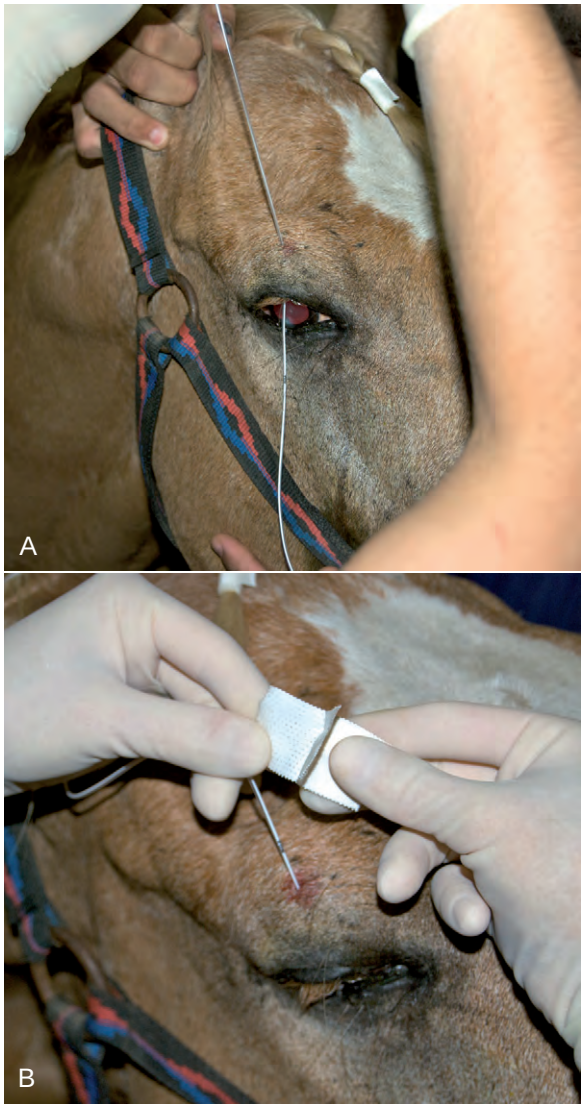


Figure 2-37. **A,** Once the lid is pierced, the trocar and the entire length of the subpalpebral lavage tubing is pulled through the eyelid. **B,** Care is taken to assure that the slanted treatment footplate is snug with the oblique angle of the eyelid fornix.

depressor, and lavage injection assembly can then be conveniently gripped and steadied with one hand while the other hand is used for medication injection (Fig. 2-40).

MEDICATION APPLICATION USING A SUBPALPEBRAL LAVAGE SYSTEM

Injection of medication is accomplished by infusing 0.1 to 0.2 mL of drug from a tuberculin syringe into the cap and catheter using a 25-gauge needle. The medication is then "chased" with 1 to 1.5 mL of air that is injected slowly into the tube (Fig. 2-41). The air pressure delivers the drug into the tears. Delivery will be apparent when the eye tears as the medication exits the tube in the fornix. Tolerance of intensive SPL medication regimes can be improved by feeding the horse carrot bits or other palatable treats at each dosing session.

Many clinicians draw up multiple medication syringes at once. It is helpful to color code the syringes with tape or label dots and keep each kind of medication in a separate cup or bag so that medications do not become confused (Fig. 2-42). Creation of a spreadsheet with boxes or circles that indicate treatment times of various medications is also useful. Checking off the boxes as treatments are completed will assure compliance and good communication between a team of treatment personnel.

Most horses with SPL tubes are treated with a number of drugs. The frequency of treatment varies with severity and chronicity of the problem but is generally 4 to 12 times a day. Medication administration should be spaced 3 to 5 minutes apart to minimize washout.

Pump devices (Infu-Disk [Mila International], www.milaint.com, 1-888-645-2468) attach to the lavage tube and infuse a small dose of a "cocktail" of medication to the globe at a continuous rate. Eight different pumps are available that deliver solutions at rates ranging from 0.06 mL/h to 1 mL/h. Depending on the rate of delivery, an individual pump will last between 10 hours and 7 days. Although use of pumps is convenient, the cost of the devices, the lack of suitable drug combinations, and propensity of horses to dislodge the pumps have resulted in their use only when traditional injections are not possible.

MANAGEMENT, REPAIR, AND REMOVAL OF SUBPALPEBRAL LAVAGE SYSTEMS

Properly managed SPL tubes can remain in place for a month or more. Catheter caps should be cleaned frequently with an alcohol wipe and replaced every 2 or 3 days. The injection assembly can be retaped as necessary. White butterfly wings or plastic guides that secure the tubing to the face should be repaired if the sutures break. The SPL tube should be checked daily. On the Mila brand of tubes, there is a label on the tubing near the foot plate that says "Mila," and this should be identified daily about 25 mm above the exit hole in the lid to assure that the tube footplate is snug in the palpebral conjunctiva and not migrating towards the cornea. Occasionally, tubes may develop small holes. If this occurs, the section with the hole can be cut out, and two adjacent intact sections of tubing can be spliced together using the lumen of a 20-gauge IV catheter as a bridge.

Many clinicians manage horses with SPL systems well with fabric fly masks (Fig. 2-43) or no facial covering. Although rarely needed, cup hoods are available in "left" and "right" models of various sizes (Eyesaver [Jorgensen Laboratories]). Optimum air circulation will occur if the plastic ocular cup is perforated with several drilled 5- to 10-mm holes so it resembles a whiffle ball. The terrycloth "tear catchers" that snap into the inner aspect of the cup should be changed and washed daily, and a new gauze pad should be snapped across the hood lumen as well. Caution is advised when using hard cup hoods, because some horses have developed severe periocular dermatitis with their use. Warm and humid environments may contribute to development of ocular surface infections in horses that wear hard cup hoods. Hoods must be checked daily and discontinued or modified if dermatitis develops (Fig. 2-44). Quiet horses with SPL systems in place may tolerate solitary turnout in small paddocks if they wear a hood or a fabric mask. The SPL injection port assembly near the withers can also be covered with a small plastic bag that is taped shut and attached to the mane

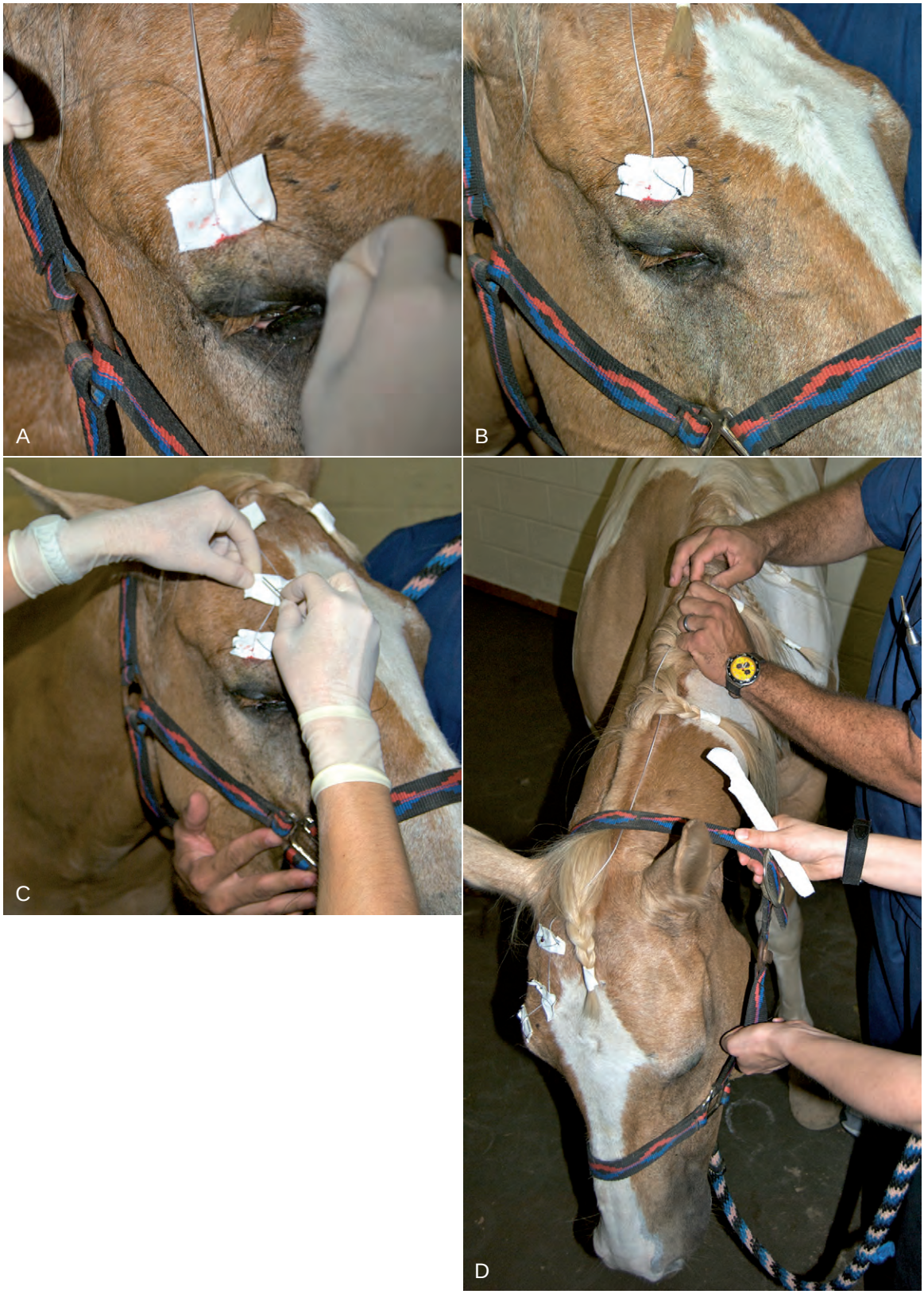


Figure 2-38. **A,** White adhesive tape is used to construct two or three "butterfly wings" that adhere to the outside of the tubing. **B,** The first "wing" is sutured to the skin directly above the exit site. **C** and **D,** Additional wings are placed between the exit site and the poll.

Figure 2-39. The trocar remains attached to the tubing until the tubing has been threaded through preplaced mane braids or tufts. The tubing is woven down to a braid close to the withers for best access for medication administration.

Figure 2-40. The injection port for the subpalpebral lavage system is created by feeding a 20-gauge, 1-inch catheter into the open tubing and inserting a standard male catheter injection cap into the catheter. The port assembly is then taped to a tongue depressor and secured to a braid near the withers.

Figure 2-41. Medication is injected into the tube using a tuberculin syringe and a 25-gauge needle. A volume of 0.1 to 0.2 mL of the drug is injected and then pushed through the tube and into the tear film by *slowly* injecting 1 to 1.5 mL of air from a 3-mL syringe attached to a 25-gauge needle. (Photograph courtesy Faith Ferguson, Silver Ridge Stables, Micanopy, FL.)

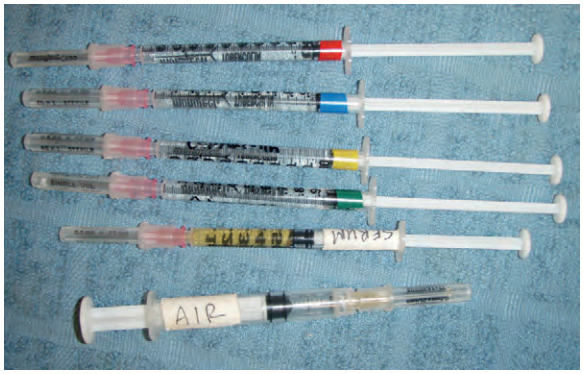


Figure 2-42. Compliance with a multidrug treatment schedule is aided if the syringes containing the various treatments prescribed are drawn up in tuberculin syringes (5 doses each) that are color coded to distinguish different medications.

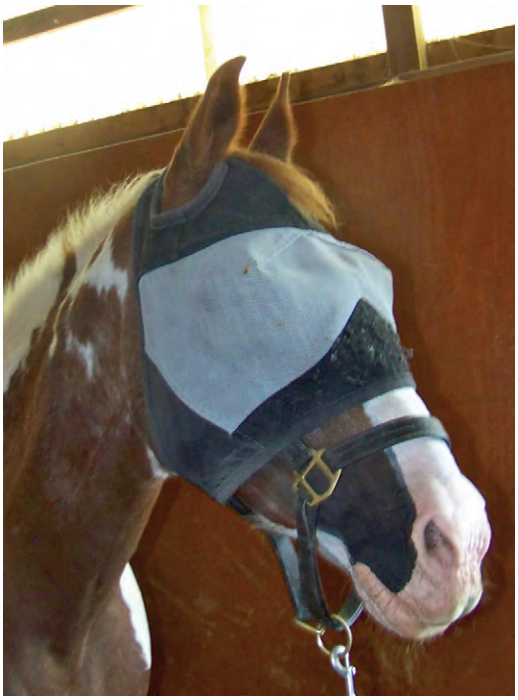


Figure 2-43. Many clinicians cover subpalpebral lavage systems with mesh-fabric fly masks. The mask protects the system from light head rubs, reduces light stimulation, and promotes cleanliness.

braid to protect the assembly parts and keep them clean if the horse inadvertently rolls.

SPL tubes are easily removed in the standing, sedated horse by cutting the tubing a few centimeters above the fornix exit site and removing all wings or guides that attach the cut section to the face. The tubing that remains attached to the footplate can be used as a "pole" to push the footplate away from the conjunctiva and into the fornix space (Fig. 2-45). A gloved finger can then be used to fish the footplate and short length of tubing out of the fornix and remove it. Occasionally the footplate will remain buried in the conjunctival tissues. In these instances, the exit site in the eyelid skin can be infiltrated with a small amount of local anesthetic, and a simple cutdown surgery can be performed around the tubing stump to retrieve the footplate and associated remnant.

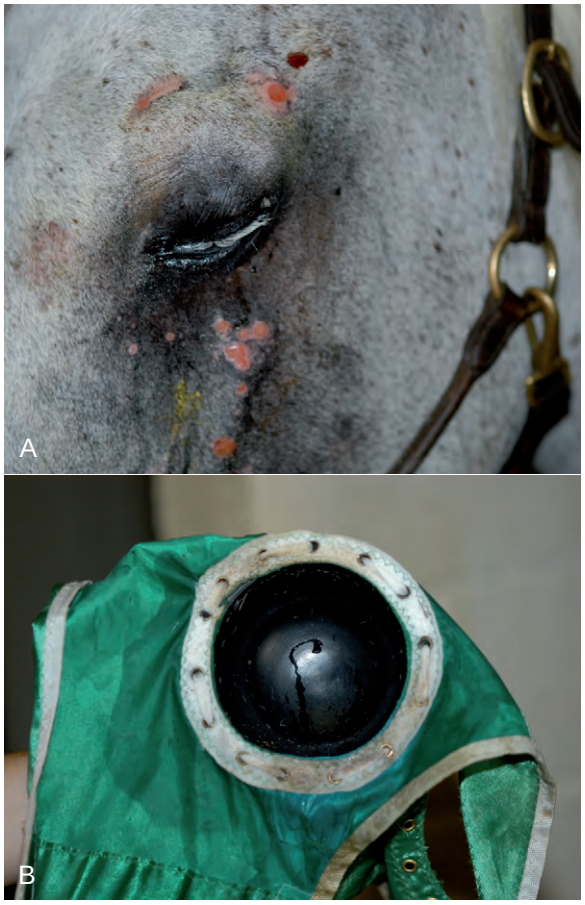


Figure 2-44. Plastic eye cups can be used to protect subpalpebral lavage systems, but they must be used with caution and checked frequently. **A,** Periocular dermatitis from use of an eye cup. **B,** Typical appearance of an eye cup after 24 hours of use. Note that the moisture that accumulates can contribute to the development of infection. (Photographs courtesy Dr. Brian Gilger.)

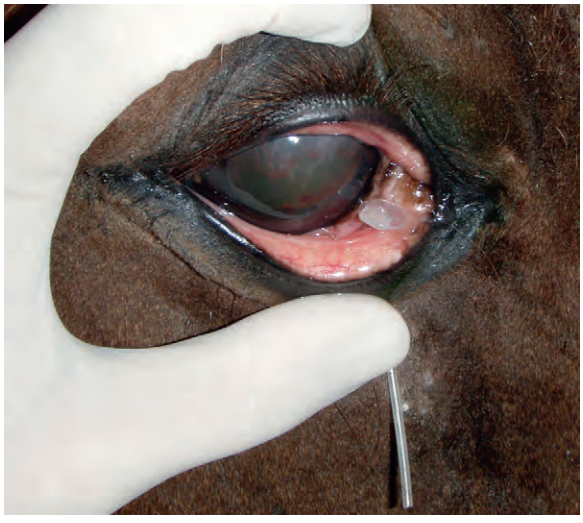


Figure 2-45. Subpalpebral lavage tubes are easily removed in the standing sedated horse. Once the tubing is cut a few centimeters above the exit site, the remaining segment that is attached to the footplate can be used as a "pole" to push the footplate away from the conjunctiva, where it can be easily removed.

STANDING SURGERY

The majority of ocular problems treated surgically by ambulatory practitioners are done as standing procedures. Standing procedures can be separated into (1) simpler surgeries performed on the adnexa or cornea that require only sedation, subcutaneous regional anesthesia, and topical anesthesia and (2) more complex procedures of the nictitans, cornea, or globe that may require retrobulbar nerve block to produce ocular immobility. The former group of procedures (Box 2-10) are readily performed in the field, but any particular procedure that will involve lengthy manipulation, sharp dissection, or very precise handling of tissue is best performed in stocks. The group of procedures that may require retrobulbar nerve block (Box 2-11) must be performed in a clinic setting with stocks for optimal restraint, lighting, environmental control, and safety.

PREPARATION FOR STANDING PROCEDURES

Simple standing procedures done on the farm are facilitated by creative use of items at hand to fashion as ideal a "surgery room" as possible (Fig. 2-46). The site should be cleared of clutter, and available lighting should be optimized. Two common but troublesome challenges that should be minimized are wind disturbance and untimely traffic from people and animals. Head support of the patient at an effective operating level is critical. Creation of a "bale table" using four to six bales of hay, straw, or bedding covered by a clean cloth can make the difference between an "adequate" procedure and an excel-

Box 2-10 | Standing Surgical Procedures That Do Not Require Retrobulbar Block

- Eyelid laceration repair
- Removal or biopsy of small eyelid masses
- Adjunctive therapy for adnexal neoplasia
- Conjunctival biopsy
- Corneal cytology sampling
- Corneal débridement
- Grid keratotomy
- Superficial keratectomy

Box 2-11 | Standing Surgical Procedures That May Require Retrobulbar Block

- Enucleation
- Third eyelid laceration repair
- Third eyelid removal
- Removal of superficial corneal foreign body
- Suture of small nonperforating corneal laceration
- Amputation of corneal flaps
- Aqueocentesis
- Intraocular injection
- Iris cyst laser ablation
- Laser cyclophotocoagulation for glaucoma
- Intraocular mass laser ablation

Figure 2-46. A makeshift "surgery room" can be created in the field if simple standing surgery or diagnostic tests are planned. Wind disturbance and traffic from people and animals should be minimized.

lent one. The surgeon should arrange the support so that the horse is comfortable, the head is stable, and a space is available to rest the elbows for hand stability as needed. Depending on the height of the horse, the surgeon may stand on the ground, stand on a bale or stool, or sit on a similar aid to perform the procedure.

All items anticipated for the procedure(s) are assembled before the horse is presented for sedation and local anesthesia. Working table space for equipment should be created. Sturdy portable folding tables (available from Champagne Pet Products, Southampton, MA [http://www.champagnetables.com/main.html] or Stonewell Bodies, Genoa, NY [http://www.stonewellbodies.com/]) can be set up on site, and extra flat storage surfaces can be fashioned from bales.

Good lighting is also critical. Incandescent light sources do not provide sufficient illumination, so supplemental halogen or LED lighting is useful. Many practitioners carry a small (250 to 750 watt) halogen work light (available at Home Depot [www.homedepot.com] or similar hardware stores) in their vehicle. This work light can be clamped or hung on a wall and aimed at the operated eye. Alternatively, the stable owner may provide a high-wattage halogen light source that is mounted on an adjustable tripod (Fig. 2-47). Automotive "trouble lights" that contain multiple light emission display (LED) bulbs are also good wall sources of auxiliary bright light.

The surgeon will be aided by focal illumination in the form of a headband light. Good, inexpensive headband lights constructed of four or more LED bulbs can be purchased at outdoor stores (L.L. Bean, Gander Mountain, etc.) (Fig. 2-48). More costly examination headlights that have xenon, solid state, halogen, LED, or fiberoptic light sources with auxiliary power supplies can be purchased through a number of manufacturers and distributors (www.shor-line.com, www.welchallyn.com, www.sheervision.com, www.accessbutler.com, www.pennvet.com, www.paragonmed.com).

Magnification is also a helpful aid in many standing surgeries. Practitioners choosing a head loupe should consider several factors when selecting a model, including resolution (the image

Figure 2-47. Halogen work lights can provide useful auxiliary lighting in dimly lit barns. Compact units that can be hung on a wall are readily available. A high-wattage halogen light source mounted on an adjustable tripod is ideal.

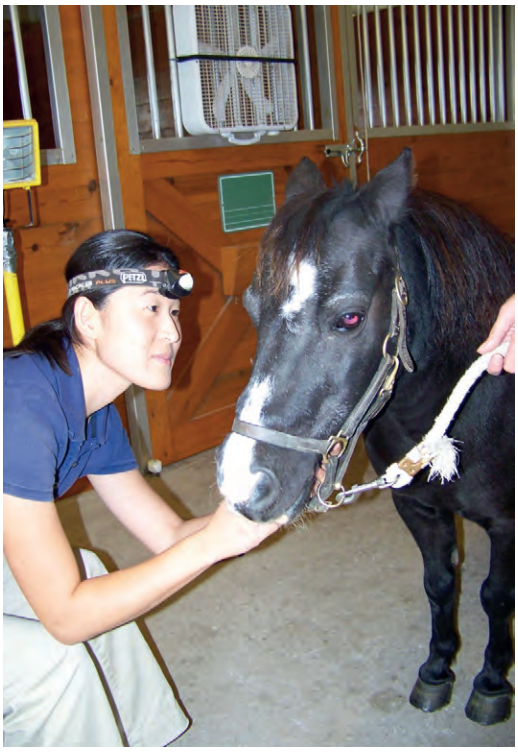


Figure 2-48. Illumination during standing surgical procedures is aided by the use of a simple headband lamp equipped with four or more LED bulbs.

should be clear from edge to edge), unit weight and comfort, field of view, degree of magnification, and depth of field. It is also important to choose a unit that is in focus at a comfortable working distance. Keeler binocular head loupes (www.keelerusa.com) are practical units equipped with frames that fit on the surgeon's head like a pair of eyeglasses. Models that deliver ×2.5 to ×5.5 magnification are available. A practical choice for field use is Keeler Model 2112-P-1012; it delivers ×2.5 magnification at a 46-cm working distance. Keeler Model 2113-P-2009 XL is a more powerful system suitable for more advanced microsurgical techniques; it delivers ×4.5 magnification with a 46-cm working distance. A newer model, K-LED, is equipped with 3W LED lights that provide a light patch of up to 18,000 lux and is powered by a rechargeable battery. Additional head loupe units are made by a variety of manufacturers (Heine, Sheer Vision, Miltex, etc.) and are available through most veterinary distributors (Fig. 2-49).

Once the environment is readied for the procedure and all supplies are assembled, the horse is brought into the designated area for surgery. Sedation is administered, and the periocular region is cleaned with 2% Betadine solution. Choice of topical or regional anesthesia is dependent on the exact procedure planned, but most procedures will require palpebral and supraorbital nerve blocks (see Chapter 1 for detailed instruction on these procedures). Specific instructions on the various conditions described in the following sections are provided throughout this text.

FIELD TIPS FOR BASIC STANDING PROCEDURES

Most acute eyelid lacerations are treated on the farm, since emergency transport is rarely practical. Eyelid laceration repair requires meticulous technique. Excision of lid tissue should be minimal and restricted to removal of devitalized tags of skin and/or minor freshening of the skin margins that will be closed.

A two-layer closure is usually best, but the sutures in the subconjunctival layer should be inserted sparingly with great care, assuring that no portion of the knot has the potential to abrade the cornea. The skin adjacent to the tarsal margin should be closed with a figure-eight pattern suture loop that apposes the torn lid margin sections exactly with no gap or step. Cosmetic results of careful repairs of acute lacerations are usually very rewarding. For more information on the technique for repair of eyelid lacerations, please consult Chapter 4.

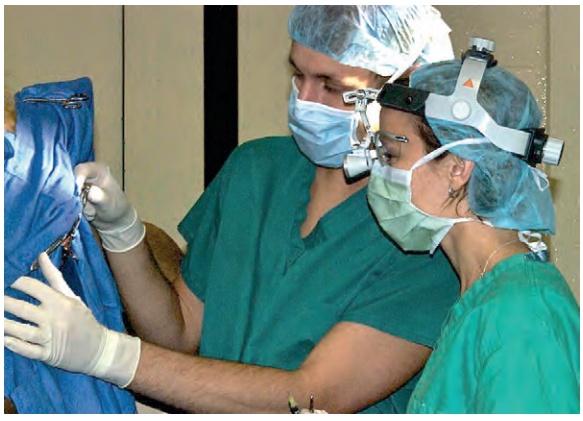


Figure 2-49. Magnification for standing surgeries is a very helpful aid. Pictured here is the 2.5X Heine HR-C Binocular Loupes (Heine USA, Dover, NH, USA) in use for a standing superficial keratectomy.

Temporary correction of entropion in neonatal foals is easily accomplished in the field as a short-term recumbent surgery. The foal should be sedated then placed in lateral recumbency with the affected eye up and the contralateral side of the face resting on a towel. Local anesthesia is infiltrated below the lower tarsal margin, using a 25- or 22-gauge needle. Three to four vertical mattress sutures of #1-0 diameter are placed in the loose skin ventral and perpendicular to the tarsal margin to tighten the tissue and evert the lid. Care must be taken to assure that the suture tags do not have the potential to abrade the cornea. The tissue will usually gain enough subcutaneous fluid and rigidity that entropion will not recur after 10 to 14 days, so the sutures should be removed in that interval.

Minor eyelid margin revision is indicated for resection of small tumors or repair of small old lid defects in adult horses. Most tarsal margin lesions that are less than 4 mm in diameter will involve straightforward wedge resection. The precision of the resection can be aided by drawing a V on the skin with a permanent surgical marker to guide creation of the incision. Lid skin is best incised with a small, curved #15 Bard Parker scalpel blade. Small blunt-tipped scissors may be used to trim the subcutaneous tissue that extends toward the fornix. Margin repair is done using the same procedure described for eyelid laceration repair.

Extensive eyelid margin revision is indicated for resection of large tumors, repair of old scars that hinder lid function, or permanent correction of entropion or ectropion in adult horses. Please see Chapter 4 for more information.

Conjunctival biopsy is indicated for investigation of masses or patches of conjunctiva with abnormal appearance. This procedure can be performed in the standing, sedated horse with topical anesthetic. Hemorrhage can be minimized by applying a few drops of 2.5% phenylephrine to the site prior to tissue excision. Palpebral and frontal nerve blocks are helpful as they eliminate blepharospasm. Access to sites on the bulbar conjunctiva can be aided by tipping the head of the horse to stimulate oculovestibular globe motion. Rolling the top of the horse's head away from the surgeon exposes the dorsal bulbar conjunctiva, and rolling the top of the head towards the surgeon exposes more ventral sites. Suturing of the parent conjunctiva is rarely necessary, since the mucosa heals well by second intention.

Corneal débridement is the most common standing ophthalmic procedure. To prevent transfer of pathogens from the surgeon's hands, sterile gloves should be worn when doing débridement or any other procedure on the ocular surface. The inner paper wrapper of the surgical glove pack provides a useful sterile field for short-term placement of débridement items and cytology slides. Débridement tools include scalpel blades (any size) with their foil wrappers, Kimura platinum spatulas, and cotton-tipped swabs.

Débridement often begins with cytology sampling of the lesion, as described earlier in this chapter. In some instances, blade débridement then continues in repeated sessions to remove any loose debris in the ulcer bed, but care is taken to avoid gouging the bed or applying any pressure that might threaten the stability of the cornea.

Blunt-blade débridement is followed by lighter débridement of the margin of the lesion with a series of sterile cotton swabs.

Each dry swab is stroked in a firm but gentle "paintbrush" movement across the damaged region of cornea, and the margin of the defect is circled with the swab tip (see Fig. 2-8, *B*). The dry swab applies enough friction on the corneal surface to loosen poorly attached epithelium and roll it away from the underlying stroma. Swabs are replaced as they become soaked with tears and lose frictional action. The character of the corneal defect will dictate the number of swabs that are used and amount of corneal debris that is removed, but gentle débridement should proceed as long as epithelium peels away easily. Débridement of small superficial lesions surrounded by very loose epithelium will create a much larger defect than the original ulcer.

Treatment of burdock bristle keratopathy on the cornea and nictitans is a common task in northeastern practices in the fall months. Horses suffering from this condition often present with multiple burdock thistles entangled in the mane or tail (Fig. 2-50). Inspection of the pasture will reveal weedy patches, often along the fence, where the larger plant is established. The tiny microscopic pappus bristles (which provided the inspiration for the adhesive hook and loop system known as Velcro) have the ability to adhere to nearly any substance and can easily become embedded on the cornea or the conjunctiva.

A typical case presents with a vascularized ulcer in the ventronasal cornea, surrounded by an opaque section of chronically inflamed stroma. The nictitans mucosa apposing the corneal defect is usually swollen and inflamed. Atypical cases may present elsewhere on the limbus as a small region of focal superficial vascularization with or without a superficial epithelial defect. Discomfort is usually mild, and the horse may have been symptomatic for several days to weeks. The tiny plant barbs are rarely visible, even with magnification. However, the condition should be suspected if the mane is tangled with burdock thistles or the conjunctiva on the inner face of the nictitans has a follicular or cobblestone appearance. Frequently, vessels on the nictitans of suspect cases will show focal hypertrophy, with the most intense vessel growth pointing to the region where the bristle(s) are probably embedded (Fig. 2-51).

Treatment involves removal of the embedded pappus bristles. Access to the surfaces that contain the bristles requires sedation, head support, and good topical sedation. If the nictitans is involved, it must be everted with a small hemostat so the inner surface can be accessed. Practice tips for successful treatment include using the open jaw of a small hemostat as a scraping instrument to débride any inflamed nictitans mucosa, paying particular attention to any focal region of high vascularity. Hemostat débridement can be followed with judicious rubbing of the inner-third eyelid mucosa with a corner of a dry gauze 4 × 4 pad stretched over a gloved finger. Any inflamed region of the cornea should be treated using standard débridement supplemented by application of a gauze-covered gloved finger to the corneal surface as a final "sweep" for embedded bristles. All débrided ocular surfaces should be lavaged with 10 to 12 mL of sterile saline or eyewash to flush out any debris that may linger on the surface.

Treatment is followed by topical application of a broad-spectrum antibiotic ointment and a mydriatic for several days. Resolution is confirmed when the ulcer bed heals, vascularization fades, and the horse becomes comfortable. A few cases require repeat treatment for full resolution.

FIELD TIPS FOR PROCEDURES REQUIRING RETROBULBAR BLOCK

The horse has powerful retractor oculi muscles that retract the globe into the orbit in response to noxious stimuli. The retraction motion results in a sudden eversion of the nictitans across the nasal portion of the cornea. Such globe and eyelid motion restricts surgical access to the nasal portion of the cornea and makes the globe unsafe to approach with sharp instruments.

Figure 2-50. Horses suffering from burdock bristle keratopathy often present with multiple burdock thistles entangled in the mane or tail.

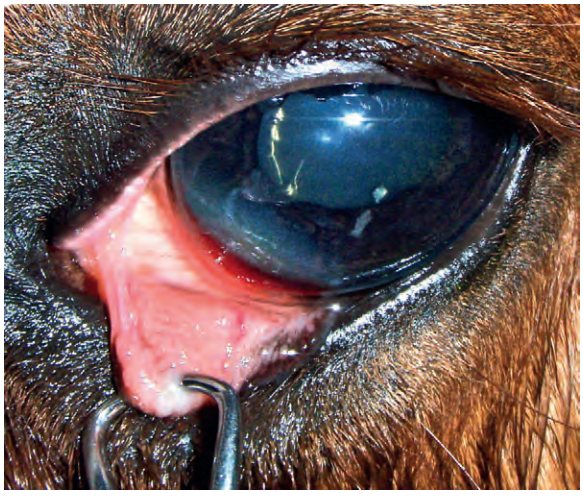


Figure 2-51. The inner mucosal surface of the nictitans is frequently inflamed on horses that suffer burdock bristle keratopathy. The vessel pattern suggests probable location of the embedded bristles.

Consequently, certain standing procedures that stimulate globe retraction require the use of a retrobulbar block.

Retrobulbar blocks, which are described in detail in Chapter 1, produce complete immobility of the globe by inducing paralysis of the retractor bulbi muscles. They also effect anesthesia of the optic nerve and ophthalmic branch of the trigeminal nerve so vision and tactile sensation are reduced. Horses that are restrained in stocks, sedated heavily, and subjected to both a retrobulbar block and various subcutaneous blocks that produce lid immobility and akinesia are good candidates for several more extensive ocular surgeries, including enucleation, removal of the third eyelid, selected microsurgical manipulations of the cornea, and a few of the simpler intraocular procedures. Standing ocular surgery may be desirable to reduce the risks of general anesthesia, especially in draft horses, geriatric patients, and horses with orthopedic disease. Standing surgery may also be chosen to treat selected conditions when the surgeon has access to stocks but not to an operating table.

Procedures that are done with retrobulbar blocks are aided by the topical application of a surface anesthetic (0.2 to 0.5 mL proparacaine HCl) and a surface vasoconstrictor (0.2 mL 2.5% phenylephrine). These topical agents enhance surface anesthesia and aid in controlling hemorrhage from conjunctival blood vessels. If necessary, the agents may be reapplied at 15- to 20-minute intervals.

ENUCLEATION

The most common surgical indication for retrobulbar block is enucleation. Standing enucleation can be performed on selected patients with tractable temperaments.[7,8] It is a reasonable option for very old patients, large draft horses, tiny ponies, and other patients that are risks for general anesthesia. Safety concerns for both the surgeon and the patient dictate that standing enucleation be performed ONLY when the patient is restrained in stocks.

Enucleation surgery is covered in Chapter 3. Field tips for smooth surgery include the instillation of an IV jugular catheter to allow rapid administration of IV medication, and good clinical judgment on initial and sequential doses of sedation. The challenge of this procedure lies in giving sufficient sedation that the horse keeps its head still, but not so much that it becomes ataxic in the stocks. Head support is critical. A padded, wedge-shaped headrest can be fashioned for the contralateral side of the face so that the horse's head is supported in both the horizontal and oblique vertical plane (Fig. 2-52). This arrangement optimizes patient comfort and provides a stable operating position for the surgeon.

Achieving a good plane of regional anesthesia is usually straightforward. The periorbit is clipped and prepped, and the local and retrobulbar blocks are administered using strict sterile technique. In addition to palpebral and frontal blocks, local anesthetic is infiltrated in a subcutaneous ring around the orbit, and a small bleb is infiltrated at the needle insertion site for the retrobulbar block. The retrobulbar block is achieved by inserting a 20-gauge, 3½-inch spinal needle* (Becton Dickinson, Franklin Lakes, NJ) into the orbital fossa just posterior to the posterior border of the dorsal orbital rim (Fig. 2-53). The needle

*For ponies, use a 22-gauge, 2½-inch spinal needle.

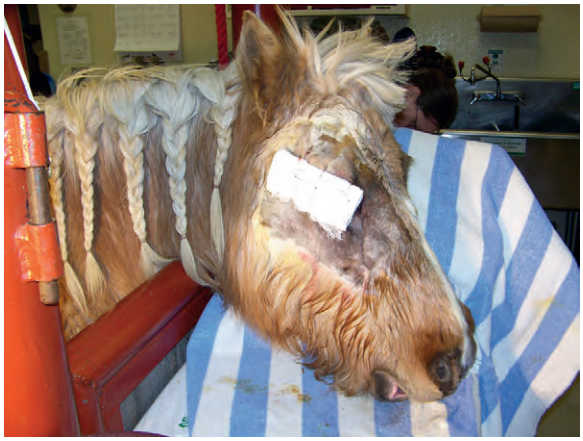


Figure 2-52. Horses undergoing standing enucleation should be restrained in stocks. Surgical positioning is helped if the patient's head is supported on a bale table and an oblique head rest is created to aid support of the contralateral side of the face.

is advanced into the retrobulbar space in a vertical direction, and a volume of 10 to 12 mL of lidocaine or mepivacaine is injected (see Chapter 1 for more details on the block technique). The periorbit is then scrubbed again, and the surgery site is draped, using the halter of the animal as an aid for securing the drapes in the sedated patient.

The enucleation surgery is as described in Chapter 3. After the surgery, the horse is placed on nonsteroidal antiinflammatory therapy for 3 to 5 days following surgery, and the skin sutures are removed in 10 to 12 days. Postoperative recovery is generally swift, and the horse may be returned to training at the time of suture removal.

NICTITANS REMOVAL

Nictitans removal is frequently required for treatment of advanced third eyelid neoplasia. The entire third eyelid can be removed in the standing patient by amputation of the gland, including a wide section of mucosa that surrounds the central T-shaped cartilage. This procedure generally does not require a retrobulbar block, but some surgeons may opt to perform one for maximum restraint and patient comfort—therefore it is recommended. Patients who are not treated with retrobulbar block must receive complete regional anesthesia of the conjunctiva of the entire nictitans. This is done by combining topical anesthesia (0.5% proparacaine sprayed onto the corneal and nictitans surface) with infiltration of the gland mucosa with 1 to 3 mL of lidocaine or mepivacaine that is injected under the mucosa with a 25-gauge needle attached to a tuberculin syringe. Amputation proceeds along the thin layers of mucosa that are closest to the globe. As the tissue sectioning proceeds, the gland is further everted so that the tissue is severed as far below the cartilage as possible. Closure of the conjunctival layers that remain in the fornix is desirable to prevent postoperative herniation of orbital fat.

Repair of nictitans lacerations and resection of small tumors of the third eyelid are procedures that are facilitated by retrobulbar block when done in a standing patient. The block will render the gland immobile, enabling precise manipulation of the target tissues. These surgeries require suturing of the gland mucosa. Absorbable suture material of very fine diameter (5-0

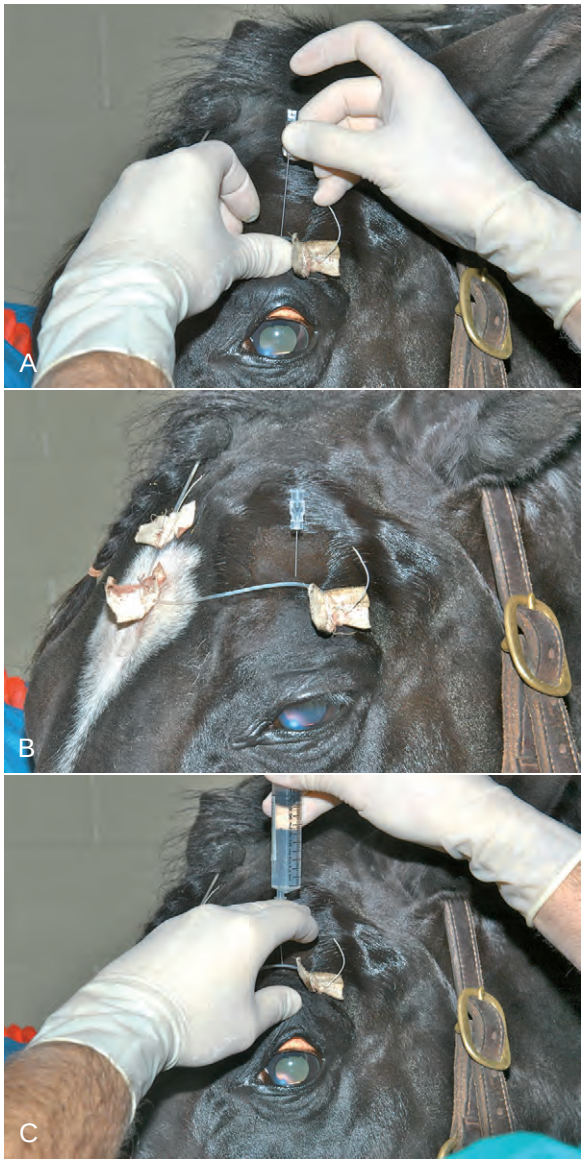


Figure 2-53. Retrobulbar block should be performed for any horse undergoing enucleation. It also provides useful local anesthesia and globe immobility for a number of advanced standing procedures listed in Box 2-11. **A,** A 3½-inch, 20-gauge spinal needle is placed behind the orbital rim in the dorsal orbital fossa. **B,** The needle is advanced perpendicularly into the orbit. **C,** Then 10 to 12 mL of lidocaine HCl or mepivacaine HCl is injected behind the globe into the orbit.

to 7-0 Vicryl or Dexon) is used to repair the lid mucosa, and great care is taken to assure that no suture tag abrades the cornea. Further description of these surgical procedures involving the third eyelid is found in Chapter 4.

CORNEAL FOREIGN BODY

Occasionally horses will present with an embedded corneal foreign body. Each case must be assessed carefully to decide if it should be referred or if the horse can be treated locally. Removal of a superficial corneal foreign body can be attempted if the object appears to be lodged in the upper third of the stroma or embedded in the epithelium. If the foreign material is lodged in the nasal quadrant of the eye, retrobulbar block may be required to avoid nictitans repulsion and allow full access to the damaged region.

A simple field technique that may help dislodge a superficial foreign body is vigorous lavage of the entry site with sterile saline or eye wash using a spray device fashioned from a 12-mL syringe attached to the hub of a broken-off 25-gauge needle. A Kimura platinum spatula, 20-gauge needle, or foreign-body spud may also be used as an aid to remove the foreign body. The surgeon must be aware that prolonged efforts at foreign-body removal may actually drive the object deeper into the cornea. If simple manipulation fails to dislodge the object, the patient must be referred for removal under general anesthesia. Further information on corneal foreign-body treatment can be found in Chapter 5.

Horses may present with corneal lacerations that have lifted up a flap of epithelium attached to stroma. Deep flaps that penetrate to a depth greater than 50% of the stromal thickness are best treated at referral facilities. Some superficial corneal flaps may be treatable in the field by amputation followed by intense topical treatment of the remaining ulcer bed. A retrobulbar block may be needed to access any part of the cornea that is close to the nictitans and may also be desirable to immobilize the globe for safe and accurate flap amputation. Deep lacerations that require suturing should be performed while the horse is under general anesthesia, using appropriate microsurgical techniques. Please see Chapter 5 for more information.

AQUEOUS PARACENTESIS

Aqueous paracentesis is an advanced procedure that may be indicated for obtaining samples for culture and cytology, protein measurement, antibody titers, and polymerase chain reaction (PCR) in cases of intraocular infection or inflammation. It can also be used to instill doses of total plasminogen activator (TPA) into the anterior chamber to treat horses that present with excessive fibrin clots in the anterior segment. If performed in the standing horse, the technique requires sedation, topical anesthesia, and in most cases a retrobulbar block. The procedure and its risks are detailed in Chapter 1.

REFERRAL

Practitioners who perform comprehensive examinations on all their patients, respond to ocular emergencies in a timely fashion, and master the basics of diagnostic testing, field medical therapy, and basic standing surgical procedures are able to handle the majority of ophthalmic conditions that present in their practice population. However, very serious or chronic ocular conditions will occur in any practice, and these should be referred to equine ophthalmology specialists if the client can afford referral and there is a specialist facility within a reasonable distance.

In general, success rates for referral cases are highest if the horse is referred early in the clinical course of the problem. Referral of horses that are presented with very severe facial trauma may result in superior cosmetic results following repair of the orbit and adnexa under general anesthesia. Specialists can often perform plastic surgery on eyelids that are deformed

as a result of previous trauma and may be able to restore normal function and comfort. Neoplasms of the periocular region receive optimum treatment at referral institutions where advanced adjunctive therapies like radiation therapy, photodynamic therapy, or temperature-regulated cryotherapy can be incorporated with skilled surgical excision.

Deep, melting, or chronic corneal infections and corneas with lesions suggesting severe immune-mediated inflammation will benefit greatly from specialist care, especially if the referral is early in the course of the problem. Procedures involving suturing or remodeling of the cornea (deep keratectomy, conjunctival grafts, excision and adjunctive therapy of corneal neoplasias, corneal rupture, or laceration repair) are referred to veterinary ophthalmic specialists.

Any type of intraocular surgery should be referred, including cataract surgery and iris resection. Most universities and specialty centers offer cataract surgery for foals, and some also perform cataract surgery on selected adult cases. Some glaucoma cases can be helped with procedures such as laser cyclophotocoagulation of the ciliary body.

Many uveitis cases benefit from referral to a boarded ophthalmic specialist. The specialist can perform diagnostic tests to fully assess the extent of the disease syndrome and may suggest novel long-term management strategies.

Practitioners may choose to refer horses requiring enucleation to specialists if they do not perform this service in-house. Referral institutions may be able to offer advanced options for cosmesis (including scleral shells and intraorbital implants) and provide optimum expertise for removal of orbital tumors.

OPHTHALMOLOGY AND THE EQUINE INDUSTRY

PREPURCHASE EXAMINATIONS

People who are deciding whether or not to buy a horse frequently request equine veterinarians to perform a prepurchase examination. Prepurchase examinations involve a thorough inspection of all observable body systems using basic equipment including an ophthalmoscope, stethoscope, hoof testers, weight tape, and bright light source. They include observation of the horse being ridden or lunged, tests to assess the neurologic status of the horse, and orthopedic flexion tests to assess gait following joint manipulation. Buyers may request additional procedures such as diagnostic imaging of the musculoskeletal, respiratory, or reproductive systems, laboratory blood analysis, or drug testing.

Guidelines for the conduct of prepurchase examinations are available online through the American Association of Equine Practitioners at http://www.aaep.org/purchase_exams.htm. The AAEP guidelines state that veterinarians should *"list all abnormal or undesirable findings discovered during the examination and give his or her qualified opinions as to the functional effect of these findings"*.[9] The standards state that the veterinarian should *"make no determination and express no opinions as to the suitability of the animal for the purpose intended"*.[9] Consequently, veterinarians do not "pass" or "fail" horses when they do prepurchase examinations. However, every examination involves discovery and disclosure of medical findings that go into the report the buyer evaluates when making the purchase decision.

THE OPHTHALMIC PORTION OF THE PREPURCHASE EXAMINATION

The ophthalmologic examination is a critical part of the prepurchase examination. Between 5% and 10% of horses have been reported to have important ophthalmic lesions that may affect vision or function.[10] An additional sizable percentage of horses have observable ophthalmic variants that are clinically insignificant. It is the responsibility of the examiner to do a thorough ophthalmic examination to discover any abnormalities and variants and render a written judgment as to the significance of the findings (Box 2-12).

The process of doing an ophthalmologic examination is basically identical to the thorough field ocular examination described in this text. Ideally an ocular history should be taken, but this may not always be possible if the seller is not present or is unfamiliar with the horse. During the moving/riding part of the examination, the horse is watched for its reaction to objects in the environment and observed for its ability to navigate obstacles such as a jumping course. Sometimes the temperament of the horse, inclement weather, or the conditions of the examination site may impair the examination. The prepurchase report should fully document any condition or situation where examination conditions were less than ideal.

No official consensus exists regarding the application of a short-term mydriatic (e.g., 1% tropicamide) to dilate the pupils during a prepurchase examination. However, mydriasis is required for a complete examination of the lens and ocular posterior segment. Response to a mydriatic also tests the range of iris mobility and checks for the presence of synechia. Pupil dilation is thus recommended for every prepurchase examination. Ocular reflex testing and inspection of the globes in an undilated state should precede the dilated exam. From a practical standpoint, the riding and moving part of the prepurchase examination should also be completed prior to the instillation of tropicamide. The mydriatic solution should be applied to both corneas after the riding exam is finished and before the standing portion of the physical examination. Mydriasis will be complete in about 15 to 20 minutes. The dilated ophthalmic examination is then performed in a dark area after the standing physical examination is completed. The prepurchase report should state that the pupils were dilated and list the findings of the dilated exam.

THE PREPURCHASE EXAMINATION REPORT

Any abnormalities in ocular reflexes or cranial nerve function are listed in the prepurchase report. Findings on the globe or adnexa are described in the report by citing the affected side and describing the lesion or variant with respect to color, shape, size, optical consistency, and location of the lesion in respect to other structures. Lesions on the adnexa or surface of the globe can be measured using the ruler on a Schirmer tear test strip or a scalpel handle. Lesions that affect the clarity of a normally transparent structure are described using appropriate adjectives: *focal, punctate, dense, diffuse, filamentous, lacelike, tangled, blotchy, linear, crystalline, fusiform, stellate,* and so forth. The location of lesions on the cornea, lens, or optic disc can be described by citing the "hour region" of the abnormality, relating the parent structure to the face of a clock. Cataractous changes can be anatomically described as capsular, cortical,

perinuclear, nuclear, or equatorial and localized with respect to the polar axis of the lens.[11] Lesions that occur in the peripapillary region can be localized by stating the percentage of a disc diameter that they occur away from the disc margin.

Regardless of the findings of any particular examination, buyers must understand that it is impossible for veterinarians to pass judgment on the visual acuity of any animal. Buyers expect the examiner to render an opinion in the report as to whether any reported finding(s) are likely to affect vision and likely to progress or recur. Usually it is not possible to give an opinion with certainty. The greatest dilemmas occur when a lesion is found that could either progress or remain static. It may be impossible to determine if these lesions affect vision to a significant degree at the time of the examination. Such is the case with many pigmentary lesions in the peripapillary region, some corneal opacities, focal cataracts, and a number of other findings (see Box 2-12).

Problems arise in prepurchase examinations when findings are missed because of an incomplete examination or inexperience on the part of the examiner. It is also problematic when a clinically insignificant variant is interpreted as a major lesion, or a major lesion is interpreted as a normal variant. Practitioners preparing prepurchase reports will be aided by consulting, and in some instances citing, information from current ophthalmic reference tests and atlases. Most practitioners opt to err on the side of caution when preparing their report of ophthalmic findings. When equivocal lesions are discovered, it is advisable to give buyers the option of obtaining a second opinion from a board-certified veterinary ophthalmologist who may be able to provide additional prognostic expertise or advanced testing. If the buyer declines this option, the report should document that referral was offered and discussed.

ISSUES SPECIFIC TO COMPETITIVE HORSES AND HORSES USED FOR COMMERCIAL PRODUCTION

Many horses are companion animals belonging to single owners or families. These animals do not participate in competitive sporting events, and if they are sold, the sale occurs under

Box 2-12 | Significance of Prepurchase Ocular Examination Findings

Unequivocally Significant Prepurchase Examination Findings

- Sarcoids or other adnexal tumors
- Dysplasia of eyelid tissue or conjunctiva
- Ectropion or entropion
- Lid motility disorder
- Trichiasis
- Chalazion
- Exophthalmos, microphthalmos, enophthalmos, or buphthalmos
- Pronounced or unilateral strabismus
- Impaired pupillary light reflex
- Large corneal axial scars
- Multiple punctate corneal opacities
- Mineralized corneal deposits
- Corneal edema
- Multiple corneal stria
- Corneal vascularization
- Flare, hyphema, or hypopyon
- Miosis
- Eccentric pupil shape
- Synechia
- Mature cataracts
- Extensive cortical cataracts
- Lens luxation or subluxation
- Elevated intraocular pressure
- Multiple opacities in the vitreous
- Vitritis
- Extensive peripapillary chorioretinitis with vessel attenuation
- Retinal detachment
- Optic nerve atrophy
- Optic neuritis
- Phthisis bulbi

Prepurchase Findings That Are Uncertain in Terms of Prognostic Significance

- Signs of past sinus trauma—dents or raised areas
- Eyelid coloring that lacks pigment
- Solar blepharitis
- Small focal corneal scars
- Single corneal stria
- Pigment deposit on the cornea or lens, with no other ocular abnormalities
- Lipid deposits in the cornea
- Large iridal cysts
- Iridal hypoplasia
- Large granula iridica cysts
- Small focal cataracts
- Vitreal syneresis
- Vitreal membranes
- Focal chorioretinopathy without other ophthalmic abnormalities
- Diffuse (butterfly-wing) peripapillary chorioretinitis without other ophthalmic abnormalities
- Proliferative optic neuropathy
- Senile retinopathy

Prepurchase Findings That May Be Variants or Minor Blemishes

- Small, healed traumatic notches in the tarsal margin
- Persistent pupillary membranes that bridge iris stroma
- Small iris colobomas or nevi
- Heterochromia iridis
- Small granula iridica cysts
- Small vacuolations in the lens
- Mittendorf's dot
- Faint retrolenticular fibroplasia
- Prominent suture lines in the lens
- Small focal inclusions in the vitreous
- Persistent hyaloid vasculature
- Variations in color of the tapetum
- Partial albinism
- Circumpapillary marginal pigment proliferation
- A few scattered chorioretinal scars
- Ectopic myelination of the disc
- Small fundic colobomas

private circumstances. Practitioners are free to examine, test, and treat these horses for the various conditions described in this text, using clinical judgment that is tempered only by the budget of the owner and the ability of the caretakers to deliver the prescribed treatment.

Other horses, however, are professional athletes. They compete on local, national, or international levels in a variety of disciplines, and most of these competitions have some form of drug testing to ascertain the presence of forbidden medications in the body fluids of competitors. Practitioners who treat these horses must have a full understanding of the medication rules that prevail at the given competition. Medications that are prescribed for chronic conditions or recent injuries may need to be adjusted or withdrawn at a certain interval before the start of a competition. Horses that sustain injuries just prior to or during a competition must be assessed and treated under prevailing medication rules if they are to continue to compete. Reports of examination findings and drug administration must be completed according to the competition standards.

The particular sporting discipline the horse participates in may carry certain risks for ocular injury. Certain sports have management issues that influence delivery of care for ophthalmic problems. Racetrack rules, for example, prohibit possession of syringes and needles by backstretch personnel, making treatment of some ophthalmic conditions difficult.

Finally, some horses are involved in the breeding industry or may be offered for sale at public auction. These groups have their own issues that influence diagnosis, treatment, and disclosure of ophthalmic problems. Medication issues, risks associated with the major sectors of performance, and issues affecting broodmares and horses destined for public auctions are discussed in the following sections.

MEDICATION RULES AT FEI EVENTS

Horses competing at the Olympic Games or at other international events in the disciplines of jumping, eventing, dressage, combined driving, endurance, reining, vaulting, and paraequestrian events compete under rules established by the Fédération Equestre Internationale (FEI, http://www.fei.org). Competitions that are hosted by the FEI follow a strict medication policy (Fig. 2-54). FEI veterinary regulations list many substances, such as local anesthetics, tranquilizers, and opioids, that are forbidden at any level in the tissues or body fluids. They also list a set of "threshold substances" that are tolerated only at low trace amounts in tissues or body fluids. Recently the FEI published a "List of Detection Times" that provides some guidance for veterinarians on minimum withdrawal times for commonly used medications, including antiinflammatory drugs, tranquilizers, and local anesthetics. See www.fei.org for this current "List of Detection Times."

FEI medication rules do not discriminate between routes of administration for forbidden substances, so the use of topical or regional ocular anesthetics is not allowed during or just prior to competition, without express permission from the Veterinary Commission.

Ocular emergencies may arise during a competition. In these instances, the treating veterinarian should administer the therapy that is needed to meet the emergency needs of the horse. Several forms must be completed and submitted to the competition Veterinary Commission and Ground Jury for review. The team of officials then convenes to determine if the horse is fit to continue to compete based on its clinical condition and the drugs required for treatment. All medications utilized to treat the ophthalmic emergency or any chronic condition are reviewed on a case-by-case basis.

Figure 2-54. The Olympic Games and several other high-level international competitions are governed by rules established by the FEI (Fédération Equestre Internationale). Practitioners treating ophthalmic issues in horses at these competitions must be familiar with the strict medication rules that prevail. (Courtesy Dr. Midge Leitch.)

Laboratories that test blood and urine samples submitted from competitions use very sensitive equipment that can detect minute trace levels of many substances. Competitors have been disqualified and have lost Olympic medals because drug testing revealed trace amounts of banned substances in the blood or urine of the horse. Any veterinarian treating an eye problem that occurs either near the start date or during an FEI competition should consult the current FEI veterinary regulations by reviewing the online rules for veterinary care (http://www.fei.org/Rules/Veterinary/Pages/Default.aspx) and the online guidelines for drug testing (http://www.fei.org/Athletes_AND_Horses/Medication_Control_AND_Antidoping/Horses/Pages/Information.aspx). They are also well advised to consult with an FEI official veterinarian on therapeutic decisions.

FEI rules allow unilateral blind horses to compete in any of their disciplines (jumping, dressage, eventing, driving, reining, vaulting, endurance, and paraequestrian events).

MEDICATION RULES AT USEF EVENTS

Horses competing in the United States in disciplines such as hunters, jumpers, eventers, and dressage horses or in certain breed competitions usually compete under rules established by the United States Equestrian Federation (USEF, http://www.usef.org). USEF medication rules allow the use of certain systemic nonsteroidal and steroidal drugs within a prescribed period before a given class. Medication reports must be submitted to the show stewards or technical delegate detailing the reason for treatment and the names, treatment route, and frequency of any drugs that are prescribed. The use of some medications, such as local anesthetics, requires withdrawal from competition if the product has to be administered within 24 hours of competition. Most topical medications are permitted in current USEF rules, but any veterinarian who has to make treatment decisions on a horse during a show should consult the prevailing medication rules by visiting the website section on medication (http://www.usef.org/ContentPage2.aspx?id=dm) or calling the USEF medication hotline at 1-800-633-2472.

Under USEF rules, horses missing one eye or unilaterally blind are permitted to compete in most English show disciplines and in eventing and dressage, but they are only allowed to compete in the hunter division at the judges' discretion.

OPHTHALMIC ISSUES FOR ENGLISH SHOW HORSES

Cosmetic appearance is paramount for horses that are shown in hand (halter and breed classes) and horses that are judged on conformation and appearance in addition to performance (hunters). Most show horses have the vibrissae (long hairs near the eyelids) clipped close to the face. Trainers of some breeds (Arabians and miniature horses) clip the skin hair of the eyelids and periorbit with a surgical clipping blade (#40) prior to shows (Fig. 2-55). They may apply a thin film of Vaseline or other shiny lubricant to the periocular skin to enhance the appearance of the eyes in classes. These practices can occasionally traumatize or irritate the periocular skin or cornea.

Show horses are frequently transported long distances and housed in show grounds that may be dusty, insect infested, windy, or humid. As a result, they have a high incidence of general irritation of the conjunctiva and cornea and often suffer chemosis, blepharitis, epiphora, and mild corneal edema. Ocular irritation and pruritus may predispose to rubbing on buckets and stall walls, leading to secondary problems such as eyelid lacerations and corneal ulcers. Blinkers, hoods, or quality fly masks may help prevent the more serious secondary problems. Show horses can also occasionally sustain blunt trauma to the skull and periorbit from trailer trauma or stabling accidents.

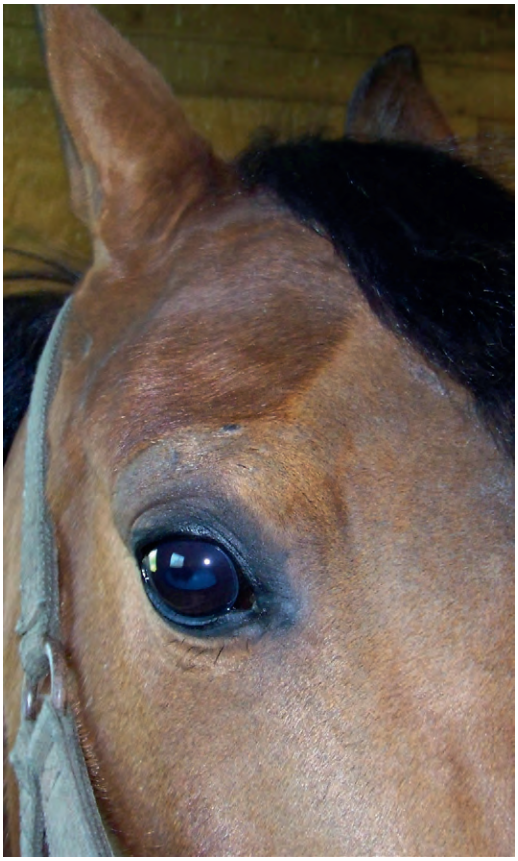


Figure 2-55. Trainers of some show breeds clip the hair of the eyelids and periorbit prior to shows to enhance the prominence of the globes. This practice carries a small risk of injury.

Many show horses compete on systemic antiinflammatory treatment (nonsteroidal drugs like phenylbutazone, flunixin meglumine, firocoxib, ketoprofen; or steroidal drugs such as dexamethasone). Often multiple agents are present systemically at substantial therapeutic levels. These may mask the signs of serious ocular trouble, such as corneal ulcers. Grooms must be alert to subtle signs of ocular swelling and pain, and seek veterinary evaluation promptly. Horse-show veterinarians should treat ocular problems as emergencies and promptly do a full examination of any horse with any ocular complaint.

Compliance with treatment plans may be difficult in a horse-show environment, and trainers must be cautioned against the use of topical corticosteroids on an irritated eye. The drug may produce short-term improvement but could have disastrous long-term effects if a secondary infection sets in. Practitioners should be aware that local anesthetics and antihistamines are banned substances in most competitive venues. If a problem occurs that necessitates use of a local anesthetic or

antihistamine, the horse may have to be scratched from competition.

Again, unilaterally blind horses are permitted to compete as jumpers but may, at judge discretion, be excluded from competition as hunters in rated shows judged under USEF rules.

OPHTHALMIC ISSUES FOR DRESSAGE AND EVENTING HORSES

Like show horses, horses that compete in dressage and eventing often travel long distances and are stabled in temporary stabling that may be dusty, windy, or humid. As such they are at increased risk for ocular irritation and blunt periocular trauma. Corneal ulcers are diagnosed occasionally.

Treatment of the eye problems that arise may be influenced by the rules governing the competition (see sections on USEF and FEI rules). Any event that is an officially sanctioned competition will require that treatment for any acute injury or inflammation be reported. Caution must be used in prescribing systemic nonsteroidal antiinflammatory medication for horses that are competing: the veterinarian must be thoroughly familiar with the prevailing rules if the horse is to be allowed to continue to compete.

Some grooms are not capable of the frequent topical therapy that may be required for some ocular problems. If frequent ocular medication is required for an eye disease, that horse should be withheld from competition until the eye has healed.

Unilaterally blind horses are permitted to compete in both dressage and eventing. A few totally blind horses have competed in dressage events as these events do not involve high speed, uneven ground, or obstacle negotiation.

OPHTHALMIC ISSUES FOR WESTERN PERFORMANCE AND RODEO HORSES

Western performance horses are at increased risk of travel-related trauma because they are often hauled long distances in trailers that may have open slats on the sides. Bucking horses, which perform in rodeos, are housed in group pens and are not closely handled or managed. They may be at increased risk for herd-related trauma. Occasionally, roping horses sustain corneal trauma from ropes (Fig. 2-56).

Corneal ulcers are the most common ocular problem seen in Western performance horses. Most respond to topical therapy, but they may develop into complex problems like fungal keratitis or stromal ulcers. Treating a corneal ulcer in a horse used as a rodeo bronc is challenging; these animals are unaccustomed to handling around the head.

Western events are governed by a variety of different sport organizations. The American Quarter Horse Association (http://www.aqha.com/) has medication guidelines that allow the use of most topical medication but restrict the use of nonsteroidal antiinflammatory medication to a single agent during competition. A medication report must be filed for most drugs administered. Use of some substances may require that the horse be kept out of competition for 24 hours. Lidocaine or mepivacaine are allowed as local anesthetics for repair of skin lacerations, but the administration of the substance must be directly observed by the show management and/or the official show veterinarian, and a report must be filed. Additional information about the medication rules that prevail at AQHA shows can be found on the Internet: http://www.aqha.com/showing/guideto-showing/theraputicmed.html.

Figure 2-56. Western performance horses who compete in roping events occasionally suffer corneal or globe injury from rope trauma. (Courtesy Beth McQuade and Evan Lesser, Manhattan, KS.)

Western events that are run by the National Reining Horse Association (http://www.nrha.com/), the National Reined Cow Horse Association (http://www.nrcha.com/), and the National Cutting Horse Association (http://www.nchacutting.com/) do not currently have medication rules that govern veterinary care for competing horses. So under current rules, ocular problems that arise during these events may be treated at the veterinarian's discretion. However, medication rules for these organizations are under review and may soon be changed to more restrictive policies. Practitioners who treat horses in these competitions should review the most up-to-date rules that are in effect and base their therapy on the prevailing medication guidelines that the host organization has adopted.

Reining has recently been added to the list of international events governed by the FEI. Horses competing in FEI reining events must comply with the strict medication rules of this organization.

Unilaterally blind or enucleated horses are allowed to compete in Western performance events. A few totally blind horses have competed in reining competitions.

OPHTHALMIC ISSUES FOR ENDURANCE HORSES

Horses competing in long-distance rides are trailered to the ride site, and on arrival are often confined in small pens. These horses are at increased risk of debris-associated conjunctivitis and corneal ulcers, as well as blunt trauma and eyelid lacerations. The ride site may be remote and wooded, so allergic and insect-related irritation is common.

In contrast to other sports where the actual event may only take a matter of minutes, endurance rides involve 6 to 24 hours of competition (Fig. 2-57). Hazards like high winds, branches, or heavy brush encountered on the trail pose a slight risk of injury during the competition. Horses that have had pupillary dilation prescribed for an ocular problem should not be ridden in endurance competition because of the discomfort that results

Figure 2-57. Endurance horses compete over varied terrain and may encounter hazards like high wind, branches, or heavy brush that pose a small risk of ocular injury. (Courtesy Dr. Nancy Loving.)

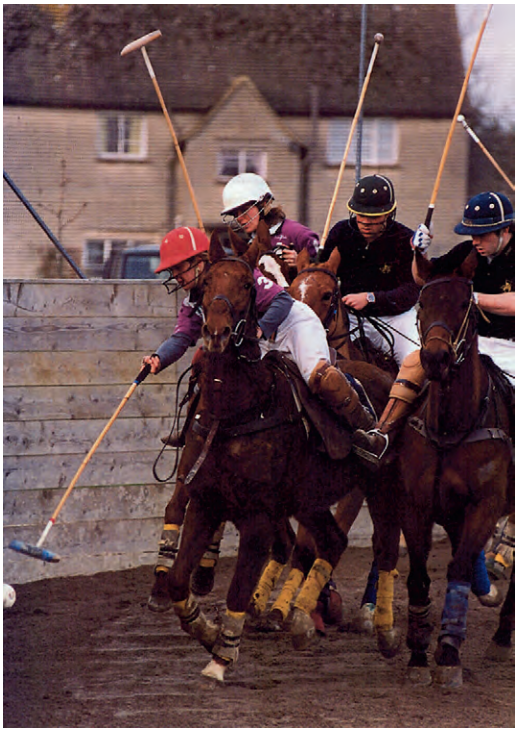


Figure 2-58. Polo ponies are at significant risk of blunt trauma to the globe and periocular region from swinging mallets, airborne balls, and collisions with other ponies. (From Hinchcliff KW, Kaneps AJ, Geor RJ: Equine sports medicine and surgery, St Louis, 2004, Elsevier LTD.)

from bright daylight. Also, atropine usage has a risk of diminished intestinal motility that may be exacerbated by dehydration or electrolyte disturbances induced by the length of the ride.

Endurance is essentially a drug-free sport. The national organization that administers rides, the American Endurance Ride Conference (http://www.aerc.org/) has an extensive list of substances prohibited during rides. The conference rules specifically state that local anesthetics and topical agents, including ophthalmic medications, are forbidden. Some officials may provide special dispensation for horses requiring topical antibiotics or topical hyperosmotics, but topical steroids and mydriatics are prohibited. Specific information relating to endurance medication and drug testing can be found on the Internet at http://www.aerc.org/AERCdrugtestingpolicy.asp. One other useful website is the Eastern Competitive Trail Riding Association site, http://www.ectra.org/. Endurance riding is now recognized as an international competition, and some prominent rides are administered by the FEI. Information on FEI drug policy is stated in the earlier section.

Unilaterally blind horses and horses that have been enucleated on one side are permitted to compete in endurance events. Many perform very well.

OPHTHALMIC ISSUES FOR POLO PONIES

Polo ponies are hauled in large trailers that accommodate the sizable string of horses required for each match. As polo is a sport that is played internationally, high-level ponies may travel by air to championship events. As such they are at increased risk for travel-related trauma.

Polo ponies are at increased risk for blunt trauma to the globe and periocular region from swinging mallets, airborne balls, and collisions with other ponies. Such trauma may be severe insofar as the mallets and balls are propelled at high speed (Fig. 2-58).

There are currently no medication rules governing the sport of polo, so horses requiring therapy for ocular problems may be treated at the veterinarian's discretion. However, competitive rules are frequently revised, so practitioners are encouraged to consult the most up-to-date guidelines before making therapeutic decisions.

The rules of the U.S. Polo Association (http://www.us-polo.org) state: "A mount blind in one eye may not be played." Collegiate rules allow half-blind or one-eyed polo ponies to participate in matches, so professional ponies who become blind in one eye may end up in collegiate strings.

MEDICATION RULES AT THE RACETRACK

Currently, each state that allows pari-mutuel wagering for flat racing or harness racing has its own laws governing medication of racehorses. Some states allow administration of specific levels of nonsteroidal medications or other therapeutic substances such as diuretics at a defined interval before the race. All states have rules forbidding the administration of tranquilizers and/or local anesthetics close to a race. All states routinely test the blood and/or urine of the front-placing horses for evidence of illegal substances or excessive levels of permitted substances immediately after the race, and most states test other horses in the race in a random fashion. Rules about many topical medications, including ophthalmic preparations, may be unclear and subject to interpretation by the trainer, owner, and practitioner.

OPHTHALMIC ISSUES FOR RACEHORSES

Racehorses are housed in stalls when they are in training and are at increased risk for eyelid lacerations. Most lacerations occur when the horse rubs its head on a water-bucket handle or other item that has a pronglike projection large enough to entrap the tarsal margin. All eyelid lacerations should be repaired meticulously with particular care to the apposition of the tarsal margin. However, the veterinarian must realize that the local anesthetics required to denervate the lid tissue for repair are banned in horses that are entered in races. Post-race drug testing is routine in all states, and detection of any local anesthetic would disqualify the horse and result in heavy penalties for the trainer. Horses that undergo local anesthetic infiltration for treatment of periocular problems must not be raced until the drug has cleared the system.

Horses that have suffered peracute lacerations just prior to a race have been managed by temporary "basting" of unblocked injured lid sections. The procedure is done on horses restrained with a nose twitch, using suture inserted through the lumen of a needle that is passed through each side of the torn lid. The suture is then tied to bridge the gap just for the duration of the race. A proper post-race repair is then achieved after all drug testing samples are obtained.[12] Eyelid injury incidents can be reduced if trainers and grooms tape up all bucket handles and feed tubs with J-shaped gaps and police the stalls for projecting nails or other objects.

Thoroughbred horses are at increased risk for blunt trauma to the orbit and periorbit from starting-gate accidents. The starting gate is an immovable metal cage with vertical posts and a gate that is closed in front of the head prior to the start of the race or gate-training session (Fig. 2-59). Horses that rear or flip over in the gate can sustain severe skull fractures or intracranial damage from contact with the metal pipes of the gate.

Both Thoroughbred and Standardbred horses are at high risk for corneal injuries caused by particulate matter from the racetrack surface. Injuries can also occur from contact with a whip or equipment that hits the eye. Injuries can occur during daily training but are particularly common during races where a number of horses are traveling at high speed in close proximity (Fig. 2-60). Those horses not in the lead are subject to debris kicked up by horses racing in front of them. Blinkers may provide a partial physical barrier, but considerable grit (sand, clay, small stones, or synthetic material) still pelts the facial area as well as the bodies of horses, jockeys, and drivers. Practitioners who work at a variety of tracks have noted patterns of corneal injury that seem related to the surface at the site, with some racetrack surfaces associated with higher rates of corneal ulcers and particular patterns of infection.[13]

Most grooms routinely "blow out" the corneal surface of each racehorse immediately upon return to the barn after a race. "Blowing out the cornea" involves pursing the eyelids of the horse between the fingers to hold them open, leaning close to the lateral canthus and blowing hard over the corneal surface several times. This practice, which all racehorses are trained to tolerate, dislodges much of the visible debris adherent to the cornea and conjunctiva. The surface of the cornea is then medicated with a generous application of a broad-spectrum topical ointment (triple antibiotic, chloramphenicol, or gentamycin). This practice may prevent many corneal injuries and infections.

Even with the noted precautions, post-race corneal injuries are common.[14] Racetrack practitioners educate grooms and trainers to recognize horses with post-race ocular discomfort and treat them as true emergencies requiring immediate veterinary care. Conscientious practitioners will institute intense topical therapy for corneal ulcers immediately and may administer many of the treatments themselves as they revisit the same

Figure 2-59. Thoroughbred racehorses are at significant risk for trauma to the orbit and globe from starting-gate accidents. The starting gate is essentially an immovable steel cage. Fractious individuals may rear or flip over inside an individual chute.

Figure 2-60. Thoroughbred and Standardbred racehorses are at high risk of corneal injury during races. Horses not in the lead are subject to trauma from track debris kicked up by horses racing in front of them. (Courtesy Dr. Eleanor Green.)

barns in the course of a day. As a result, most corneal injuries heal quickly as long as the personnel who care for the horse alert the veterinarian to any problem in a timely fashion.

However, some corneal traumas are deep and extensive, and some are not noted promptly. If not treated, these may go on to become complex problems, developing into melting ulcers, fungal keratitis, or stromal abscesses. Treatment of complex ocular problems on the racetrack may be dictated by economic as well as medical concerns. Racehorses have short athletic careers, and many trainers and owners are reluctant to take them out of training for any significant length of time. Use of SPL systems is difficult, since many racetracks prohibit the possession of syringes and needles by nonveterinary personnel, and night oversight is usually limited to security personnel who are unable to administer eye therapy. As a result, many horses that develop complex eye problems are either taken out of training and sent to a layup facility or are subject to enucleation of the affected eye. Return to training following enucleation can be as soon as a few weeks without a significant difference in performance level.

Enucleated horses are permitted to race at all levels in most states; however, the unilateral blind condition should be declared to the betting public.

OPHTHALMIC ISSUES FOR BROODMARES

Broodmares are usually shipped to a stallion or an artificial insemination facility for breeding and thus are at slightly increased risk for ocular trauma related to transport. Once confirmed in-foal, broodmares in large breeding operations are often turned out in a band for the duration of their 11-month period of gestation and are at additional risk for ocular trauma from herd interaction. Broodmares may not be closely observed, so ocular problems may not be noticed promptly. Compliance in treating serious problems may be a challenge if the mare is not routinely stabled.

Mares that live in temperate climates near dairy farms or deer herds may be at increased risk for leptospiral-associated uveitis if they ingest spirochetes while grazing or drinking contaminated groundwater from creeks or ponds. Increased incidence of blindness related to uveitis, added to the population of mares retired because of blindness for other reasons, means that it is common to encounter blind broodmares. Blind mares will not respond to photoinduction of estrus and may ovulate later in the year than mares that are responsive to light stimulation of their heat cycles, but most are experiencing normal heat cycles and are ready to breed by April of any given year. They usually show normal maternal behavior but become very anxious if they lose track of their foals. Attaching a bell to the foal's halter will enable the mare to locate her offspring and help reduce her anxiety.

OPHTHALMIC ISSUES FOR HORSES SOLD AT PUBLIC AUCTION

Yearlings, weanlings, and other sales horses are managed intensively in the weeks prior to the actual sale. They are at increased risk for ocular trauma because of the stress of confinement and transport from pasture to the preparatory barn and sales pavilion. Sales horses are observed closely during the presale period, so eye problems are usually noticed quickly. The most common issues are blunt trauma, lid lacerations, and corneal ulcers. Acute eyelid lacerations have been repaired under general anesthesia within 24 hours of successful auction in the sales ring.[6]

All sales horses are housed on the sales company grounds and are available for prospective buyers to examine for a few days prior to auction. Many consignors will not allow their sales prospects to be tranquilized for examination because sedation could adversely affect the results of endoscopic evaluation of the upper respiratory tract (a common presale procedure). Thus, most on-site ocular examinations of these young, often fractious individuals are limited to inspection of undilated eyes with a bright light and direct ophthalmoscope in a stall in the sales barn where lighting cannot be adjusted easily.

Auction rules dictate that all deviations from the norm must be declared by the consignor (seller). The consignor gives a statement to the sales administration that then becomes part of the "repository record" of the horse being auctioned. This repository record, which also includes a standard set of radiographic images on the individual and any endoscopic reports or other declarations, is available to any prospective buyer and the buyer's veterinarian during the presale examination period.

All blind eyes, corneal scars, and congenital defects must be declared. Statements are usually prepared by a veterinarian familiar with the horse. The statement describes the problem but is not required to include a prognosis. Corneal scars are the most common ocular issue declared at sales (Fig. 2-61). Buyers who purchase a horse with a significant ocular defect that was NOT declared have the right to return the horse to the seller.

CONCLUSIONS

VETERINARY EXPERTISE AND CLIENT CONTINUING EDUCATION

Through a combination of diligent study and daily practice, equine veterinarians can acquire solid field expertise in equine ophthalmology. The ocular system is special in that much of the tissue that is responsible for receiving visual stimuli can be directly observed with simple equipment, and many pathologic processes are also readily observable. As such, the science of equine ophthalmology is very rewarding for the field practitioner, despite the various challenges field care presents.

A noble goal for any practitioner is to perform screening eye exams on each patient in the practice as part of a basic "wellness" program. Routine screening eye examinations provide a valuable baseline and allow the veterinarian to educate the owner about ophthalmic findings such as old orbital or lid trauma, corneal opacities, pupil irregularities, synechia, cataracts, lens displacements, vitritis, and fundic abnormalities that may compromise sight, alter cosmesis, or signal chronic or recurrent inflammation.

Stallside client education on equine ocular problems can be combined with periodic formal client education using newsletters, websites, and client seminars as a way to expand client knowledge of equine ophthalmology. Most equine eye problems can be explained by comparing them to human perception

Figure 2-61. All blind eyes, corneal scars, and congenital ocular defects must be declared to potential buyers of Thoroughbreds sold at public auction. Buyers may arrange a veterinary ophthalmic examination during the presale inspection period. (Courtesy Dr. Eleanor Green.)

and anatomy. Presentations on equine vision, eye anatomy, and eye problems are of great interest to all riders, especially those who train and compete their horses. Images of the serious consequences of unchecked ocular infection, untreated trauma, or advanced neoplasia provide powerful reinforcement of the message that early attention to these problems is critical.

Well-educated clients who understand their horses' ophthalmic status rarely delay in calling their veterinarian about a painful or abnormal eye. They are more accepting of the expense of the diagnostic workup that accompanies serious problems and exhibit superior compliance with prescribed treatment protocols. They are also more willing to refer very serious problems. The extra effort involved in screening horses for eye disease and educating horse owners about eye problems will pay off in the long run.

Acknowledgment

The author thanks and acknowledges the following individuals for their contributions to this chapter: Dr. Midge Leitch, Cochranville, PA; Dr. Sally Hyman, Middleburg, VA; Dr. Sharon Spier, Davis, CA (Eventing and Dressage, FEI issues); Dr. Steven Soule, Palm Beach, FL; Dr. Reynolds Cowles, Free Union, VA (Hunters and Jumpers); Dr. Robert Tugel, Farmington, NY; Dr. Tom Brokken, Ft. Lauderdale, FL; Dr. John Mitchell, Boca Raton, FL; Dr. Kathy Anderson, Elkton, MD (Racing); Dr. Lane Easter, Whitesboro, TX; Dr. Douglas Corey, Adams, OR (Western Performance); Dr. Nancy Loving, Boulder, CO; Dr. Heather Hoyns, Reading, VT (Endurance Horses); Dr. Claire Latimer, Lexington, KY; and Dr. Katharine Garrett, Lexington, KY (Public Auctions).

References

1. Kalf KL, Utter ME, Wotman KL: Evaluation of duration of corneal anesthesia induced with ophthalmic 0.5% proparacaine hydrochloride by use of a Cochet-Bonnet aesthesiometer in clinically normal horses, Am J Vet Res 69:1655–1658, 2008.
2. Cutler T: Ophthalmic findings in the geriatric horse, Vet Clin North Am Equine Pract 18:545–574, 2002.
3. Giuliano E: Eyes and ocular adnexa. In Cowell R, Tyler R, editors: Diagnostic cytology and hematology of the horse, St. Louis, 2002, p 43.
4. McMullen RJ, Jr, Clode AB, Gilger BC: Infrared digital imaging of the equine anterior segment, Vet Ophthalmol 12:125–131, 2009.
5. Ramirez S, Tucker RL: Ophthalmic imaging, Vet Clin North Am Equine Pract 20:441–457, 2004.
6. Latimer C: Personal Communication. 2009.
7. Hewes CA, Keoughan GC, Gutierrez-Nibeyro S: Standing enucleation in the horse: a report of 5 cases, Can Vet J 48:512–514, 2007.
8. Pollock PJ, Russell T, Hughes TK, et al: Transpalpebral eye enucleation in 40 standing horses, Vet Surg 37:306–309, 2008.
9. AAEP: American Association of Equine Practitioners 2009 Resource Guide: guidelines for reporting purchase examinations, 44, 2009.
10. Hurn SD, Turner AG: Ophthalmic examination findings of Thoroughbred racehorses in Australia, Vet Ophthalmol 9:95–100, 2006.
11. Matthews AG: Lens opacities in the horse: a clinical classification, Vet Ophthalmol 3:65–71, 2000.
12. Mitchell J: Personal communication. 2009.
13. Brokken T: Personal communication. 2009.
14. Wada S, Hobo S, Niwa H: Ulcerative keratitis in thoroughbread racehorses in Japan from 1997 to 2008, Vet Ophthalmol 13(2):99–105, 2010.

Chapter 3

Diseases and Surgery of the Globe and Orbit

Brian C. Gilger

Diseases of the equine orbit may not be as common as diseases in other parts of the equine eye, but the impact of orbital disease is very high. Not only do diseases of the equine orbit result in profound cosmetic changes such as exophthalmos or strabismus, but in almost all cases, vision loss occurs. Unfortunately, these cosmetic changes and vision loss are commonly permanent, and prognosis of orbital disease in general is poor. The globe and orbit are subject to trauma, inflammation, neoplasia, congenital disease, and extension of disease into the orbit from adjacent cranial cavities, particularly the sinuses. Recent advances in imaging techniques and their wider availability have opened the door for more elaborate medical and surgical therapy. The desire for better cosmetic outcomes after serious ocular injury and trauma has resulted in better surgical repair of orbital fractures and a greater variety of surgical prostheses. In this chapter, diseases of the orbit and globe surgery are described, with emphasis on diagnostics, medical therapy, and surgical management.

CLINICAL ANATOMY AND PHYSIOLOGY

SKULL AND FORAMINA

The horse is unusual in having a complete bony orbital rim (Fig. 3-1). The orbit and globes are positioned laterally on the head and are ideally situated for a wide and panoramic visual field exceeding 340 degrees.[1] This seems appropriate for the horse's ecologic niche as a grazer and consequently a prey animal, but perhaps it is less perfect for the activities it is commonly tasked in today's society. The visual field is binocular, permitting stereoscopy, and the wide separation of the two globes provides greater depth perception than most other

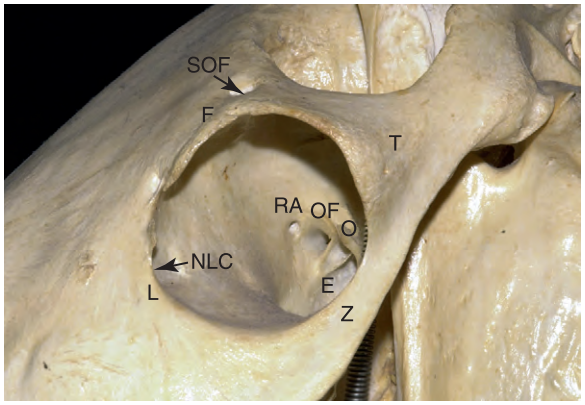


Figure 3-1. The horse has a complete bony orbital rim. The orbital bones include the frontal *(F)*, lacrimal *(L)*, zygomatic *(Z)*, and temporal *(T)*. The sphenoid and palatine bone forming the medial wall of the orbit separates the orbit from the calvarium. The nasolacrimal duct canaliculi *(NLC)* course through the lacrimal bone. The orbital foramina through the sphenoid bone includes, from anterior to posterior, the rostral alar *(RA)*, orbital fissure *(OF)*, optic *(O)*, and ethmoidal *(E)* (see Table 3-1). The supraorbital foramen *(SOF)* exits through the frontal bone.

Table 3-1 | **Structures Perforating the Orbit and Contents**

STRUCTURE	OSTEUM
Maxillary artery and nerve	Rostral alar foramen
Ethmoidal artery, vein, nerve	Ethmoidal foramen
Optic nerve (II)	Optic foramen
Oculomotor nerve (III)	Orbital foramen
Trochlear nerve (IV)	Orbital foramen
Abducens nerve (VI)	Orbital foramen
Supraorbital artery, vein, nerve	Supraorbital foramen
Major palatine artery, vein, and nerve	Caudal palatine foramen
Infraorbital vein, artery, and nerve	Maxillary foramen
Sphenopalatine artery and vein and pterygopalatine nerve	Sphenopalatine foramen

domestic species can attain. The main visual axis is approximately parallel with the long axis of the skull.[2] Equine vision is explored more thoroughly in Chapter 11.

The equine globe is among the largest of the mammalian kingdom, perhaps eclipsed in size only by the giraffe's eye. The axis of the globe in the horse is nearly perpendicular to that of the skull and angled with respect to the long axis of the orbit. The average dimensions of the adult horse globe are 43.68 mm anterior-posterior, 47.63 mm vertically, and 48.45 mm horizontally.[3] The globe of the mule is almost identical in size, measuring 43.0 mm, 47.5 mm, and 48.5 mm in the same orientation. The globe is not a sphere, but rather is compressed from anterior to posterior, with the ratios of the dimensions previously given being 1:1.09:1.10 for the horse and 1:1.10:1.12 for the mule.[3] The globe is located at the anterior border of the rather large orbit, which averages 62 × 59 × 98 mm. The orbits are separated by 172 mm across the anterior surface of the frontal bone.[3] The remainder of the orbital cavity is filled largely by fat and muscle and is divided into pockets by layers of connective tissue that coordinate ocular mobility.

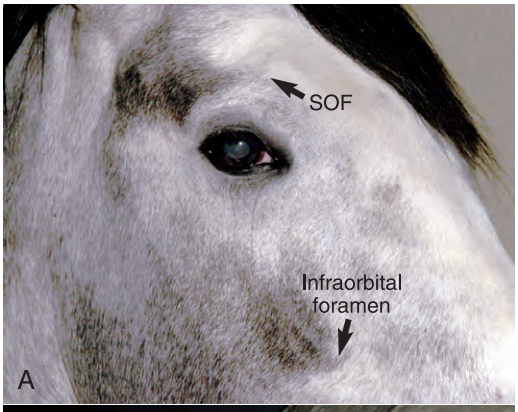
The orbital bones are the frontal, lacrimal, zygomatic, and temporal bones (clockwise for the right orbit), with the sphenoid and palatine bone forming the deeper internal wall of the orbit that separates it from the calvarium (see Fig. 3-1). The complete bony rim temporally and dorsally is composed of the frontal process of the zygomatic bone and zygomatic processes of the frontal and temporal bones. The supraorbital foramen is located in the anterior aspect of the frontal bone that forms the dorsal orbital rim. The lacrimal gland is closely adhered to the internal orbit near the dorsotemporal orbital rim. Inferiorly the zygomatic bone forms the lower rim, and nasally it is fused to the lacrimal bone, wherein embedded canals provide refuge to the nasolacrimal duct canaliculi (see Fig. 3-1). Beneath the globe, cushioning is provided by orbital fat that separates the globe from the palatine bone. Caudally the orbital floor is angled inferiorly until it is composed of soft tissues only, including the large pterygoid muscles that exert closing motion for the lower jaw. The bony floor of the orbit ends directly beneath the caudal aspect of the dorsal rim.

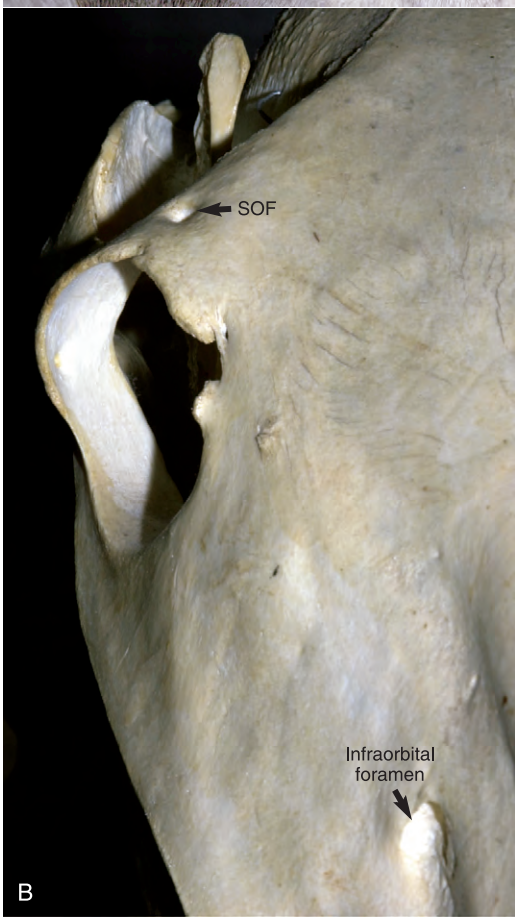
Various foramina provide conduits between the orbit and other compartments of the head, particularly through the calvarium to the brain. The efferent foramina are arranged curvilinearly along the sphenoid bone that forms the medial orbital wall. From anterior to posterior they are the rostral alar, orbital fissure, optic, and ethmoidal (Table 3-1) and are evident in Fig. 3-1. The clinical significance of the location of the foramina lies in avoiding their contents during biopsy and exploratory procedures. The foramina appear to provide relatively minimal risk for extension of orbital infection or neoplasia, but they may be severely damaged during trauma to the calvarium, with serious consequences for vision. Fracture of the basisphenoid and basioccipital bones frequently occurs in blunt trauma to the poll. Afferent foramina are located in the extreme anteromedial portion of the orbit; they are the caudal palatine (major palatine artery and nerve), the maxillary (infraorbital artery, vein, and nerve), and sphenopalatine (sphenopalatine artery and vein and pterygopalatine nerve).

The *infraorbital foramen* is the point of egress of the infraorbital nerve, artery, and vein from the orbit, which can be palpated 1 cm rostral and 3 cm dorsal to the rostral edge of the facial crest, a third of the distance to the nostrils (Fig. 3-2, *A* and *B*). It may be partially obscured by the overlying muscular belly of the levator nasolabialis.[4] The infraorbital nerve arises from the maxillary branch of the trigeminal to provide sensory innervation to the upper lip, nostril, and cheek. Its major significance is in desensitization for laceration repair of those tissues, and infrequently for nerve blockade to evaluate the contribution of trigeminal summation in clinical head shakers.[5] The infraorbital canal bisects the maxillary sinus (see Fig. 3-2, *C*).

PERIORBITUM

The orbit is completely lined with a strong, multilayered periosteum/periorbitum. This dense fibrous connective tissue has surgical importance because it provides a formidable barrier to the extension of orbital disease beyond the soft-tissue contents into the bone architecture. Even moderately extensive stages of squamous cell carcinoma may be sufficiently contained by the periosteum, allowing successful and complete surgical removal of the neoplastic expansion. The periorbitum is retained in enucleation, and its anterior portion is preferably completely reapposed in closure. In the exenteration procedure, the major-





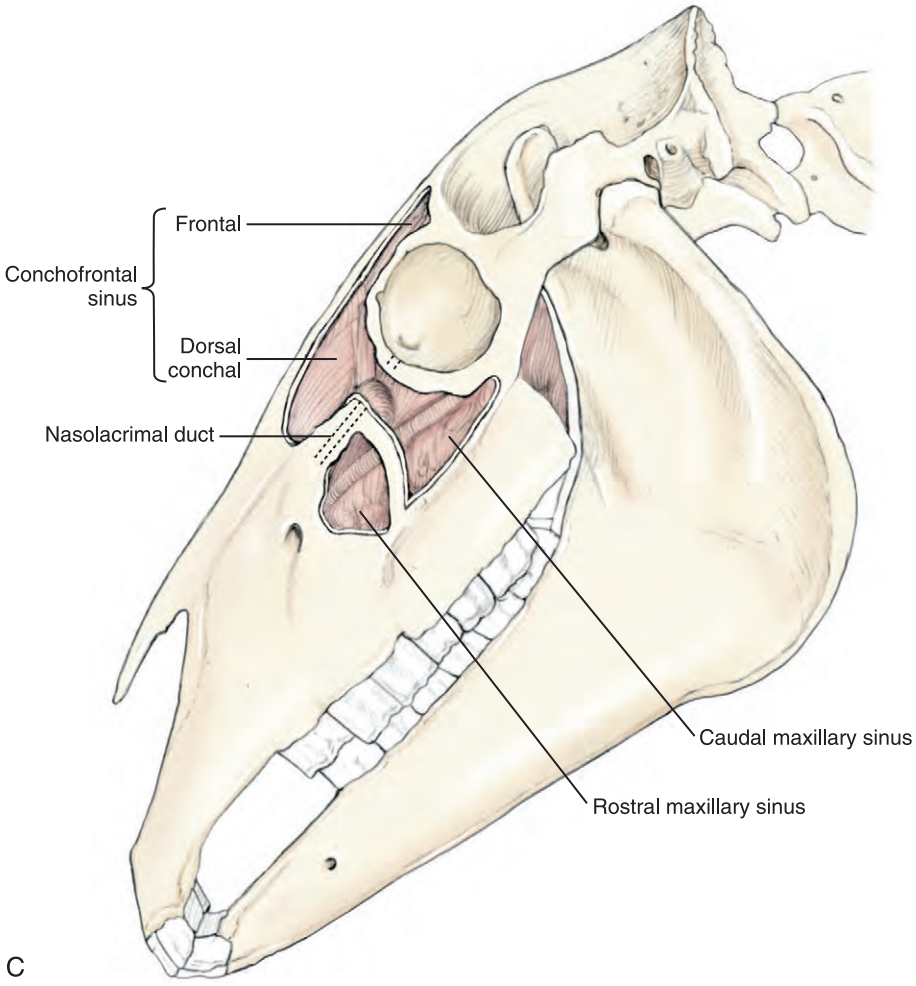


Figure 3-2. **A,** The infraorbital foramen is the point of egress of the infraorbital nerve, artery, and vein from the orbit. It can be palpated 1 cm rostral and 3 cm dorsal to the rostral edge of the facial crest, a third of the distance to the nostrils *(arrows)*. *SOF,* Supraorbital foramen. **B,** Equine skull viewed from the front, demonstrating the left orbit and infraorbital foramen *(arrow)*. **C,** The infraorbital canal bisects the maxillary sinus.

ity of the periorbitum is removed. If the periosteal surface overlying orbital bone has lost its thin glossy appearance, suggesting pathology, it should be elevated and removed; deeper lesions should be explored and treated appropriately.

GLOBE

The equine globe resides anteriorly within the orbit, supported by loosely packed retrobulbar tissues. Reflections of the periorbitum together with smooth muscle attach the globe to the orbital rim. The external wall of the globe is a trilayer, with the sclera and cornea forming the outer predominantly fibrous tunic, the highly vascular uvea forming the middle layer, and the neural layers of the retina being most internal. The thickness of the sclera is 1.05 mm where the optic nerve penetrates the posterior pole, 0.31 mm at the limbus, and 0.5 mm at the equator of the globe.[6] Consequently, during traumatic events, the sclera most frequently ruptures at the limbus, the potentially

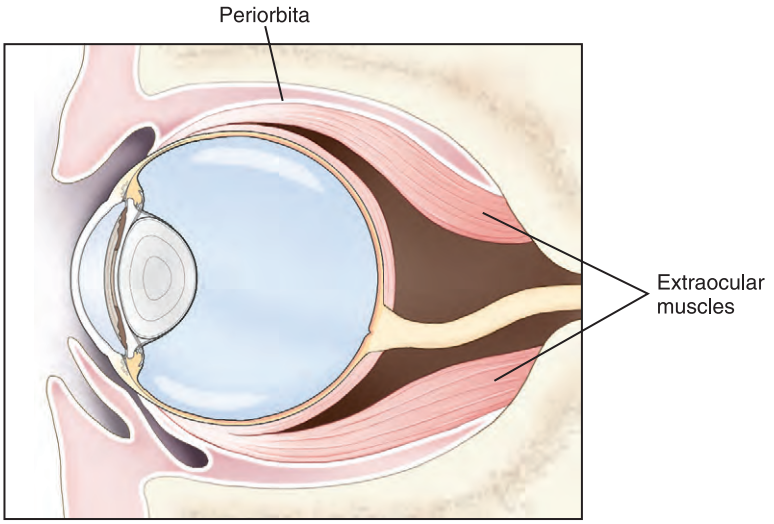


Figure 3-3. Illustration of the extraocular muscles of the horse. The multiple large bellies of the retractor bulbi muscle (not illustrated), attach extensively around the posterior half of the sclera and surround the optic nerve.

weakest area of the sclera. The adult cornea measures 29.7 to 34.0 mm horizontally and 23.0 to 26.5 mm vertically.[7] When measured by ultrasonic pachymetry, the corneal thickness averages 0.793 to 0.893 mm, with no effect of gender or age but a tendency to be thicker in the dorsal and ventral quadrants.[8,9] Recently these values have also been reported for Miniature horses, where average corneal thickness was 0.785 mm, horizontal diameter was 25.8 mm, and vertical diameter was 19.4 mm.[10] Mean intraocular pressure was 26.0 mm Hg.[10] The internal volume of the equine globe is large. In one study, the mean aqueous humor volume measured in six adult equine eyes was 3.04 ± 1.27 mL, and the mean vitreous humor volume was 26.15 ± 4.87 mL.[6] Total internal volume of the globe has been reported up to 45 to 50 mL with a weight of 100 mg.[6]

The multiple large bellies of the retractor bulbi muscle, which attach extensively around the posterior half of the sclera and are innervated by cranial nerve VI, dominate the extraocular muscles (Fig. 3-3). The globe retraction reflex provides one of the major methods of evaluating this nerve's function. The other six muscles have typical attachments (Table 3-2) but more extensive bulk and insertion than is the case in many other species. Muscular attachments are seldom avulsed in orbital trauma (in contrast to the dog), but they may become entrapped and be unable to function after orbital fractures.

Table 3-2 | **Orbital and Ocular Muscles: Function and Innervation**

EXTRAOCULAR MUSCLE	FUNCTION	INNERVATION
Dorsal rectus	Upward motion of globe	Oculomotor (III)
Ventral rectus	Downward motion	Oculomotor (III)
Medial rectus	Medial motion	Oculomotor (III)
Lateral rectus	Lateral motion	Abducens (VI)
Dorsal oblique	Rotation nasally and inferiorly	Trochlear (IV)
Ventral oblique	Rotation laterally and superiorly	Oculomotor (III)
Retractor bulbi	Posterior motion of globe	Abducens (VI)
EYELID	**FUNCTION**	**INNERVATION**
Levator palpebrae superioris	Elevates upper eyelid	Facial (VIII)
Levator angularis oculi	Elevates nasal eyelid/eyebrow	Oculomotor (III)
Malaris	Opens lower eyelid	Facial (VII)
Orbicularis oculi	Forceful closure of eyelids	Facial (VII)
Retractor angularis oculi	Retracts lateral canthus	Facial (VII)
Arrectores ciliorum	Elevates eyelashes	Sympathetic
Orbitalis (Muller's): superior and inferior tarsus and circular fibers	Retracts eyelid (smooth)	Sympathetic
Corrugator supercilii	Elevates upper eyelid	Facial (VII)

ORBITAL VASCULAR SUPPLY

The vascular system of the equine orbit has been described in detail, and the reader is referred to the excellent work of Simoens.[11] Most vessels cross through the orbit inferiorly and nasally and may be avoided by aspirating and biopsying the orbit only from the dorsal, lateral, or dorsomedial directions. The orbital branches of the external ophthalmic artery are variably derived from the internal maxillary artery deep within the orbit (Fig. 3-4). Two functional groups—the ciliary arteries rostrally and the chorioretinal arteries caudally—perfuse the globe. Posterior ciliary arteries enter the sclera behind the equator in the cardinal positions to perfuse the choroid and continue forwards toward the anterior segment within the sclera. Anterior ciliary arteries enter superiorly and inferiorly caudal to the limbus. Multiple chorioretinal arteries (10 to 20) surround the optic nerve at its entry through the sclera, supplying retinal arteries and contributing to local choroidal perfusion.[11] The primary venous drainage of the eye is through the ophthalmic, orbital, supraorbital, and reflex veins.[3] The superior vortex vein, palpebral, and lacrimal veins course into the dorsal ophthalmic vein before more caudal contributions from the anterior ciliary, supraorbital, muscularis, and infratrochlear

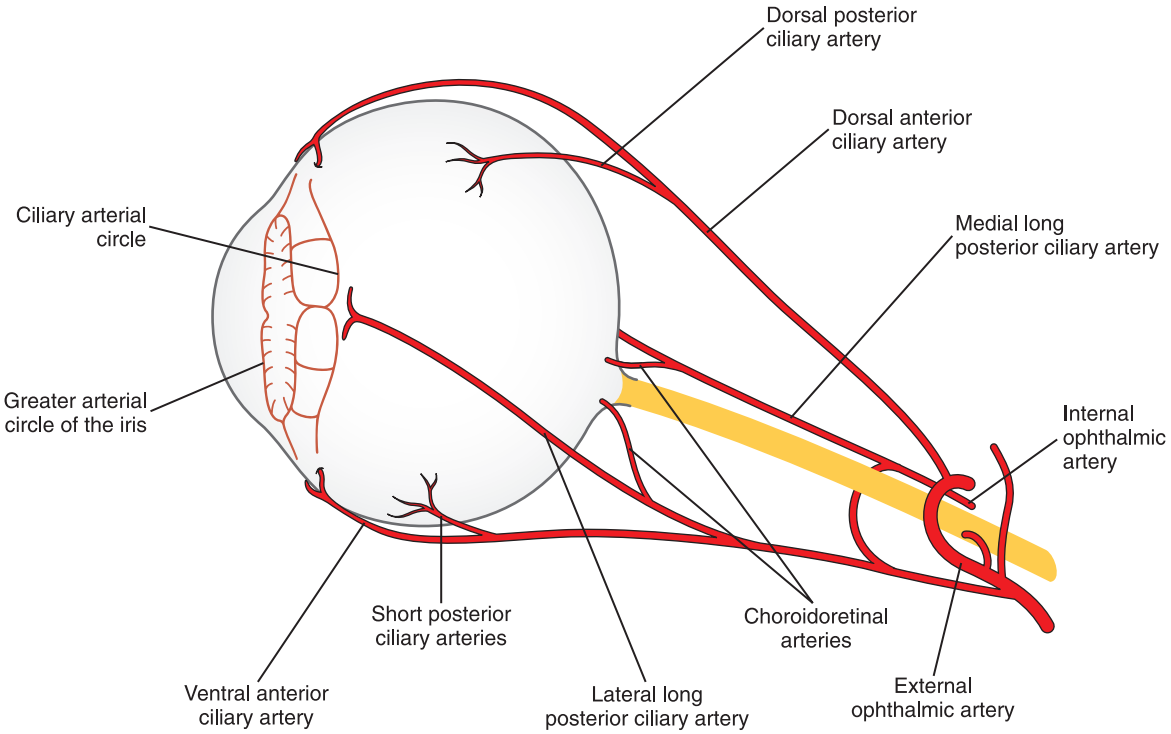


Figure 3-4. Arterial vascular supply to the equine orbit.

veins, and ultimately from the ophthalmic vein at the apex of the orbit. The orbital and internal maxillary vein then provides venous drainage. The inferior vortex vein anteriorly drains into the reflex vein, which also receives venous return from the muscular and palpebral veins, the great palatine, sphenopalatine, and infraorbital veins in the anterior orbit before entering the facial vein.

STRUCTURES ADJACENT TO THE ORBIT

ORAL/BUCCAL CAVITY

The buccal cavity is separated from the orbit in horses because of skull thickness and size and because of the complete bony orbit. Dental disease may still impact the orbit via the sinuses, but it must be substantial to do so. The last premolar and first three molars arise in the maxillary sinus, and the last molar abuts the sphenopalatine sinus. If oral disease is present or suspected, the buccal cavity should be opened and examined, and the horse's ability to prehend food should be further evaluated. Manipulation of the mandible on the maxilla will often elicit information about functional quality of apposition of the dental arcades. An oral speculum is necessary for more detailed analysis and should be performed if malodorous breath, evidence of food retention/packing, or chronic rhinorrhea or purulent discharge is present.

GUTTURAL POUCH

The guttural pouch is a diverticulum of the eustachian tube that occupies the area posterior to the mandible and is the site of multiple fragile structures. It extends anteriorly to closely approximate the orbit and enters the pharynx through a slitlike opening. Therefore, disease of the guttural pouch may directly impact the orbit. More commonly, ocular disease may result from damage to the internal carotid artery that passes through the guttural pouch or to the cranial cervical ganglion of the autonomic nervous system. The major diseases of the guttural pouch are bacterial or fungal infection and empyema, and some of the surgical and medical managements of that condition. Rupture of the internal carotid artery is a life-threatening condition. See Chapter 13, Ocular Manifestations of Systemic Disease, for more information on guttural pouch disease.

NASOLACRIMAL DUCT

The nasolacrimal duct system originates proximally via large puncta in the upper and lower eyelids and is joined by canaliculi to the lacrimal sac, which is embedded in the lacrimal bone. Damage by fracture, direct blunt trauma, infectious or inflammatory disease at this site may cause epiphora and chronic irritation. Treatment of nasolacrimal disease is described in Chapter 4. The nasolacrimal duct traverses the maxillary sinus, and sinusitis resulting in increased sinus pressure may functionally obstruct the duct, resulting in epiphora.

PERIORBITAL SINUSES

Periorbital sinuses, the frontal (conchofrontal), maxillary (caudal and rostral), and sphenopalatine, are in close anatomic proximity to the orbit (see Fig. 3-2, *C*). Primary sinus diseases may secondarily affect one or both orbits.[12-16] The *frontal sinus* is a shallow, wide sinus parallel with the frontal bone; it extends anteriorly from a line joining each temporomandibular joint forward almost to the dorsal turbinate bone that represents the conchofrontal sinus. The sinus system is lined with epithelium and is air filled, therefore an open fracture of any sinus is clinically relevant because it is considered a contaminated wound.

The *maxillary sinus* extends ventrally from an imaginary line joining the medial canthus and the nasomaxillary notch, to just below the facial crest. The rostral border is the rostral extent of the facial crest, and the caudal border is the midline of the orbit. Diminutive *ethmoidal* and *sphenopalatine sinuses* are present medial to the internal wall of the orbit and are more difficult to identify from external landmarks. Infection of the sphenopalatine sinuses may cause swelling and distention that can compress the optic nerve and chiasm, resulting in blindness.[17] Together with the frontal sinus, drainage is into the caudal maxillary sinus. Ultimately, drainage occurs from these sinuses into the nasal cavity. When surgical drainage is indicated for sinus disease, trephination dorsal to a line between the infraorbital foramen and the medial canthus can result in nasolacrimal duct damage and must be avoided (see Fig. 3-2, *C*).[18]

ETHMOID TURBINATES

The ethmoid turbinates are located axially and inferiorly to the orbit at the caudal end of the nasal cavity within the skull. This area receives a very rich vascular supply and may be the site of origin of ethmoidal hematomas (which cause chronic nasal disease) as well as aggressive carcinoma.

ORBITAL DIAGNOSTICS

OCULOKINETIC REFLEXES

Although the horse typically does not display much independent globe motion, entrapment or compression of the globe within the orbit may be evaluated by taking advantage of the oculokinetic reflexes of the vestibular system. While standing at one side, the skull is grasped near the distal extremity, and gentle sweeping motions are made while observing for primary and secondary adjustments in globe position. Finally, a spiraling motion may be used to attempt to determine if tertiary motions are normal or not, although this maneuver may be more challenging for the examiner than the subject.

FORCED DUCTION TESTS

Passive forced duction testing requires desensitization (e.g., use of topical 0.5% proparacaine) and gentle retraction of the globe in the direction of interest (the motion is passive for the horse). Failure to achieve globe motion is regarded as a positive test result and indicates entrapment or disease of the muscle (restrictive muscle disease). *Active forced duction testing* requires participation of the patient, and the examiner observes and feels for attempted motion of the globe by muscle contraction in the direction of interest.

FINE-NEEDLE ASPIRATION

Fine-needle aspiration for cytology and biopsy for histopathology are highly desirable when attempting to make a diagnosis of the cause of an orbital mass lesion. Preferably a thorough physical examination and imaging studies (e.g., computed tomography [CT], magnetic resonance imaging [MRI], and orbital ultrasound; see later in this chapter for more details) are performed prior to the aspiration or biopsy to specifically define the lesion location. Real-time, B-mode ultrasonography is recommended to guide sampling, permit observation of needle placement, and reduce the risk of iatrogenic trauma. Strabismus or globe displacement suggests the location of an intraorbital mass, which typically must be extensive to compress or decenter the globe. Intraconal masses displace the entire globe anteriorly, whereas extraconal masses cause strabismus and ocular displacement. Biopsy of orbital contents may be performed from the supraorbital fossa, from 1 cm lateral to the lateral canthus, and from the medial canthus parallel to the orbital wall, avoiding the inferior quadrant. Avoiding the major vessels and structures of the orbit is critical. Several samples may be acquired if the mass is firm, but hemorrhage may impede later sample acquisition.

Bacterial culture is indicated for samples acquired from any paranasal sinus, and potentially from orbital masses in younger animals where an abscess or septic cellulitis is suspected. Where generalized orbital cellulitis is present, microbial culture is desirable, but an appropriate sample is difficult to acquire, and the entire orbital contents appear homogenously expanded on ultrasonography; in such cases a small biopsy may be preferable to an aspirate for culture purposes. Even when a systemic leukocytosis is demonstrated, blood cultures are highly unlikely to be useful unless a severe fever is present concurrently (>105°F).

ORBITAL IMAGING

Orbital disease may be more challenging to diagnose because many of the structures are hidden from direct examination. In addition to appearance, displacement of adjacent structures permits deduction of involved structures and suggests the tissue of interest. Imaging systems provide confirmation of suspected diagnoses and are frequently an essential part of the diagnostic process. Imaging is described in greater detail in Chapter 1.

ULTRASONOGRAPHY

Ultrasonography is convenient, efficient, performed in real time, inexpensive, and readily available to most practitioners.[19,20] Although a 10- or 7.5-MHz probe is necessary for adequate imaging of the globe, the deeper aspects of the orbit may require a 5- or 7.5-MHz probe (Fig. 3-5). However, orbital ultrasonography is not very sensitive or specific, and other imaging modes such as CT may be more diagnostic. In fact, even moderately large orbital lesions may not be apparent on some ultrasound examinations. Please see Chapter 1 for the technique on how to perform the ocular and orbital ultrasound.

Aspiration of a lesion (e.g., mass, fluid) in the equine orbit can be performed for cytology, culture, and histopathologic examination. An 18-gauge, 10-cm, slightly curved needle is inserted 1 cm lateral to the lateral canthus and then directed posteriorly in a line parallel to the medial canthus.[21] Approaching the retrobulbar space via the supraorbital fossa as described for retrobulbar block is also possible, especially if the lesion is in the dorsal retrobulbar area.

Exophthalmos and orbital trauma are the two most common indications for orbital ultrasound examination in the horse. After trauma to the orbit and associated structures, ultrasound may be used to evaluate the retrobulbar space for displaced fractures, hemorrhage, swelling, compression of the optic nerve, and integrity of the posterior wall of the globe.[22]

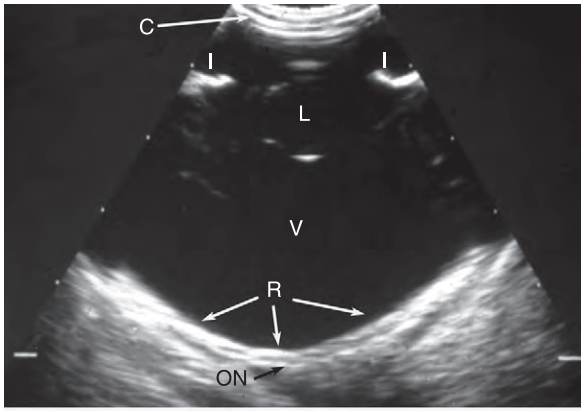


Figure 3-5. Transcorneal ocular ultrasound of a normal equine eye using a 7.5-MHz transducer. The deeper aspects of the orbit may require a 5- or 7.5-MHz transducer. *C*, Cornea; *I*, iris; *L*, lens; *R*, location of retina; *ON*, location of optic nerve; *V*, vitreous.

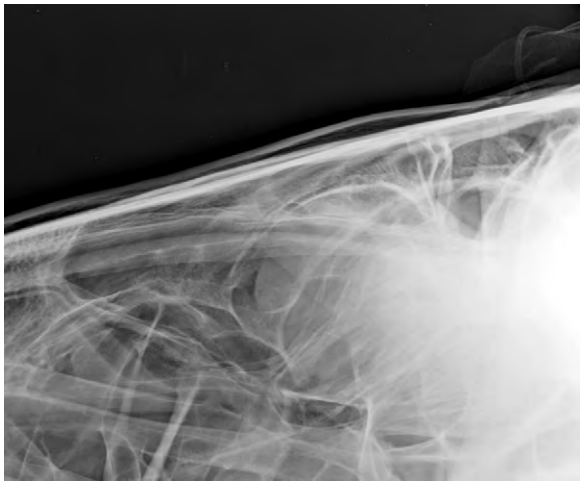


Figure 3-6. Skyline radiographic technique may isolate the bone of interest against an air-filled background (e.g., frontal sinus). This radiograph is of a frontal sinus fracture from blunt trauma demonstrating subcutaneous emphysema.

RADIOGRAPHY

Radiography is indicated primarily to identify bone fractures in the acutely traumatized individual, bone deformation in invasive neoplasia or sepsis, and to localize cellulitis if gas production is evident. Precise radiographs require general anesthesia to avoid motion, although screening images may be obtained in the standing sedated patient, particularly with the advent of digital radiography. Specific skyline techniques to highlight the orbital bones of interest (Fig. 3-6) may identify a lesion against an air-filled background (e.g., frontal sinus). Contrast orbitography may be performed by artificially introducing air into the orbit, although routine CT and MRI are much more sensitive diagnostic procedures. Other injectable contrast materials are seldom indicated and risk creating complications. Fluid/air interfaces within the sinus indicate pathology that is directly relevant to the orbit.

Although infrequently necessary, radiography is also useful for localizing metallic foreign bodies such as gunshot within the orbit. In general, such foreign bodies are preferably left in position unless direct damage to a blood vessel results in substantial hemorrhage or the object is migrating.

COMPUTED TOMOGRAPHY AND MAGNETIC RESONANCE IMAGING

Advanced imaging such as MRI and CT provide the best images to localize the orbital lesion precisely (Fig. 3-7). The use of cross-sectional and three-dimensional reconstruction of CT equine skull images overcomes the superimposition of the complex anatomic features of the equine skull that make conventional radiographic interpretation difficult.[23,24] The large amount of low-density fat in the equine orbit provides good natural contrast for differentiating various soft-tissue structures by CT, although the primary advantage of CT over MRI is its ability to detect osseous changes.[23] Disadvantages of CT over skull radiography in the horse include the need for general anesthesia and the risks associated with recovery from anesthesia, increased cost, and limited accessibility.[24] There have been several reports of CT examination of the equine orbit, including evaluation of the periorbital sinuses, orbital masses, and skull fractures.[17,24-26] See Chapter 1 for more information on CT imaging.

IMPACT OF ORBITAL DISEASES ON THE EQUINE INDUSTRY

Orbital disease is uncommon and of relatively low financial impact in general, although it is of very substantial and potentially life-threatening impact to the individual. Diseases of the equine orbit result in profound cosmetic changes, and in almost all cases, vision loss occurs. Most treatable orbital diseases occur in juvenile and young horses and are predominantly traumatic or congenital, whereas the debilitating progressive orbital diseases that occur in older adult horses may be difficult to manage and often are impossible to cure. No epidemiologic studies are available to record the potential annual economic impact of orbital disease, but the major costs are likely to be related to loss of use because of loss of vision, cosmetic defects, or possibly even loss of life. To minimize globe or orbital disease, preventive management strategies to reduce ocular trauma, cautious introduction of new horses into group confinement, and early diagnosis, referral, and imaging of orbital disease is needed. It is possible that more routine use of advanced imaging, such as CT and MRI, and earlier surgical intervention may improve the prognosis or medical and surgical treatment of orbital disease.

There are no significant contagious or infectious diseases of the orbit that pose a threat to livestock in the United States. Among exotic diseases, African horse sickness, equine infectious anemia, and infectious diseases causing vasculitis may cause retrobulbar and supraorbital swelling and distension in multiple individuals (see Chapter 13). Quarantine, importation restrictions, and routine serologic testing are the major source of protection against these diseases in the United States, Australia, and nonendemic areas of Europe.

CLINICAL SIGNS OF ORBITAL DISEASE

ABNORMALITIES OF GLOBE POSITION

Strabismus is the deviation of the visual axis from the expected orientation, which is straight ahead in the horse. When both

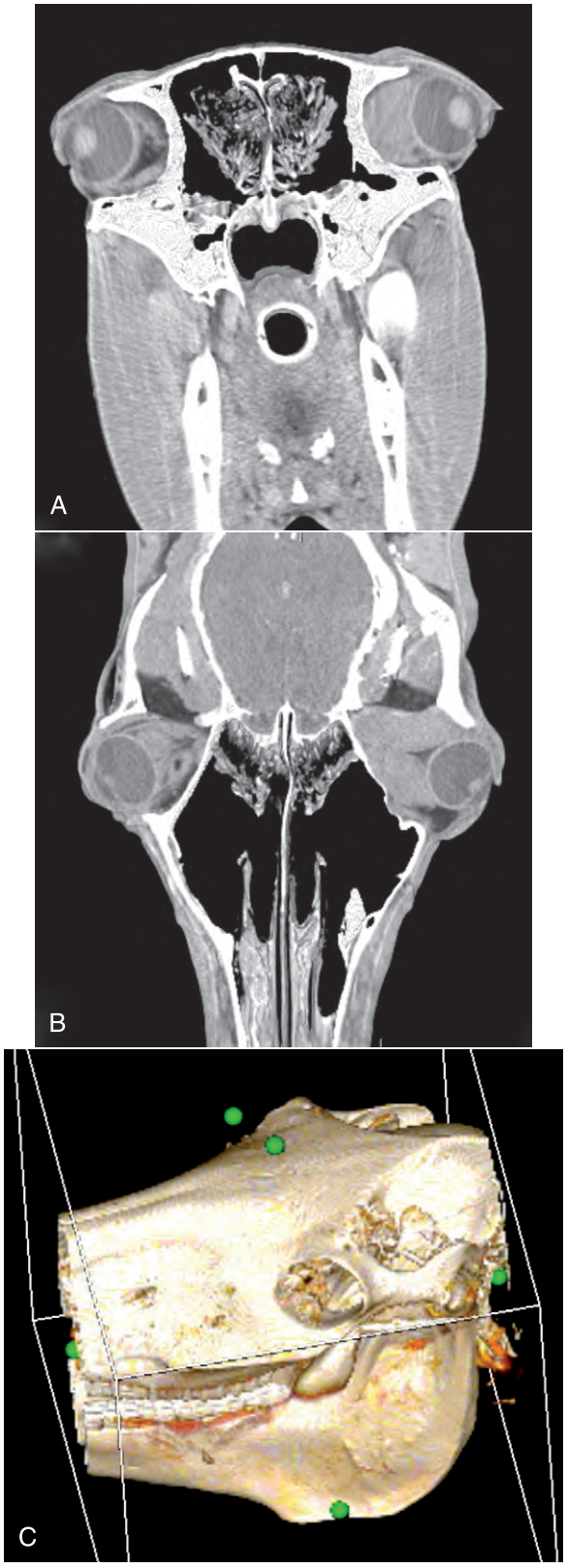


Figure 3-7. **A,** Transverse and **B,** saggital views of a computed tomography (CT) image of a horse with left-sided exophthalmos caused by a retrobulbar neoplasm. Note the increased soft-tissue density in the left orbit compared to the right orbit. **C,** Three-dimensional CT image reconstructed from transverse-plane CT images of the horse in **A.**

globes are focused ahead, the conjugate gaze has an overlap of the visual fields, allowing for binocular vision and good depth perception owing to the wide globe separation (see Chapter 11). The deviation induced by strabismus presumably disturbs the collation and overlap of visual field information from each eye when it is interpreted in the midbrain and visual centers. In people, misdirected visual axes result in diplopia or double vision. Strabismus generally occurs from a space-occupying mass of the orbit, distorting the globe from its resting position, or possibly it may result from disturbance of the ocular muscle innervation or activity due to stricture, contraction, or mechanical entrapment. Strabismus in young individuals is uncommon and likely to be congenital or breed related.

Neonatal foals most frequently have a *physiologic rotational strabismus* that resolves to the adult orientation within the first 2 to 4 weeks of life. The horizontal pupil is rotated so that the nasal portion is ventral to the temporal portion, and the globe may also be rotated medially. The strabismus is considered physiologic and requires no therapy. The cause is unknown, and no therapy is possible. Appaloosa foals afflicted with *congenital stationary night blindness* (CSNB) may also exhibit a dorsal strabismus (Fig. 3-8).[27,28] The relationship of the strabismus to CSNB is unclear.

Acquired causes of strabismus are traumatic in origin typically, due to muscle entrapment post fracture, or less likely due to avulsion of a rectus muscle attachment. The most anterior rectus muscle attachments are for the ventral (8 mm behind limbus) and dorsal (9 mm) rectus muscles, while a portion of

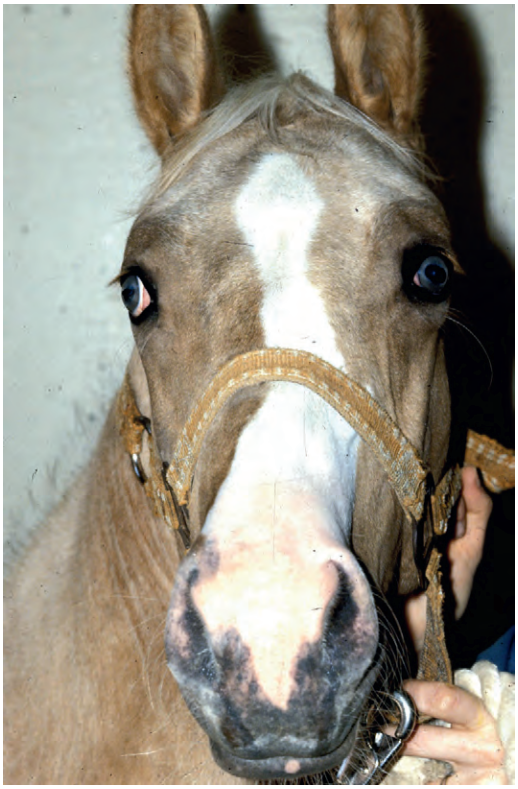


Figure 3-8. Appaloosa affected with congenital stationary night blindness (CSNB), demonstrating dorsomedial strabismus and an unusual gaze associated with head elevation (termed *star gazing*). The relationship of the strabismus to CSNB is unclear. (Photograph courtesy Dr. David Wilkie.)

the lateral rectus attaches within 5 mm of the limbus.[29] Occasionally, central nervous system infections may result in strabismus, most commonly with equine protozoal myeloencephalitis (see Chapter 13).[30-32] Midbrain (oculomotor) lesions most commonly result in a lateral strabismus.[33] Peripheral vestibular disease may result in strabismus rather than nystagmus and is often accentuated by elevation of the horse's head. Strabismus may be the only residual sign after recovery from vestibular disease.[33]

Postinflammatory stricture of an ocular muscle may result in moderate or severe strabismus but is uncommonly identified. In forced duction tests, the globe cannot be moved in the direction opposite the strabismus. In contrast, muscle avulsion will permit a freely mobile globe, at least until the partner muscle atrophies and fixes the globe position. This strabismus is occasionally identified in horses after severe blunt trauma from the side or front.

NYSTAGMUS

Nystagmus is an oscillatory movement of the globe which may be horizontal, vertical, or rotational. Physiologic nystagmus is a normal compensatory reaction that occurs when the head turns and is a direct response to differential stimuli within the inner ear and the vestibular system. This involuntary motion of the globe permits a more stable visual horizon and enhances stability of the visual field. Pathologic forms of nystagmus reflect damage to the vestibulocochlear apparatus (horizontal, rotatory) or central nervous system disease (vertical). Nystagmus most frequently accompanies central disease in the horse, which is most often infectious in etiology. Potential etiologies include equine protozoal myeloencephalitis (EPM), the viral encephalitides (Eastern equine encephalitis [EEE], Western equine encephalitis [WEE], Venezuelan equine encephalitis [VEE], West Nile Virus), aberrant parasite migration, or bacterial sepsis. Peripheral causes include EPM; trauma fracturing the petrous temporal, basisphenoid, or basioccipital bones; conditions afflicting the guttural pouch diverticulum (empyema, mycosis, chondroids); temporohyoid osteopathy (THO); and osteomyelitis adjacent the inner ear and orbit. Concurrent depression substantially worsens the prognosis. Refer to Chapter 13 for more details of the specific diseases and their treatment.

ABNORMALITIES OF GLOBE LOCATION, SIZE, AND FUNCTION

EXOPHTHALMOS

Exophthalmos describes the anterior displacement of a normal-sized globe within the orbit. The most common causes are retrobulbar masses, orbital cellulitis, and trauma that reduces the orbital space (Fig. 3-9 and Table 3-3). Exophthalmos is most easily identified by viewing the head from the front and comparing the angle of eyelashes, the relative prominence of the globe, and the size of the palpebral fissure (Fig. 3-10). In contrast to other domestic species, there is minimal additional benefit from observation from above the skull. An exophthalmometer is a device used to measure relative globe prominence within the orbit, but it is seldom of clinical relevance. Palpation of the globe relative to the orbital rim may achieve similar results to an exophthalmometer.

Figure 3-9. Exophthalmos of the right eye due to an orbital mass. Note the prominence of the nictitans and mild dorsomedial strabismus, which suggests the mass is extraconal within the orbit.

Figure 3-10. Exophthalmos of the right eye due to orbital cellulitis. Note the distorted contour of the eyelids, mydriasis, supraorbital fossa swelling, and eyelash angle asymmetry of the right eye compared to the left.

Digital retropulsion, or pushing the globe caudally into the orbit by digital pressure through the eyelids, should be attempted in every individual exhibiting exophthalmos. The extent and ease of retropulsion reflects the tissue pressure within the orbit. It is easier to move the globe directly posteriorly than inferiorly. Painful exophthalmos typically suggests inflammatory disease (e.g., orbital cellulitis), whereas nonpainful exophthalmos is more commonly observed in slowly expanding neoplastic or cystic masses.

ENOPHTHALMOS

Enophthalmos, or globe abnormally deep or caudally displaced in the orbit of the globe, is typically secondary to the loss of orbital contents. It is most commonly found in older horses that are reabsorbing orbital fat, but it should be differentiated from phthisis bulbi occurring in a chronically inflamed eye. Neonatal foals are enophthalmic if dehydrated (Fig. 3-11) and may develop entropion due to lack of globe support to the eyelids. This neonatal foal enophthalmos reverses rapidly with return to normal homeostasis. Enophthalmic globes should be comfortable and visual, but vision may be reduced by the prominence or elevation of the nictitans, which is no longer held in position by the globe. The supraorbital fossa is more prominent and deep. It has been suggested that fat mobilization occurs

Table 3-3 | **Literature Review of Causes of Exophthalmos in the Horse**

PRIMARY LOCATION	DISEASE TYPE	NUMBER OF ANIMALS AFFECTED	REFERENCE
PERIORBITAL SINUS			
Cysts	Sinonasal cyst	1	Annear et al., 2008[72]
	Hydatid cyst	1	Barnett et al., 1988[57]
Inflammation	*Cryptococcus* granuloma	3	Roberts et al., 1981[53] Scott et al., 1974[13]
	Chronic bacterial sinusitis	1	Kanda et al., 2007[71]
	Masseter muscle myonecrosis	1	Step et al., 1991[64]
Neoplasia	Adenocarcinoma	3	Hill et al., 1989[16] Dixon et al., 1999[75] Davis et al., 2002[32]
	Adenoma	2	Dixon et al., 1999[75]
	Osteoma	2	Scotty et al., 2004[79] Schaaf et al., 2007[112]
	Squamous cell carcinoma	1	Dixon et al., 1999[75]
	Fibrosarcoma	1	Dixon et al., 1999[75]
	Undifferentiated sarcoma	1	Dixon et al., 1999[75]
	Lymphosarcoma	1	Dixon et al., 1999[75]
	Esthesioneuroblastoma	1	Dopke et al., 2005[113]
ORBIT			
Neoplasia	Neuroendocrine tumor	7	Van Maanen et al., 1996[12] Basher et al., 1997[80] Matiasek et al., 2007[81]
	Extra-adrenal paraganglioma	7	Goodhead et al., 1997[82] Miesner et al., 2009[26]
	Anaplastic sarcoma	5	Baptiste et al., 2000[86]
	Squamous cell carcinoma	4	Dixon et al., 1999[75] Baptiste et al., 2000[86]
	Lymphosarcoma	2	Rebhun et al., 1998[83]
	Malignant rhabdoid neoplasia	1	Hong et al., 1999[94]
	Angiosarcoma	2	Bolton et al., 1990[92] Bischofberger et al., 2008[93]
	Fibroma	1	Colitz et al., 2000[25]
	Adenocarcinoma	1	Baptiste et al., 2000[86]
	Primitive neuroepithelium.	1	Bistner et al., 1983[85]
	Melanoma	1	Moore et al., 2000[90]
Inflammation	Abscess	2	Hubert et al., 1996[54] Van den top et al., 2007[55]
	Granuloma caused by *Halicephalobus gingivalis*	1	Pearce et al., 2001[59]
	Strongylus edentatus	1	Walde et al.[58]
Cysts	Dermoid cyst	1	Munoz et al., 2007[46]

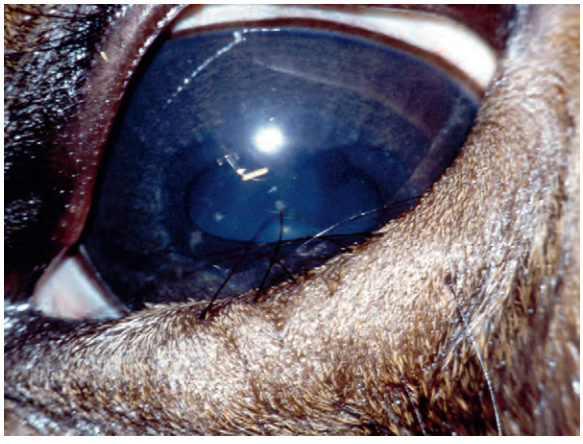


Figure 3-11. Dehydrated neonatal foal with enophthalmos and lower-eyelid entropion. Tacking sutures to roll out the lower eyelid and systemic support will allow the globes to rapidly return to their normal position. (Photograph courtesy Dr. Riccardo Stoppini.)

preferentially from sites with the greatest variation in individual fat-cell size. The orbital fat and supraorbital fossa fat cells are the smallest in the body, suggesting that fat resorption in this area occurs as a late outcome.[34]

Trichiasis and chronic ocular discharge from misalignment of the eyelid and puncta are management problems in enophthalmos. Entropion of the lower eyelid may be addressed to prevent direct abrasion of the hair on the cornea. (See Chapter 4 for more information on management of entropion and trichiasis.) Strategies include primary entropion repair, which may result in inappropriate gapping between the globe and the eyelid and accumulation of mucoid debris. Alternatives are cryosurgery of irritating hairs, injection of collagen intradermally to increase eyelid rigidity, or placement of retrobulbar silicone devices to propel the globe forward. The latter procedure is subject to later displacement of the silicone prostheses and recurrence. Addressing the sequelae in this manner is likely to only be temporarily successful. Pars intermedia dysfunction in horses may accentuate reabsorption of fat and worsen enoph-

thalmos. Orbital fracture may result in enophthalmos if the ventral floor of the orbit is displaced. Finally, enophthalmos may be associated with sympathetic denervation to the smooth muscle between the globe and orbital rim, which is typically somewhat subtle in appearance but may be associated with nictitans prominence (see Chapters 4 and 13 for more information on Horner's syndrome).

PHTHISIS BULBI

Phthisis bulbi, gradual shrinkage of the globe, is due to chronic inflammation and hypotony of the globe resulting from severe damage to the ciliary body epithelial cells responsible for fluid production (Fig. 3-12). Generally, eyes that are phthisical should be enucleated to prevent ocular discomfort. When a cosmetic appearance is desirable, phthisical globes may have an intrascleral prosthesis inserted to replace the intraocular contents. It is not possible to expand the size of the globe, but further shrinkage may be avoided. A cosmetic shell with or without enucleation and orbital prosthesis placement may also result in reasonable cosmetic outcomes (see technique later in chapter).[35] See chapters on uveal diseases (see Chapter 6) and equine recurrent uveitis (see Chapter 8) for more information and treatment of intraocular inflammatory diseases.

ATROPHIA BULBI

Atrophia bulbi describes a smaller globe than normal, suggesting a gradual decline in globe size secondary to chronic inflammation. In contrast, *phthisis bulbi* refers to an end-stage, blind eye. Again, Chapters 6 and 8 offer more information on diagnosis and treatment of intraocular inflammatory diseases.

Figure 3-12. A, Phthisis bulbi of the horse's right eye, front view. **B,** Phthisis bulbi, or shrunken globe, from chronic ocular inflammation associated with equine recurrent uveitis. (Photograph courtesy Dr. Stacy Andrew.)

HYDROPHTHALMOS (BUPHTHALMOS)

Hydrophthalmos refers to an unusually enlarged globe, which is associated with chronically increased intraocular pressure secondary to glaucoma. Technically, the term *buphthalmos* indicates a globe typical of a bovine, which purists would observe is generally smaller than that of the horse. *Hydrophthalmos* indicates that the globe is larger than normal and may be the preferred term in the horse. In adult horses, globe enlargement occurs slowly and is associated with other clinical signs of glaucoma, including corneal edema and endothelial striae (Fig. 3-13). Vision may be present, reduced, or absent at the time of diagnosis. It is not uncommon in horses for vision to return when intraocular pressure (IOP) is subsequently controlled, even if the condition is chronic and mild globe enlargement has occurred. Glaucoma may also be congenital, in which instance hydrophthalmos may occur rapidly with only a temporary retention of ocular function. Congenital glaucoma is usually severe and blinding in the early stages. Hydrophthalmos should be differentiated from exophthalmos of a normal-sized globe. See Chapter 9 for more information on the diagnosis and treatment of glaucoma in horses.

MEGALOPHTHALMOS

Megalophthalmos refers to a distortion of the globe and has been used to describe the grouping of abnormalities found in Rocky Mountain horses with multiple congential ocular anomalies. These clinical signs include increased corneal curvature, iris hypoplasia, congenital miosis, uveal cysts, cataracts, and retinal dysplasia. Persistent pupillary membranes may also be present.[36]

OTHER SIGNS OF ORBITAL DISEASE IN THE HORSE

In addition to the clinical signs of orbital disease already described, other typical signs include a prominent nictitans, epiphora, subcutaneous emphysema, reduced airflow from the ipsilateral nostril, altered sinus percussion, episcleral vessel enlargement, bone deformation, keratoconjunctivitis sicca, and distention of the supraorbital fossa.

Figure 3-13. Hydrophthalmos (buphthalmos) in an adult horse with chronic glaucoma in the left eye. Note additional typical signs of chronic glaucoma such as corneal edema.

PROMINENT NICTITANS

The nictitans in the horse can be elevated passively with orbital space-occupying masses (Fig. 3-14). This temporary physiologic displacement may become chronic and persistent if orbital contents are altered in position due to a mass or absence of adequate globe support resulting in enophthalmos. The prominence of the nictitans in Horner's syndrome is associated with enophthalmos and may not always be obvious in the horse. Clinical cases of tetanus often exhibit spasm of the nictitans, particularly in response to sudden stimulation. Globe retropulsion should always be performed when nictitans prominence is observed.

EPIPHORA

Epiphora is commonly associated with orbital disease, but it should be differentiated from eyelid swelling and distortion such as that due to dacryocystitis, neoplasia, or infection (see Chapter 4). In orbital and extraorbital disease, the nasolacrimal duct may be obstructed functionally or anatomically (i.e., by sinusitis, fracture, or neoplasia), or the eyelid puncta may become misaligned due to blepharoedema, blepharoconjunctivitis, or exophthalmos. Normal tear flow through the nasolacrimal duct depends in part upon vacuum development in the duct, created by the orbicularis oculi during eyelid closure. Functional obstruction may be differentiated from occlusion by irritation of the nasolacrimal duct.

EMPHYSEMA

Accumulation of subcutaneous air is due to unidirectional aspiration of air and entrapment between the skin and calvarium (Fig. 3-15). The most common cause is a sinus fracture, which should be considered an open contaminated wound. A depression or displaced fracture is almost always palpable, but radiography with skyline views or a CT scan should be performed if the fracture is not identified clinically. Infrequently, anaerobic bacterial sepsis may result in gas production, although this is uncommon in the equine head.

REDUCED AIRFLOW FROM IPSILATERAL NOSTRIL

This may be more subtle, but airflow may be detected by holding a piece of cotton in front of the nostril, or a cool glass slide to detect condensation of warm exhaled air. Partial occlusion of the nasal cavity by a large expanding mass should be suspected if airflow is altered.

Sinus Percussion

The mandible should be opened to reduce the mass of tissue being percussed, which improves the sonic qualities, and the bones overlying the sinus are rapidly percussed to determine if a fluid pocket, or solid density can be localized by a more bass tone to the echoing sound. Each side is percussed in sequence for comparative purposes.

EPISCLERAL VESSEL ENLARGEMENT

If direct compression of the retrobulbar optic cone results in venous stasis, episcleral vessels may become quite prominent (Fig. 3-16). Elevated intraocular pressure, or glaucoma, may also develop and it is typically poorly or unresponsive to hypotensive medications, despite the importance of uveoscleral outflow in the horse. Exophthalmos may or may not be present. Retropulsion may not be abnormal because the functional obstruction surrounds the cone in the caudal orbit. Blindness may result from concurrent optic nerve compression, even if retropulsion is still possible.

BONE DEFORMATION

Sinus neoplasia or inflammation may result in deformation of adjacent bone, which is typically uncomfortable during firm or deep palpation. Radiographic confirmation of the localized area is usually diagnostic and permits further sample acquisition.

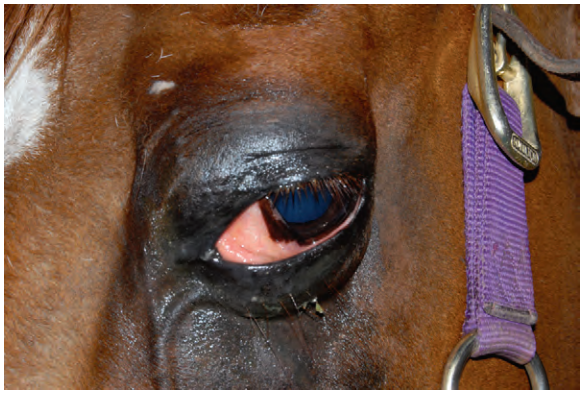


Figure 3-14. Elevated or prominent third eyelid in a horse with exophthalmos from an orbital neoplasm.

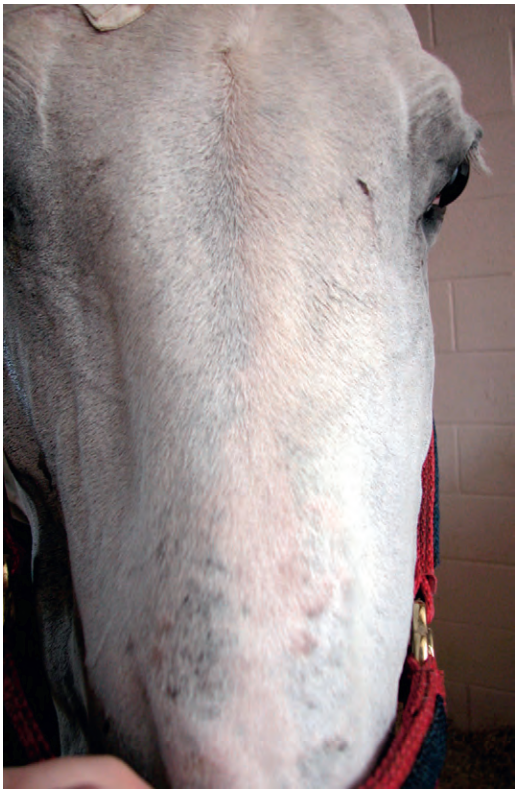


Figure 3-15. Subcutaneous emphysema from blunt trauma to the left frontal sinus. The accumulation of subcutaneous air is due to unidirectional aspiration of air and entrapment between the skin and calvarium.

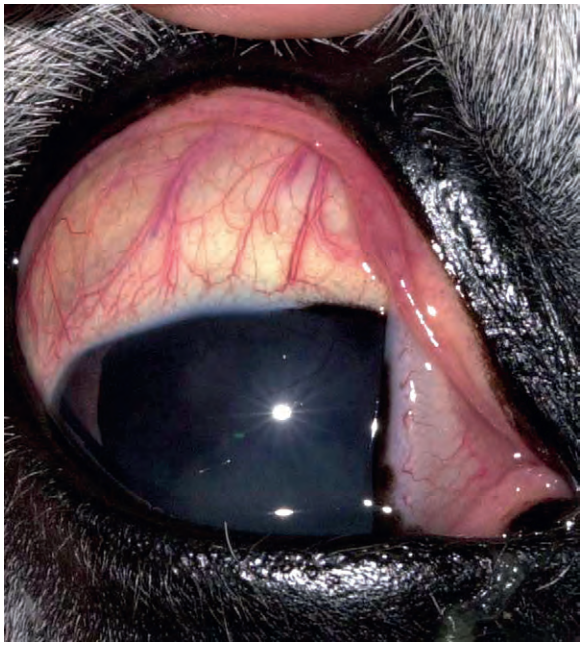


Figure 3-16. Episcleral vascular congestion in a horse with a retrobulbar mass causing venous stasis.

Periosteal reaction is less smooth and uniform than the normal bone margin and bone sutures.

KERATOCONJUNCTIVITIS SICCA

Keratoconjunctivitis sicca together with ipsilateral facial nerve paralysis suggest trauma to the facial nerve proximal to the geniculate ganglion. Neuroparalytic keratitis results from more distal lesions. The vestibulocochlear nerve (VIII) should be evaluated critically if facial (VII) nerve disease is identified, because they are commonly injured together in proximity to the petrous temporal bone[29] or the ramus of the mandible.[37]

SUPRAORBITAL FOSSA DISTENSION

Supraorbital fossa distension may accompany exophthalmos and space-occupying masses of the orbit (see Fig. 3-10). It is a particularly prominent feature of the exotic disease African Horse Sickness, where hemorrhagic edema causes great distension. Equine viral arteritis results in a panvasculitis and secondary edema that appears similarly (see Chapter 13 for further details).

CONGENITAL DISEASES

MICROPHTHALMOS

Microphthalmos is a congenital or developmental anomaly in which the globe is abnormally small.[20,38-43] Microphthalmos may be simple or complicated, referring to whether it has compound abnormalities or not. Embryologically, microphthalmos may result from incomplete closure of the optic fissure, preventing normal sealing and inflation of the globe, or it may be the consequence of a mistimed union of the migrating embryologic tissues. Microphthalmia occurred in 14.7% of foals in one study[39] and 7% in another.[44] A case of microphthalmia with brachygnathia has been reported in an older Friesian mare that received griseofulvin in the second month of gestation, similar to microphthalmia due to intoxication in other breeds.[42] Multiple ocular colobomas may accompany microphthalmia and result in severely debilitated and blind globes.

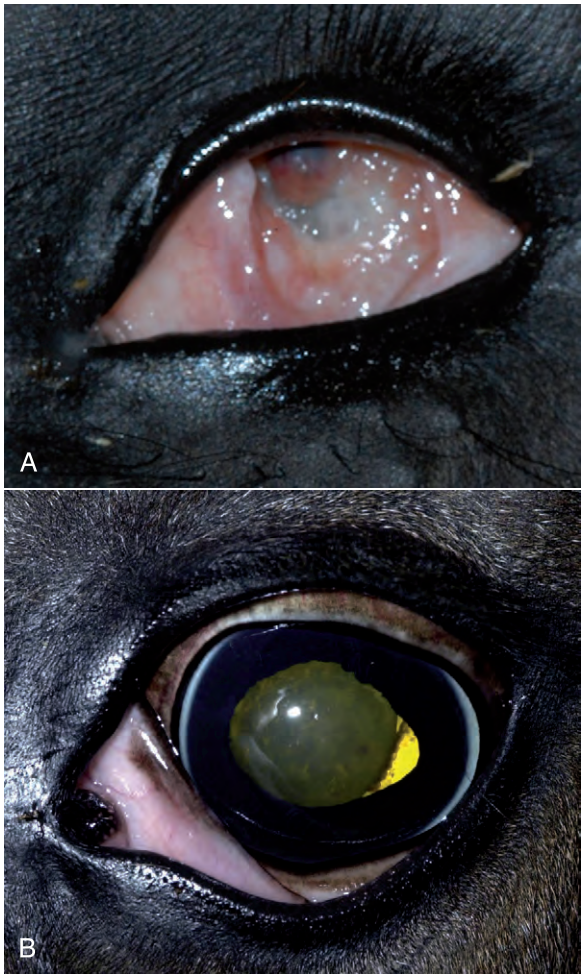


Figure 3-17. A, Congenital microphthalmos, a developmental anomaly in which the eyeball is abnormally very small. The globe may not be visible, as seen in this foal. **B,** In this foal, the globe is visible but small, and temporally there is a lens coloboma. (Photograph courtesy Dr. David Wilkie.)

CLINICAL APPEARANCE AND DIAGNOSIS

Microphthalmic eyes appear variably smaller than normal (Fig. 3-17) and commonly have additional abnormalities including cataract and other congenital abnormalities such as retinal coloboma. *Nanophthalmos* refers to a globe that is functional but smaller than normal. *Anophthalmos* is the furthest degree of microphthalmos and is extremely uncommon. More commonly, it is an excessively small globe that is barely recognizable and usually present as a very diminutive and heavily pigmented spherical mass. In such cases, the predominant tissues identified are conjunctivae and nictitans. In the adult animal, differentiating mild microphthalmos from phthisis bulbi as the cause of the small globe may be difficult; however, a poorly developed, small orbit and historical reports of a small or absent globe are most common with microphthalmos. Phthisical globes typically exhibit intraocular changes suggestive of prior substantial uveitis (see Chapters 6 and 8).

TREATMENT

If the lens is cataractous but the globe approaches normal size, has appropriate light responses, and a normal electroretinogram, it is often possible to restore useful vision with the removal of the cataract if surgery is performed early (see Chapter 7). If practical management is a substantial issue and the condition is unilateral, the globe may be removed and possibly replaced with a prosthetic device (see later). For a more normal development of the orbit, stepwise increase in orbital conformer size may assist in the approximation of normal orbit size in the adult horse.

LONG-TERM PROGNOSIS AND INHERITABILITY INFORMATION

Prognosis for vision depends on severity and the presence of other ocular defects. Microphthalmos is more common in Thoroughbreds, and in this breed it is frequently associated with cataract. Inheritance is suspected, but the mode is unknown. Conventional wisdom is to avoid repeating the same sire/dam combination.

CONGENITAL GLAUCOMA

Congenital glaucoma occurs uncommonly in foals but is often quite dramatic. The globe may rapidly enlarge and become a management problem before it becomes blind. Therapy usually carries a poor prognosis for maintaining vision. (For more information see Chapter 9.)

ORBITAL DERMOIDS

Orbital dermoids are particularly rare in horses but may cause congenital or juvenile unilateral exophthalmos. Skin with or without hair embedded within the orbit may result in a fluid-filled cystic mass that expands.[41,45,46] In one report, exophthalmos did not develop until the horse was 4 years old.[46] More commonly, noncystic dermoids are located in the dorsotemporal conjunctiva or limbus; they are frequently pigmented but not always haired.

CLINICAL APPEARANCE AND DIAGNOSIS

Clinical presentation is as for any other space-occupying mass in the orbit. Progressive enlargement and increasing exophthalmos develop, including supraorbital fossa distension.[46] Fine-needle aspiration of orbital dermoids may result in the collection of serous brown, discolored, poorly cellular fluid.[46] The specific diagnosis is likely to be determined at surgery with biopsy confirmation but may be suspected on presurgical imaging (i.e., ultrasonography and CT) in a juvenile horse with appropriate history.

TREATMENT

A space-occupying mass in the orbit requires surgical excision of the mass or orbital exenteration. The surgical approach depends on location of the mass, but a dorsal-lateral approach through the supraorbital fossa, with retraction of the temporal muscle, was successful in removing the mass in one report.[46]

LONG-TERM PROGNOSIS

Prognosis depends on the size of the mass, extent of exophthalmos, and damage to the ocular surface. In general, the prognosis for saving the globe is good for small or moderately sized masses. There is no known genetic component in horses. Dermoids of the globe have an excellent prognosis if the dermoid is excised and is not full thickness. Surgical removal of a 5-cm retrobulbar dermoid cyst was successful and did not recur during 18 months of follow-up.[46]

VASCULAR ABNORMALITIES OF THE ORBIT AND GLOBE

Pulsatile exophthalmos has been described to cause prominent exophthalmos post strenuous activity in several non-horse species. Orbital vascular anomalies occur uncommonly as a component of intracranial and extracranial congenital disease in humans. A variety of neuroectodermal dysplasias have been reported in people, but specifically Sturge-Weber disease has been reported in a young horse.[47] In that individual, prominent arterioles affected the choroid plexus of the ventricles intracranially, together with milder vascular abnormalities in the orbit. That case presented with intermittent seizures and was euthanized. Orbital varices are often ascribed to traumatic origins.

CLINICAL APPEARANCE AND DIAGNOSIS

Exophthalmos with a palpable or auscultable bruit diagnoses arterial abnormalities. External orbital vascular abnormalities are very obvious (Fig. 3-18), but orbital and intracranial arteriovenous anastomoses are harder to identify unless seizure or neurologic abnormalities are prominent and imaging studies are performed. Contrast venogram or arteriogram of the orbit may be performed with CT to recreate a three-dimensional image.

TREATMENT

If nonessential arteriovenous anastomoses can be identified, an intravascular coil may be placed to precipitate embolization. Venous sinus dilatations may be reduced surgically, but access is often limited.

PROGNOSIS

Unknown.

ACQUIRED DISEASES

Clinical signs of nontraumatic orbital disease are gradual exophthalmos with local orbital distension or deformation. Additionally, signs may extend to deviate and involve the

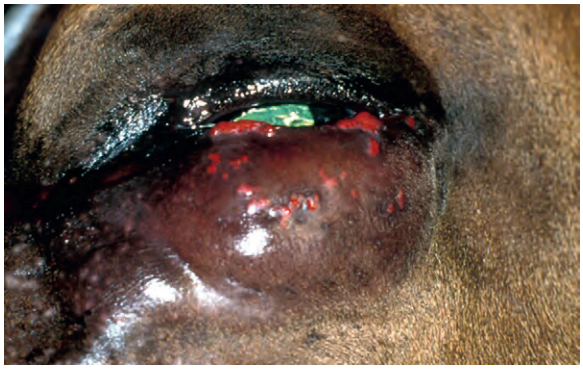


Figure 3-18. Juvenile Quarter Horse filly with unilateral vascular anomalies of the left eyelids and orbit.

frontal or maxillary sinus, adjacent tooth roots (of the caudal upper cheek teeth), nasal cavity, ethmoid turbinate bones, or guttural pouch. Processes beginning in these structures that impinge on the orbit may present primarily because of exophthalmos, strabismus, or blindness. Direct extension of guttural pouch disease is more commonly due to secondary effects rather than direct mechanical extension.

TRAUMATIC ORBITAL DISEASE

Traumatic damage to the orbit occurs more commonly in younger animals, males, and those with fractious personalities or subjected to group confinement. Athletic performance and transportation increase the risk of injury. In particular, rearing and panic-stricken behavior increase the likelihood of sudden blunt trauma, especially to the poll. The dorsal orbital rim and zygomatic arch are at greatest risk of fracture because of their prominent location on the skull of the horse (Fig. 3-19). The poll of the skull may transmit displacing forces to the sphenoid bones that form the internal orbital wall. Fracture of the frontal or maxillary bones may be further complicated by exposure of the extensive sinuses of the equine head and laceration of the profuse vasculature at the turbinate bones in close proximity to the orbit. Traumatic injury to the ethmoid turbinates or sinuses can result in epistaxis, and entrapped hemorrhagic clots may become septic and possibly result in facial swelling. Palpation and sinus percussion to compare both sides may be supplemented with radiography to localize fractures, hematomas, and fluid. The dental arcade should specifically be evaluated on radiographs to identify periapical tooth root abscesses, fractures of the roots or surrounding maxilla, or other lesion that may greatly affect the outcome. The thin periapical bone overlying the molars may be incomplete, predisposing that area to abscessation. The constant eruption of equine molar and premolar teeth contributes to the increasing size of the maxillary sinus and likely reduces the impact of dental disease inducing orbital disease.

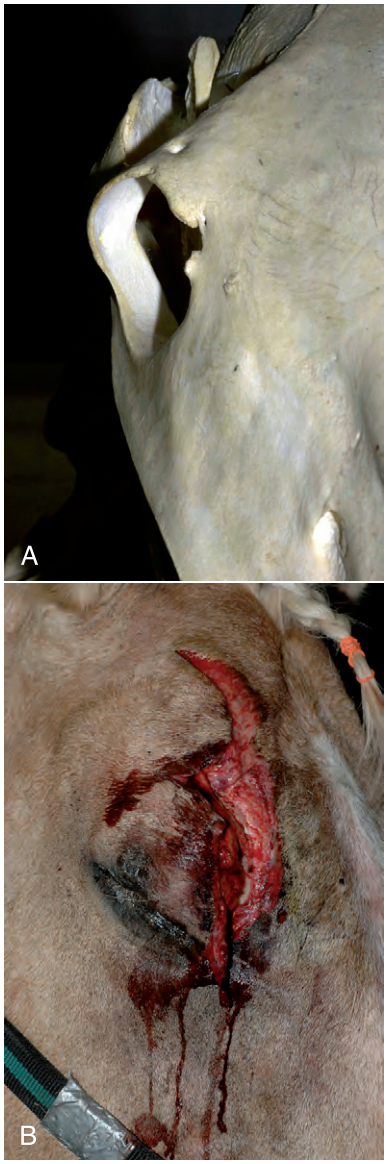


Figure 3-19. **A,** The dorsal orbital rim, especially laterally, has a prominence that is prone to trauma due to its lateral projection, as seen on a frontal view of this equine skull. **B,** Traumatic fracture of the dorsal orbital rim associated with facial lacerations secondary to blunt trauma.

GLOBE PERFORATION

INTRODUCTION AND CLINICAL APPEARANCE

A soft, fluctuant ocular surface may indicate corneal or scleral perforation if the area is hemorrhagic or if a focal protrusion of tissue is present. Iris prolapse is typically darkly colored, but frequently fibrin and hyphema are also present, resulting in a tan-red surface (Fig. 3-20). A dense red appearance to the entire anterior chamber indicates total hyphema or hemorrhage into the globe because of perforation or severe blunt trauma (Fig. 3-21). Hyphema due to blunt trauma without an ocular perforation commonly develops into glaucoma and has a poor prognosis. A perforation may initially reseal but remains mechanically unstable and may leak intermittently. Fluid leakage may be confirmed by the Seidel test (Fig. 3-22). Rupture of the globe from blunt trauma most frequently occurs at or near the limbus. A scleral rupture site may be completely covered with conjunctiva and therefore be difficult to visualize on ophthalmic examination. A scleral rupture is suspected if the globe is very soft despite complete hyphema, and no corneal defect is visible. Scleral perforation posterior to the equator is thankfully uncommon. Extrusion of vitreous or the lens extraocularly indicates severe trauma has occurred, vision will not return, and the perforation is likely too large to repair. Enucleation of the eye should be considered to avoid sepsis and continued severe pain. Keratomalacia, or melting ulcer, presents with a very soft gelatinous appearance, but the corneal surface bulges forward and is colored blue, gray, or tan with an undulant but intact surface. Rupture of such an ulcer is recognized by a central brown-tan protrusion of iris, fibrin, and hyphema through the corneal perforation site (see Fig. 3-20, *A*). Corneal disease and rupture are discussed more extensively in Chapter 4.

DIAGNOSIS

The globe's ability to transmit a pupillary light reflex (PLR) to the other eye (i.e., consensual PLR) implies that retinal function persists; this is a positive indication that vision may be saved. An absent consensual PLR may reflect severe intraocular disease or intense miosis of the pupil and opacity of the intra-

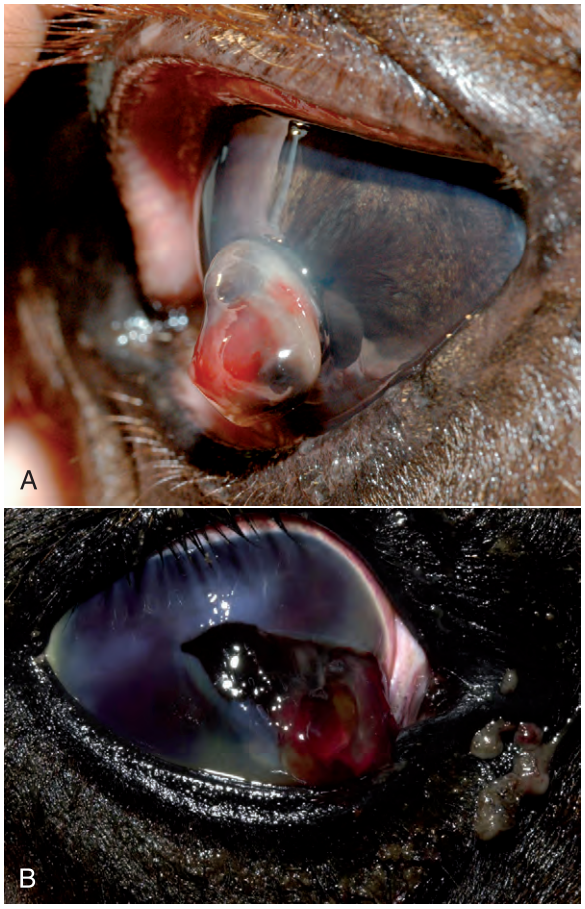


Figure 3-20. **A,** Red-tan material (fibrin, blood, iris) exiting a perforation of the cornea. The anterior chamber is collapsed, and the globe has hypotony and hyphema. **B,** Dark uveal prolapse from a horizontal linear corneal laceration.

Figure 3-21. Limbal rupture and uveal prolapse following severe blunt trauma to the eye. Note the complete hyphema.

ocular fluids. Other criteria should also be evaluated critically, such as a dazzle reflex and ocular ultrasound (see Chapter 1) to determine if surgical intervention should be aimed at preserving vision, a cosmetic globe, or enucleation. With appropriate restraint, and if not contraindicated by lack of globe integrity, cautious transpalpebral ultrasonography permits evaluation of lens and retinal position (detachment), vitreal or subretinal hemorrhage, posterior globe rupture, and possibly intraocular

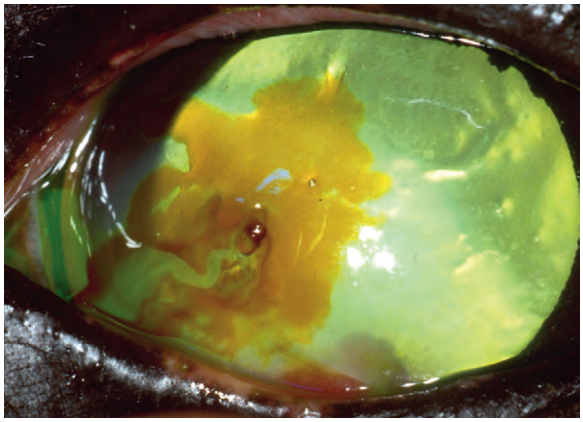


Figure 3-22. A Seidel test can be used to determine if a corneal wound is leaking aqueous humor. Concentrated, minimally diluted fluorescein is placed on the corneal surface such that the fluorescein has an orange appearance. Leaking aqueous humor will create a "river" of green, or diluted, fluorescein in the orange-concentrated fluorescein. (Photograph courtesy Dr. Dennis Brooks.)

foreign bodies. Caution is necessary to avoid complicating the injuries present. The probe position may be altered (e.g., placed laterally) to avoid complications, and even ultrasonography through the supraorbital fossa may be contributory. Radiography, especially CT, is more useful to determine the extent of fractures and whether bone displacement is present. If the patient is ataxic, depressed, or somnolent, a neurologic examination and head radiographs should be performed to confirm or refute fracture of the calvarium, which greatly impacts outcome.

TREATMENT

Treatment for globe perforations depends on the severity and prognosis for vision. Globes with a chance to regain vision (e.g., normal posterior segment, dazzle reflex, and PLR) should have the perforation(s) repaired, usually by suturing the defect and covering it with a conjunctival flap. If corneal closure is excellent and the laceration not excessive, a conjunctival flap may be bypassed to reduce long-term fibrosis. It is more difficult to close the surgical margins when they are caused by globe rupture rather than a surgical incision because of irregular directional changes (see Chapter 4). It is important to thoroughly evaluate the globe for other areas of rupture, including beneath the conjunctiva. It is not uncommon for multiple independent scleral tears to be present. A peritomy should be performed and the sclera examined in the vicinity of lacerations. If an ulcer perforates, a corneal transplant is the procedure of choice to avoid tissue distortion, and is usually supplemented by a conjunctival flap. Eyes with retinal detachments, large corneal or scleral ruptures, substantial vitreal hemorrhage, or severe endophthalmitis have very poor visual prognosis and are painful. These horses should have an intraocular or hydroxyapatite prosthesis placed or have the globe enucleated. Unfortunately, globe removal is usually associated with the least complications and cost. Nonetheless, it is remarkable the degree of trauma the globe may sustain and yet retain/regain vision and comfort after meticulous surgical repair if performed early.

LONG-TERM PROGNOSIS

The prognosis for regaining sight after corneal perforation depends on the length of the prolapse (<10 mm), whether it arose from blunt trauma or ulcer perforation, the presence of a consensual PLR, and whether the limbus is involved.[48] Severe blunt trauma to the globe usually has a worse prognosis for vision and saving the eye than sharp penetrating injuries (Fig. 3-23). Unrepaired globe lacerations have poor prognosis for maintaining a comfortable eye.

OCULAR INJURY ASSOCIATED WITH FACIAL TRAUMA

Facial trauma commonly involves ocular injury because of the prominent orbital location. The greatest risk is from lateral blunt impact. After trauma, the globe itself should be evaluated for normal motion and inflation, any possible mechanical entrapment of extraocular muscles, vision, and ocular discharge. Concurrent clinical signs to be evaluated include presence of lagophthalmos, emphysema, displacement of skull sutures/bones resulting in an open fracture, appearance of facial asymmetry or deformity, presence or absence of air flow through the nostrils, and ability to masticate and swallow. The appearance of viscous yellow fluid in the external ear in tandem with a head tilt should be regarded as a particularly serious sign.

CLINICAL APPEARANCE AND DIAGNOSIS

Globe examination should be sufficiently thorough to ensure that no serious injury is hidden by eyelid, nictitans, and surface swelling. An auriculopalpebral nerve block and sedation will likely be necessary. Initial therapy may allow a better examination within 1 or 2 hours. Diagnostics of value in determining the extent of facial trauma include palpation, oral examination, radiography with air as an inherent contrast agent, and more elaborate imaging techniques as required. Ocular ultrasonography is the alternative approach for determining whether the globe is inflated or a perforating injury has been sustained. Measurement of IOP may be of indirect value, but normal IOP does not exclude a perforating injury. Temporary closure may occur by dislodging intraocular contents into the void, and it is possible to sustain an IOP approaching normal despite slow leakage of aqueous humor, particularly if hemorrhage is extensive.

The close proximity of the orbit to the frontal, maxillary, sphenopalatine, and ethmoidal sinuses, the nasal cavity, and tooth roots provides ample opportunity for extension of trauma to adjacent cavities. Air may be introduced into the orbit and result in pneumophthalmos and subcutaneous emphysema. Aspiration occurs in a valved manner, entrapping air beneath the skin. Differentiation of anaerobic sepsis from air may be difficult, but if clinical signs are suggestive (febrile, leukocytosis, change in mentation, rapid progression), aspiration of fluid for cytologic examination and culture may be most useful. Metronidazole should be administered while test results are pending (Table 3-4).

TREATMENT

Therapy includes stabilizing the area of damage to prevent further globe injury, ensuring adequate corneal protection and lubrication, and verifying vision or identifying the need to perform decompression. If eyelid lacerations or other open skin wounds are present, they should be cleaned, clipped, and apposed if appropriate. Eyelid margin defects should be realigned cautiously to ensure that no step defect is introduced, and to prevent any sutures from abrading the corneal surface. Specific examination of the tongue is worthwhile because even extensive lacerations may pass unnoticed in the horse. Deep lacerations may require suturing, and the results may be very rewarding because of the degree of vascular perfusion.

Initial medical therapy should include aggressive systemic antiinflammatory agents (flunixin meglumine 1.1 mg/kg intravenously or orally [IV/PO]) and broad-spectrum systemic antibiotics if a skin break or sinus fracture is present

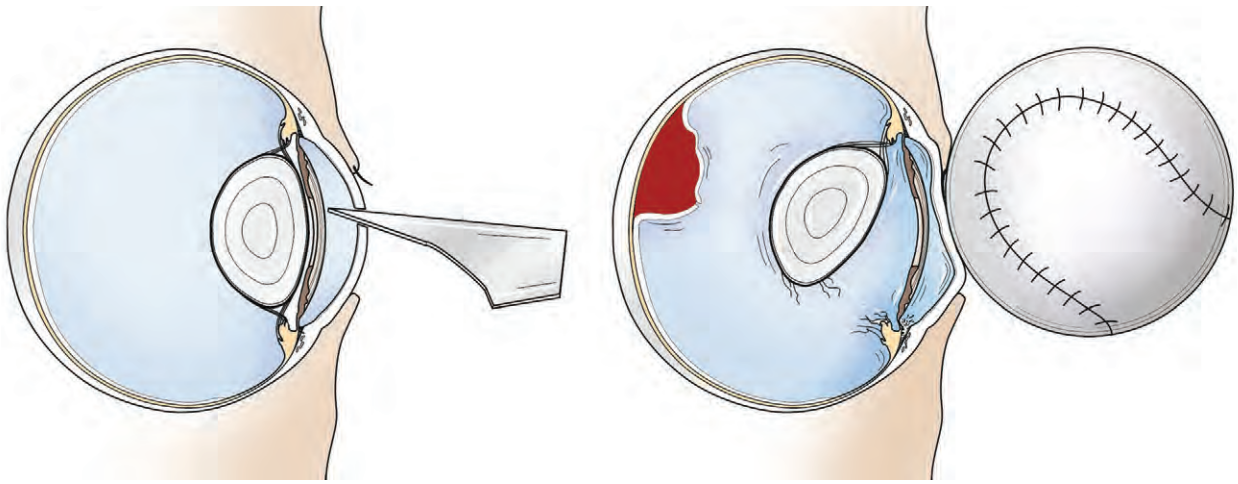


Figure 3-23. Severe blunt trauma to the globe *(right)* usually has a worse prognosis for vision and saving the eye than sharp penetrating injuries *(left)* because of intraocular damage that more commonly occurs, such as retinal detachment.

Table 3-4 | **Parenteral Medications for Orbital Disease**

MEDICATION	DOSE	NOTES
IV ANTIBIOTIC		
K-penicillin	22,000-44,000 IU/kg IV q6h	
Gentamicin	6.6 mg/kg IV, IM q24h or 3.3 mg/kg IV, IM q12h	
Ampicillin sodium (trihydrate for IM use only)	20-50 mg/kg TID	Useful if K-penicillin is unavailable
Tetracycline	5-7.5 mg/kg IV q12h	Risk of anaphylaxis; recommend dilution
ORAL ANTIBIOTIC		
Trimethoprim sulfate	15-30 mg/kg PO q12h	Broad spectrum, well tolerated
Doxycycline	10 mg/kg PO q12h	
Enrofloxacin	7.5 mg/kg PO q24h	Off-label use; if indicated on sensitivity
Metronidazole	15 mg/kg PO initial dose 7.5 mg/kg PO q6h	Occasionally indicated for anaerobic infection
ANTIINFLAMMATORY		
Flunixin meglumine (Banamine)	1.1 mg/kg PO, IM, IV q12h 0.5 mg/kg q8h	
Phenylbutazone	2.2-4.4 mg/kg PO q12h	
Aspirin	15-30 mg/kg PO q24h	Least antiinflammatory effect
GASTRIC PROTECTANT		
Omeprazole (Gastroguard)	4 mg/kg PO qd 2 mg/kg PO qd (low dose)	For individuals on chronic NSAIDs; low dose may be effective
ANTHELMINTIC		
Ivermectin	0.3 mg/kg PO	Habronemiasis
Ivermectin	1.2 mg/kg PO	May repeat at 2-3 week intervals for halicephalobiasis, resistant habronemiasis
Fenbendazole (Panacur)	10 mg/kg PO × 5 days, or 50 mg/kg PO every 3rd day	For aberrant strongyles and other nematodes

IM, Intramuscular; *IU*, international units; *IV*, intravenous; *NSAIDs*, nonsteroidal antiinflammatory drugs; *PO*, by mouth; *q6h*, every 6 hours; *q8h*, every 8 hours; *q12h*, every 12 hours; *q24h*, every 24 hours; *qd*, daily.

(see Table 3-4). Surgical interventions to repair bony and soft-tissue trauma of the orbit are discussed later in this chapter.

PENETRATING ORBITAL FOREIGN BODIES

INTRODUCTION AND CLINICAL APPEARANCE

Penetrating orbital foreign bodies such as gunshot that become lodged in the orbit may be identified by radiography, CT, and possibly ultrasonography. Organic foreign bodies are more difficult to detect but may be identified on ultrasonographic evaluation if they cast an acoustic shadow. A penetrating tract may be apparent. Orbital cellulitis may occur as a delayed complication.

TREATMENT

Metal fragments embedded in the globe may be surgically excised under general anesthesia if they are readily accessible. Foreign bodies embedded within orbital bones should be monitored and not excised unless they result in an unstable fracture, threaten vessels or other structures, or orbital cellulitis is present. Metal fragments within the orbital soft tissue should also be treated with benign neglect unless they are clinically unstable and present a risk of further damage. Gunshot is typically sterilized by the high temperature, whereas metal shards or organic materials that are lodged in the orbit should be treated with broad-spectrum systemic antibiotics as well as systemic antiinflammatories. Organic material should be removed as expeditiously as possible, and aggressive antimicrobial administration is warranted. MRI should not be performed where an intraocular foreign body may be magnetic.

LONG-TERM PROGNOSIS

The prognosis for vision is usually good unless the foreign bodies have penetrated the globe. Certain metal types may oxidize and discolor, inducing an inflammatory reaction.

ORBITAL FAT PROLAPSE

Orbital fat may herniate through weakened episcleral fascia or as a result of trauma to form a fluctuant subconjunctival mass (Fig. 3-24).[49-51] Aspiration or biopsy is recommended if the diagnosis is uncertain. Therapy is to resect the mass in toto and suture closed the conjunctival surface over the exposed area.[52] Future herniation of fat may be avoided by closure of a fascial layer beneath the conjunctiva if sufficient tissue is available.[49-51] Iatrogenic fat prolapse may follow removal of the nictitans if the resulting conjunctival and fascial wounds are not sutured, but this is easily repaired by resecting and closing the herniation site.

ORBITAL PROPTOSIS

INTRODUCTION AND CLINICAL APPEARANCE

Proptosis is the physical displacement of the globe from the orbit (Fig. 3-25). Fortunately, proptosis is an uncommon incident in horses; it is a devastating injury. If the eyelid margins become entrapped posterior to the equator of the globe, the prognosis for vision substantially worsens. Arterial flow and venous drainage are restricted, and the globe is completely exposed to mechanical trauma and corneal abrasion. Traumatic

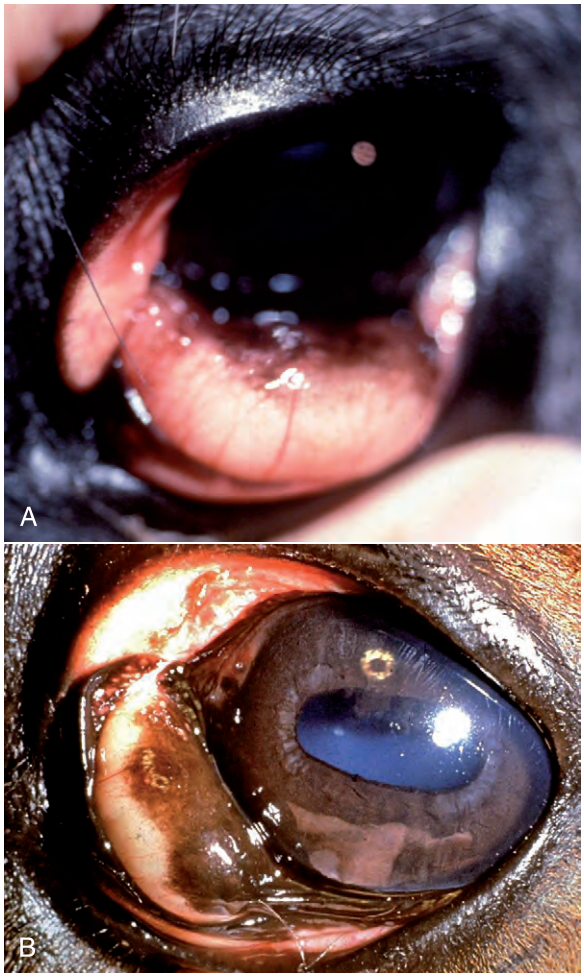


Figure 3-24. **A,** Orbital and conjunctival swelling associated with fat prolapse. **B,** Pigmented mass from fat prolapse under the third eyelid. (**A,** Courtesy Dr. Mike Davidson.)

optic neuropathy results in blindness when the optic nerve is overstretched or suffers a severe whiplash or contrecoup injury, even if proptosis does not occur. It is diagnosed funduscopically as extrusions around the optic disc and subsequently by optic nerve head atrophy (see Chapter 9).

TREATMENT

The earliest possible decompression (by performing a canthotomy if necessary) and return of the globe to the confines and protection of the orbit should be attempted. If the globe has been expelled from the orbit, sedation and extensive local anesthesia are given immediately, and a brief surgical preparation is performed. General anesthesia may be necessary for repair, but decompression of the proptosis should be performed urgently. Lidocaine 2% is administered at the lateral canthus and infiltrated along the eyelid margins. The globe should be vigorously cleansed and lubricated. A canthotomy may be performed. With adequate exposure, the fornices are examined for foreign bodies and other lacerations that require intervention. The orbital margin should be evaluated for fractures. A subpalpebral lavage system may be placed to permit medication delivery and complete tarsorrhaphy. If no other injuries are present, the globe is gradually retropulsed into the orbit using broadly applied pressure. Multiple broad tarsorrhaphy sutures are placed with stents and closed in steps to ensure complete apposition of the eyelids (see Tarsorrhaphy). The canthotomy is closed routinely. Control of ocular and orbital inflammation by systemic antiinflammatory medication is essential if vision is to be preserved (see Table 3-4). Oral corticosteroids have been advocated by some authors and may be more effective if no microbial contamination can be identified (dexamethasone 5 to 20 mg PO daily). Oral antibiotics are commonly administered. Use of topical therapy should be determined based on concurrent cornea ulceration (Table 3-5).

Table 3-5 | **Topical Medications for Globe or Orbital Disease**

LUBRICATION	FREQUENCY	SPECIAL NOTES
Artificial tears ointment	q1h-tid as needed	If excessive exposure, may become desiccated
Refresh pm	q1h-tid	More frequent administration necessary than ointment. Aids prevention of desiccation
Serum, autologous, homologous	q1h-tid	Refrigerate; viscous lubricant with anti-enzymatic properties
0.5% Hyaluronic acid	q2h-tid	Good viscosity
Hypertonic saline ointment 3% or 5%	bid-tid	If concurrent corneal edema or bullae at risk of ulceration
ANTIMICROBIAL		
Neomycin-polymyxin B-bacitracin ointment Neomycin-polymyxin B-gramicidin solution	tid-qid	Broad spectrum; rare drug-induced reaction to neomycin
Gentocin or tobramycin 0.3% solution or ointment	tid-qid	Moderate spectrum with minimal epithelial toxicity
Erythromycin ointment	tid-qid	Occasionally irritating, bacteriostatic

bid, Twice daily; *q1h*, hourly; *q2h*, every 2 hours; *qid*, 4 times daily; *tid*, 3 times daily.

LONG-TERM PROGNOSIS

Prognosis for vision is poor if the globe is displaced from the orbit, and very guarded if the eyelids are entrapped behind the globe. If the optic nerve is transected or multiple extraocular muscles are ruptured (see Fig. 3-25), enucleation or cosmetic implant should be considered.

INFECTIOUS ORBITAL DISEASE

ORBITAL CELLULITIS

Perforation by a foreign body, direct trauma, and seeding by septic emboli are among the more common causes of orbital cellulitis. The globe is at risk only in the more severe cases where therapy has been delayed or where additional complications have occurred (e.g., an orbital fracture). An initial innocuous superficial wound adjacent the orbital rim may be the only

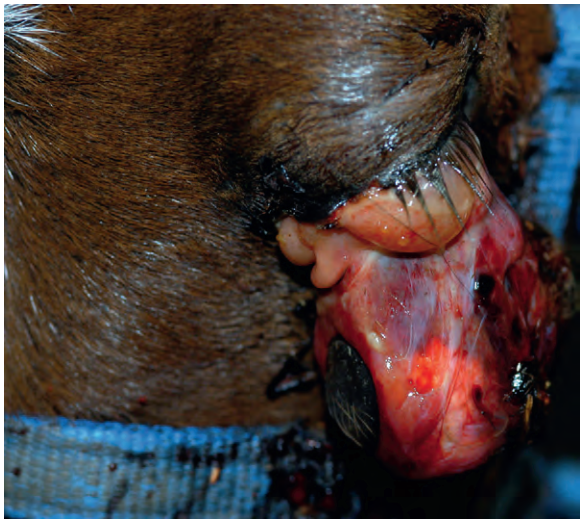


Figure 3-25. Displacement of the globe from the orbit, or proptosis, due to severe trauma. In this horse, the optic nerve and multiple extraocular muscles were transected, so the globe had to be enucleated.

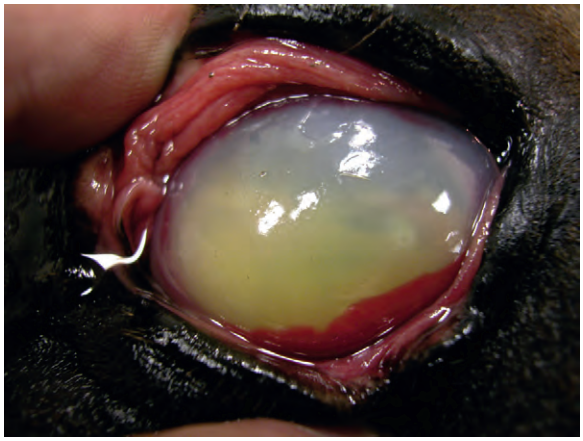


Figure 3-26. Septic panophthalmitis may extend to the orbit, resulting in exophthalmos.

external indicator and may rapidly heal. Deeper extension of the penetrating tract and sepsis subsequently result in more dramatic clinical signs. Extension of inflammatory and infectious conditions from adjacent sinuses and cavities also occurs commonly. If septic endophthalmitis is untreated or poorly responsive to therapy, it may progress to panuveitis and orbital cellulitis, in which case the etiology will be apparent. In particular, septic panophthalmitis (Fig. 3-26) may lead to devastating spread of bacterial or fungal agents; enucleation to prevent microbial colonization of deeper tissues may be necessary. In contrast, orbital cellulitis does not readily induce uveitis within the globe. A more localized chronic process will result in the formation of a true abscess rather than generalized cellulitis, so a systemic response (leukocytosis, hyperfibrinogenemia, fever) is less likely to manifest. Granulomas resulting from *Actinomyces* spp. and the nematode *Habronema* may also occur deep in the orbit. *Cryptococcus* infection is reported uncommonly in the orbit and elsewhere in the skull in horses; it should be considered as a differential diagnosis for nonresponsive orbital cellulitis.[13] Protracted therapy without attempt at removal allowed survival for 26 months in one case until the granuloma expanded through the nasal cavity and paranasal sinus and abutted the orbit.[53] *Cryptococcus* infection initiates through the respiratory or gastrointestinal tracts and travels via lymph nodes until it subsequently localizes in the orbit. Phycomycosis occurs uncommonly in the orbit, but it may spread from the guttural pouches or nasopharynx where it may result in substantial obstruction to respiration and cause secondary clinical signs by local expansion. Organisms include *Conidiobolus* and *Basidiobolus* spp. Granulomas are very persistent, locally expansive, and ultimately may be difficult to control.

CLINICAL APPEARANCE AND DIAGNOSIS

The entire orbital contents are distorted and enlarged, being forced forwards through the palpebral fissure and restrained only by the eyelids. Blepharedema or blepharitis may be severe, venous drainage may be obstructed, and epiphora may be serous or mucoid, depending on the underlying condition, and is often profuse. The nictitans is displaced anteriorly. The conjunctivae are engorged and may be displaced above the eyelid margin. If the fundus is visible ophthalmoscopically, small white exudates may be present overlying the optic nerve, where orbital cellulitis intimately involves the orbital cone. Severe exophthalmos may result in lagophthalmos. Intraocular pressure is normal until vascular compromise begins and retrobulbar tissue pressure begins to rise, which indicates an unusually severe condition. The only other aperture of the orbit is the supraorbital fossa, which may become turgidly distended. Diagnostic tests of value include a CBC to evaluate the degree of systemic inflammatory response (leukocytosis, hyperfibrinogenemia, hypergammaglobulinemia) and imaging to determine if a section of foreign body is still embedded within the orbit. Fever and general malaise may result from orbital cellulitis or even endophthalmitis; nonetheless, a thorough physical examination including thoracic rebreathing examination should be performed to identify primary or secondary disease elsewhere. Orbital ultrasonography, CT, and fine-needle aspiration may also be helpful in the diagnosis.[54,55]

TREATMENT

Antimicrobial agents should be administered systemically at the highest tolerable doses based upon diagnostic findings. Aggressive initial nonsteroidal antiinflammatory drug (NSAID) use should attenuate the high intraorbital tissue pressure and preserve globe health. Cold compresses may improve comfort and reduce local inflammation. Abscesses that are truly lined by a capsule are uncommon in the horse, but if one is identified, external surgical drainage may be established under general anesthesia,[55] with or without lavage with broad-spectrum antibiotics such as K-penicillin. Where possible, the area should be debrided of malacic material. Considerable caution is necessary to avoid iatrogenic damage, and drainage is more difficult to establish than in other domestic species. Systemic therapy is as for other cases of cellulitis.[54] Therapies proposed for pythiosis include direct intralesional injection of antifungal agents (such as amphotericin B),[56] intravenous sodium iodide and oral potassium iodide, and laser ablation. Prolonged therapy should be anticipated.

LONG-TERM PROGNOSIS

Prognosis depends on severity of disease, response to therapy, and the degree and duration of orbital vascular compromise that

arises prior to initiation of therapy. Enucleation may be necessary to control pain from persistent endophthalmitis.

PARASITIC ORBITAL DISEASE

Parasitic disease of the orbit presents as a space-occupying mass and exophthalmos. Hydatid cysts have been reported in Europe in the United Kingdom and Germany and have been associated with optic nerve atrophy and blindness.[57] Aberrant migration of other nematodes including *Strongylus vulgaris, Halicephalobus gingivalis,* and *Draschia megastoma* are more common in the central nervous system (CNS) but may be found in the orbit. *Strongylus edentatus* has been reported in the orbit.[58] *Halicephalobus gingivalis* (syn. *H. deletrix*, syn. *Micronema deletrix*) is a ubiquitous saprophytic soil nematode that appears to enter the body through damaged mucosal barriers and sporadically causes orbital, neurologic, and diffuse disease in horses and other species.[59] Invasion of the CNS is a common and grave complication. An expanding granuloma present subcutaneously at the orbital rim was successfully removed surgically and medically in one report.[60] Renal involvement is also common with halicephalobiasis. Nematodes are surrounded by macrophages, some eosinophils, a fibrous lining, and localized calcification that may be visible radiographically. *Echinococcus granulosus equinus* is not of public health significance and cycles between horses and dogs/foxes. Habronemiasis (summer sores) may cause very severe blepharoconjunctivitis, predominantly nasally, but rarely involves the orbit more deeply (see Chapter 4, Equine Ocular Adnexal and Nasolacrimal Disease).

CLINICAL APPEARANCE AND DIAGNOSIS

Clinical appearance is typical of a retrobulbar mass. History of inadequate or infrequent deworming is noteworthy. Systemic abnormalities including neurologic signs, hematuria, or other renal signs are poor signs with migrating nematode infestation. Uveitis and chorioretinitis has been reported with *H. deletrix*,[61] with diagnosis occurring after histopathologic evaluation. Urine sediment should be examined for rhabditiform nematodes.[62] Ultrasonography or CT which reveal a cystic structure are highly suspicious for a hydatid cyst of *Echinococcus* spp., and aspiration should typically be avoided to prevent dispersal of the organism.

TREATMENT

Administration of higher doses of ivermectin (see Table 3-4) is appropriate for many parasitic orbital conditions. For migrating strongyles, or where ivermectin has already been administered, very high doses of fenbendazole may be administered orally but may not be effective. Orbital hydatid cysts are ideally excised surgically with very cautious dissection to avoid inadvertent puncture and dispersal of the contents. Percutaneous aspiration has been reported as an alternative to removal[63] and should be combined with anthelmintic therapy. *Halicephalobus gingivalis* may be treated by ivermectin (1.2 mg/kg PO every 2 weeks for 3 or 4 treatments).[59] Surgical debulking is indicated if the mass is large or if it is easily accessible.

LONG-TERM PROGNOSIS

Hydatid cysts are well tolerated unless exophthalmos present, and cysts are frequently found in other organs at necropsy. Recurrence may accompany cyst rupture. Prognosis for halicephalobiasis depends on severity of disease and response to therapy. Large granulomas may cause blindness, especially if the optic nerve or retina is infiltrated. If signs of central nervous system involvement are apparent, the prognosis is very poor. Intraocular infection also carries a poor prognosis.[61]

NONINFECTIOUS INFLAMMATORY DISEASES OF THE EQUINE ORBIT

Inflammatory orbital disease is less common in horses than other domestic animals, owing in part to the greater separation from the buccal cavity and the greater bony demarcation of the orbit. Penetrating foreign bodies from the oral cavity are considerably less likely to enter into the orbit because of the length of the oral cavity. Sinusitis extending from the maxillary or frontal sinus is more common. Ethmoidal masses may also secondarily induce an inflammatory orbital condition. Control of the primary disease process together with symptomatic orbital therapy is usually sufficient. When the orbit is invaded directly, the condition is managed as a primary orbital cellulitis (see earlier).

NUTRITIONAL MYOPATHY

Uncommonly, nutritional myopathy associated with inadequate dietary selenium and/or vitamin E may result in severe myonecrosis. Cases localized to the muscles of mastication (particularly the bulky masseter) have been reported. The condition is very painful, especially upon deep palpation. A history of inadequate fresh forage and limited pasture access is typical. It has been suggested that stall confinement may protect other muscle groups and predispose the masticatory muscles.[33,64] The condition is less common than masticatory myositis in canines but equally severe.

CLINICAL APPEARANCE

A reported case presented with acutely swollen masseter and temporalis muscles, exophthalmos, passive displacement of the nictitans, and severe chemosis resulting in herniation of the conjunctiva into the palpebral fissure. Supraorbital fossae were distended. The mouth could only be opened 3 to 4 cm.[64] In general, trismus and an inability to prehend together with a distressed facial expression were apparent.

DIAGNOSIS

Clinical appearance is strongly suggestive of masticatory myositis. Other muscle groups should be evaluated, and the possibility of cardiac myositis should considered. Evaluation of the affected individual's diet, including feed analysis and blood selenium and vitamin E, will confirm the diagnosis. Serum chemistry reflects the severity of the myositis, and urine may be discolored from myoglobinuria.

TREATMENT

Treatment of nutritional myopathy entails higher-quality forage feeding, initial supplementation with selenium (25 to 50 mg), and subsequent daily selenium supplementation to reach 0.3 mcg/g of dietary intake per day. Daily oral supplementation of vitamin E (5000 to 10,000 IU PO daily) would also be reasonable. Supportive care to manage the myonecrosis includes NSAIDs, diuresis (possibly with IV fluid administration), and

warm compresses of the affected muscles. Nutritional supplementation may be necessary until normal feeding behavior is possible. In the reported case, oral dexamethasone and IV dimethyl sulfoxide (DMSO) were necessary to control the inflammation. Prognosis is poor if debilitation is present, and muscle atrophy may become profound if the patient survives.

PERIOSTITIS

INTRODUCTION AND CLINICAL APPEARANCE

Periostitis of the nasofrontal bone anastomoses/suture line may result in secondary periocular swelling and severe chemosis. Although predominantly of cosmetic interest,[65] periostitis in the region of the nasolacrimal duct may result in partial or total obstruction and secondary overflow epiphora.[66] Clinical signs may be asymmetric or unilateral. Etiology has been suggested to be instability of the junctions of the frontal, nasal, and maxillary bones, although specific traumatic history is often not identifiable.[65]

DIAGNOSIS

Radiography may be indicated to exclude a depression fracture and determine the extent of the periostitis. Age and history of the patient are important.

THERAPY

Therapy involves the use of systemic NSAIDs to control clinical signs as necessary.

PROGNOSIS

A permanent raised distortion of the suture line is likely, similar to a callus. The significance of this disorder depends on the location of the lesion and its severity but is usually cosmetic only.

OTHER INFLAMMATORY ORBITAL DISEASES

Other orbital diseases reported in other species may occur uncommonly in the horse (e.g., immune-mediated/eosinophilic myositis and pseudotumor), although they have yet to be reported in the literature. *Pseudotumor* is the term used to describe a particularly aggressive inflammatory condition of people and cats that poorly responds or is unresponsive to antiinflammatory therapy.[67-69] The pathogenesis is reminiscent of neoplasia because of its inexorable progression. Reduced retropulsion and dramatic exophthalmos may result, and enucleation may be necessary for control.

PERIORBITAL NASAL AND SINUS DISEASES

SINUSITIS

INTRODUCTION AND CLINICAL APPEARANCE

Sinusitis or empyema (i.e., purulent material within the sinus) is one of the most common nonneoplastic diseases of the equine head. Clinical signs of sinus disease, other than possible exophthalmos, includes unilateral nasal discharge, facial swelling, and decreased nasal airflow.[70] Primary bacterial sinusitis usually develops from upper respiratory tract infections.[70] Deformation or protrusion of maxillary bone may also be present, and this change is usually associated with chronic disease. In one case, exophthalmos and protrusion of the maxillary bone was observed in a 12-year-old Thoroughbred for 6 months prior to clinical evaluation.[71] In another series, three horses presenting with unilateral or bilateral blindness were found to have infectious sphenopalatine sinusitis with subsequent distension and compression of adjacent optic nerve(s) and optic chiasm.[17]

DIAGNOSIS

Diagnosis is based on typical clinical signs of sinusitis. Definitive diagnosis is made based on skull radiographs or CT. Frequently the exudate needs to be removed prior to radiology or CT to better localize the underlying cause (i.e., primary or secondary sinusitis). Sinocentesis, or sampling of the sinus fluid, should be attempted for cytologic examination and culture.[70] CT or MRI were the only antemortem diagnostic methods to diagnose sphenopalatine sinusitis in three horses with associated blindness.[17]

THERAPY

In primary infectious maxillary sinusitis, the fluid should be drained, the sinus lavaged, and appropriate systemic antimicrobial agents given. In secondary infectious sinusitis, the primary underlying disease—which may include dental disease, facial fractures, granulomatous disease, or neoplasm—should be corrected if possible.[70]

PROGNOSIS

For primary sinusitis, clearing up the disease generally makes for a good prognosis. For secondary sinusitis, prognosis depends on the underlying cause.

NASAL AND SINUS CYSTS

INTRODUCTION AND CLINICAL APPEARANCE

Maxillary sinus cysts may appear clinically similar to neoplastic masses (i.e., slow-growing, expansile) but are readily differentiated on imaging studies; they are more amenable to surgical control and removal. Cysts in the caudal maxillary sinus may result in exophthalmia.[70,72] In one report of a horse with exophthalmos, CT revealed a large demarcated mass within the caudal maxillary and conchofrontal sinuses that resulted in lysis of the sphenoid and palatine bones and extension into the retrobulbar space.[72] *Dentigerous cysts*, or cysts from the dental arcade, occur uncommonly in the horse but may result in exophthalmos or deformation of the orbit. They typically are in close approximation to the petrous temporal bone, near the base of the external ear.

DIAGNOSIS

Diagnosis is based on clinical signs, radiology, and/or CT. Dentigerous cysts have a pathognomonic appearance on radiographs.[73]

TREATMENT

Surgical resection is generally curative for sinus cysts. Sinus trephination, using a Steinmann pin and Jacobs chuck, resulted in the drainage of copious amounts of turbid, yellow fluid from the trephination site in one report.[72] A frontonasal osteoplastic

flap[74] was performed exposing a sinonasal cyst in the maxillary and chonchofrontal sinuses. Removal of the cyst was possible (histology revealed ciliated pseudostratified columnar epithelium with mucus-producing goblet cells), and no recurrence was noted.[72]

SINUS AND NASAL CAVITY NEOPLASIA

INTRODUCTION AND CLINICAL APPEARANCE

Unilateral nasal discharge, facial swelling or deformation, and epistaxis are the most common clinical signs in cases of neoplasms of the sinonasal structures.[75-77] Exophthalmos occurs in approximately 20% of cases of sinus neoplasia.[75-77] The most common neoplasms of the periorbital sinuses that cause exophthalmos are, in order of frequency, adenocarcinoma, adenoma, osteoma, squamous cell carcinoma, fibrosarcoma, undifferentiated sarcoma, lymphosarcoma, and esthesioneuroblastoma (see Table 3-3).[75-79] Exophthalmos has also been reported from nasal neoplasia. In one case, a 9-year-old Trakehner gelding had exophthalmos associated with undifferentiated nasal adenocarcinoma affecting the orbit, with metastases to the right parotid gland, cranial cervical lymph nodes, fascial planes of the neck, and lungs.[32]

DIAGNOSIS

Skull radiographs and CT are used to make a diagnosis of a sinus or nasal mass. Sinocentesis or biopsy is needed for definitive diagnosis. In one study of three sinus neoplasms, CT provided more information about the extent and severity of lesions than conventional radiography.[77]

THERAPY

Surgical excision and adjunctive radiation therapy is generally recommended.[75,76]

PROGNOSIS

The lesions are usually large and advanced with much tissue destruction prior to definitive diagnosis[77]; therefore, in general, the prognosis for elimination of the neoplasm is poor. In one series, surgical treatment alone of seven malignant neoplasms resulted in recurrence within 6 months, but four out of five benign tumors did not recur.[75]

NEOPLASIA OF THE ORBIT

Neoplasia of the equine orbit is much less common than in other domestic species. The most common neoplasias of the orbit are neuroendocrine tumors and extraadrenal paraganglioma.[12,26,80-82] Anaplastic sarcoma, lymphosarcoma (see Fig. 3-26), and squamous cell carcinoma (Fig. 3-27) are also common (see Table 3-3). Squamous cell carcinoma (SCC) of the orbit arises as an extension of neoplasia from another part of the globe. The index of suspicion is raised substantially by identifying a tumor on the globe or eyelids. Belgian and other draft breeds are at increased risk of developing SCC. Lymphosarcoma is a secondary neoplasia which is frequently more insidious and less obviously neoplastic because it frequently presents as gross blepharedema and a reduced palpebral fissure aperture. In one study, ocular lymphosarcoma represented 21 of 79 cases.[83] Eyelid involvement was recorded in 11 cases,

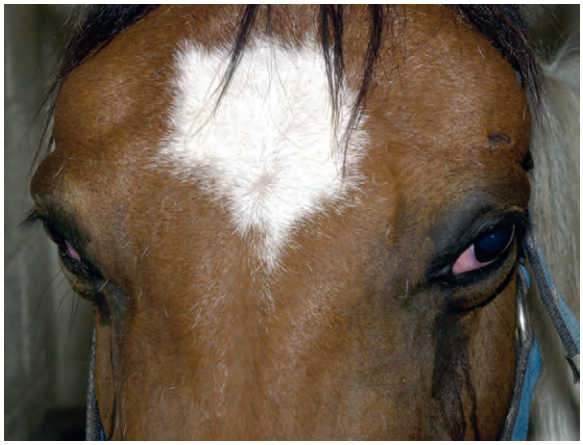


Figure 3-27. Bilateral exophthalmos in a yearling horse. Note the prominence of the nictitans, epiphora due to punctal misalignment, bulging of the supraorbital fossa, and distortion of the normal eyelid contour. Generalized lymphosarcoma was diagnosed at necropsy.

nonspecific uveitis in 4, corneoscleral masses in 2, and diffuse retrobulbar infiltration in 2. As is the case in other species, the implication is that early suspicion and confirmation of lymphosarcoma will make early therapy possible and result in an improved short- to medium-term survival for these cases. Biopsy for histopathologic evaluation should be performed early when there is clinical suspicion. Lymphosarcoma may also occur as a solitary orbital mass and proceed to rapidly enlarge and result in orbital proptosis.[84]

Other less commonly reported neoplasias of the orbit include malignant rhabdoid neoplasia, fibroma, angiosarcoma, adenocarcinoma, and primitive neuroepithelium.[19,25,32,80,85-88] See later in this chapter more information on these individual neoplasm types.

CLINICAL APPEARANCE AND DIAGNOSIS

Clinical signs of orbital neoplasia are exophthalmos, prominent displacement of the nictitans, orbital swelling, bone surface distortion (possibly with pain on palpation), strabismus if the mass is extraconal, anisocoria and/or blindness (if directly compressing the optic nerve), displacement of chemotic conjunctiva through the fissure, and less commonly, epistaxis and signs referable to the involvement of adjacent cavities (Figs. 3-28 and 3-29; see Fig. 3-27).[25,26,88] Blindness may result from intracranial compression of the optic nerve by pars intermedia masses. The tissue infiltrate may be diffuse and severe and be restricted to the orbit, or it may also be present in other locations. Clinical examination should include palpation of the orbital rim to identify evidence of periosteal reaction and bone infiltration. Local lymph nodes should be evaluated by palpation and cytology if abnormalities are suspected. Exophthalmos may be pronounced, and distortion of the eyelids and palpebral conjunctivae may be profound (see Chapter 4 for more information on primary ocular adnexal neoplasia). Exophthalmos may be the presenting complaint for neoplasia that secondarily affects the orbit but arises elsewhere, such as the sinuses. In such cases, respiratory stridor, epistaxis, purulent discharge, or a fetid odor may be present concurrently and raise clinical suspicion. CT is the best method to determine the extent of the tumor and the most appropriate treatment.[24,26,32,89] Orbital ultrasound is generally

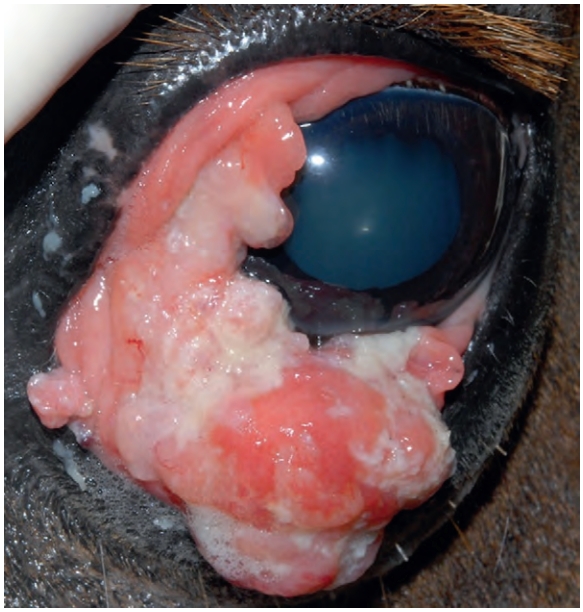


Figure 3-28. Exophthalmos from extensive medial canthus squamous cell carcinoma that has extended into the orbit.

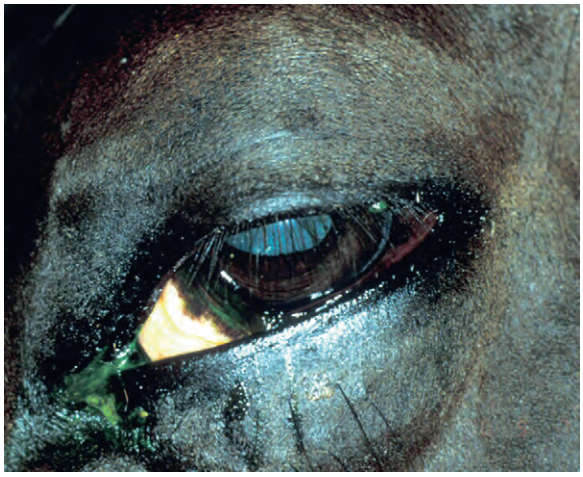


Figure 3-29. Exophthalmos, elevation of the nictitans, periorbital swelling, and dorsal strabismus with a ventral orbital mass.

only helpful in the diagnosis of orbital neoplasia to direct fine-needle aspiration for cytologic examination. A biopsy is the only definitive method to confirm the presence of neoplasia.

TREATMENT

Treatment consists of surgical removal with or without adjunctive therapies (see later in chapter for information on specific neoplasia and Chapter 4 for information on treatment of adnexal neoplasia). If therapy to preserve the globe and eyelids may be of interest to the client, early referral for imaging and surgery is strongly encouraged, and histopathologic samples should be obtained prior to initiating therapy. Current medical control of lymphoma is relatively poor but improving, and some individuals will respond well for weeks to months with aggressive use of corticosteroids and other anticancer treatment protocols. Consultation with an oncologist is warranted if therapy may be attempted.

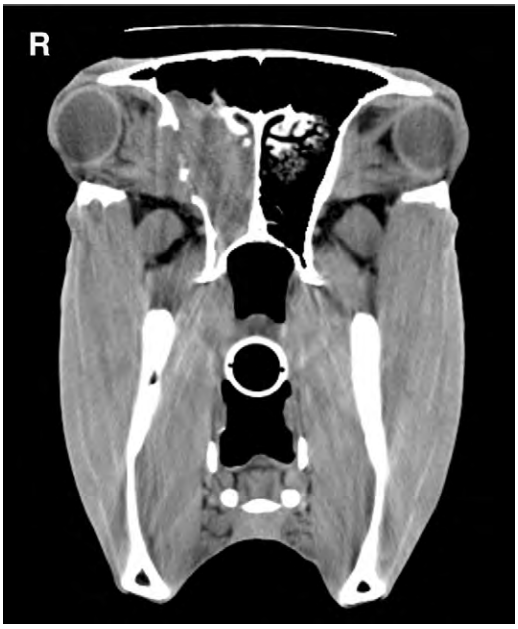


Figure 3-30. Transverse computed tomography of a horse with exophthalmos. An adenocarcinoma arose from the maxillary, sphenoid, and frontal sinuses to occupy the orbit and subsequently invaded the calvarium.

PROGNOSIS

Progress of the disease may be relatively rapid from the point at which the tumor is first recognized as a clinical problem, because the tumor may become quite advanced within the extensive capacity of the equine orbit before clinical signs are apparent. Similarly, masses within the sinus and nasal cavities have considerable space for local expansion prior to gross deviation of the skull surface or exophthalmos occurs. Consequently, when the tumor becomes overt, much of the normal physiologic function has already been compromised. This is an issue when palliative care and nursing might be an option to allow a short extension in a breeding career, or to reach and survive the exertions of foaling.

SPECIFIC ORBITAL NEOPLASIA

NASAL AND ORBITAL ADENOCARCINOMA

Extensive nasal and orbital adenocarcinoma can cause exophthalmos, strabismus, loss of physiologic nystagmus, and neurologic signs.[32] A grave prognosis should be attached to secondary metastases to the orbit that also induce neurologic signs and/or any paraneoplastic syndrome. In one reported case,[32] CT revealed that the mass arose from the maxillary, sphenoid, and frontal sinuses to occupy the orbit and subsequently invade the calvarium (Fig. 3-30). Imaging confirmed parenchymal brain involvement and avoided subjecting the patient to an impossible surgery. Of significance, metastasis was identified in the parotid gland and in fascial planes to the thorax, although no evidence of such involvement was present antemortem. The cranial cervical lymph nodes were infiltrated. This case underscores the importance of imaging and consideration of distant metastases as well as local extension. Thorough palpation may not evidence even sizeable masses, but

aspiration and cytology should be performed if even subtle asymmetries are identified on palpation. Thoracic radiography may be of value to identify masses, but negative findings do not exclude metastasis.[32] Adenocarcinoma of the frontal sinus in a 15-year-old horse expanded through the cribriform plate to enter the orbit and result in exophthalmos.[16] Adenocarcinomas of respiratory epithelium are typically very aggressive in horses, and the delay to diagnosis which occurs while the tumor expands to completely occupy the sinus permits substantial destruction before the tumor is manifest. Prognosis is particularly poor when multiple structures are involved.

Neuroendocrine tumors may occur more commonly than previously thought[26,80,81] and are the most common orbital neoplasia reported in the literature (see Table 3-3). Neuroendocrine tumors, including extraadrenal paragangliomas and undifferentiated neuroendocrine tumors, were the neoplasms identified in six of seven (86%) horses evaluated for primary orbital disease in one study.[26] These horses exhibited nonpainful exophthalmia, and two had anisocoria and dilation of the pupil of the affected eye. Neuroendocrine tumors of the orbit grow slowly, and metastasis is rare. Recurrence within the orbit is also rare after exenteration.[26,80] Caution is recommended during surgery; reports of severe intraoperative hemorrhage and a decrease in mean arterial blood pressure, possibly from handling the neoplastic tissue, are commonly encountered during exenteration.[26,80] The site of origin may be hard to define because the tumors often involve the orbit, nasal cavity, and paranasal sinus by the time of diagnosis.[12]

Osteosarcoma occurs uncommonly and is typically associated with early distortion of the bone surface. It has been reported with dramatic distortion of the frontal bone, and radiographic studies are confirmatory.[84]

Melanoma of ocular tissues is frequently benign, and primary excision is curative. However, a subset of these tumors is aggressively recurrent and may invade the orbit. A conjunctival melanoma recurred twice, necessitating orbital exenteration that was curative for at least 5 years.[90] Specific typing of cell surface receptors may permit identification of more aggressive melanoma types and indicate which individuals require close scrutiny postoperatively. Another report of melanoma invading the extraocular muscles appeared to arise from the globe.[91] A melanoma of the periorbital sinuses has also been reported.[75]

ANGIOSARCOMAS AND HEMANGIOSARCOMAS

A case of medial canthal hemangiosarcoma progressed to invade the orbit and maxillary sinus in one individual.[92] Hemangiosarcoma more frequently arises from the globe surface temporally, but it may rapidly progress caudally and perforate the fascial tunics to invade the orbit. An angiosarcoma of the eyelids in one report resulted in exophthalmos.[93]

A case report of a malignant rhabdoid tumor was treated with exenteration in a 2-year-old filly.[94] The tumor was present multifocally within the globe and orbit and had spread to lymph nodes, salivary glands, and locally within the subcutaneous tissues of the head.

Medulloepithelioma may involve the orbit in young horses, resulting in exophthalmos and intraocular distortion. Medulloepitheliomas also may arise from the uveal tract and optic nerve and require exenteration.[85,87,95]

Meningioma occurs rarely in horses as a neoplastic cause of blindness. It may become bilateral because the neoplasm often arises close to the optic chiasm. One report involved the tumor obliterating the maxillary, frontal, and sphenopalatine sinuses, but it did not invade the calvarium.[78] The diagnosis in that horse was made histologically. Nervous-tissue tumors in horses are predominantly peripheral, and the risk reaches a peak at just 4 to 6 years of age and remains stable thereafter.[96]

IATROGENIC ORBITAL DISEASE

GUTTURAL POUCH DISEASE

Guttural pouch disease in the horse may be remarkably difficult to contain and resolve. Guttural pouch empyema continues to be a challenging condition, and its therapy often involves mechanical as well as antimicrobial therapies. The use of formalin injection has been advocated for many years and undoubtedly has resulted in control of clinical cases. However, it is important to advise the client that thrombosis of the ophthalmic artery is a possible complication, which is quite likely to result in blindness. Specific cases of severe endophthalmitis have resulted from the occlusion of the internal carotid artery, requiring enucleation to achieve control of severe pain (Fig. 3-31). Surgical occlusion of the external and internal carotid and greater palatine arteries for the treatment of guttural pouch mycosis may cause ischemic optic neuropathy and blindness.[97] However, no ocular complications were observed in clinical or experimental animals treated with transarterial coil embolization of the internal and external carotid to prevent hemorrhage associated with guttural pouch infection.[98]

Direct extension of guttural pouch disease is less common, but a case of guttural pouch mycosis resulted in blindness due to expansion of the plaque to involve the optic nerve and optic chiasm within the calvarium as well as the retina and orbit.[99]

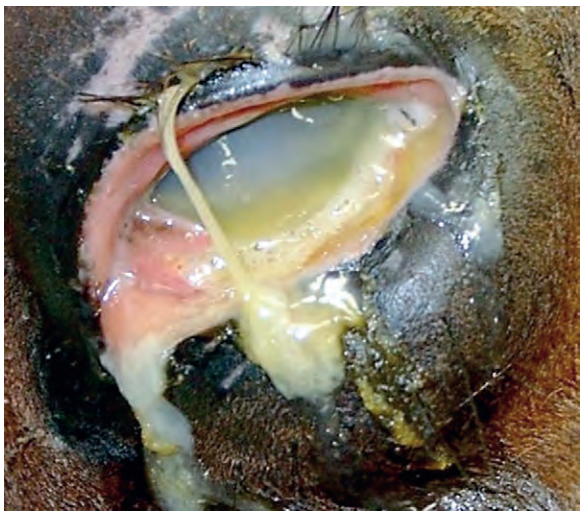


Figure 3-31. Severe endophthalmitis following use of formalin injection for treatment of guttural pouch empyema.

GENERAL THERAPY OF ORBITAL DISEASE

TOPICAL MEDICATIONS

Corneal complications of orbital disease are relatively common and may be addressed by frequent use of topical ophthalmic ointment or solutions (see Table 3-4). If the epithelial surface is intact, protecting the ocular surface tissues with ointment formulations to prevent complications from exophthalmos and possibly lagophthalmos becomes of substantial importance. Failure to adequately lubricate the cornea results in desiccation, trauma, and ulceration that may progress to stromal loss and even globe perforation. Topical ointments are preferred to solutions for increased coating ability. Petroleum-based lubricants are ideal if exposure is the primary indication. However, if exposure is sufficient to result in desiccation of the ointment base between administration, then a gel-based lubricant should be used in addition. If lagophthalmos is significant, support beyond medical therapy is likely to be necessary unless the lagophthalmos will rapidly resolve.

SYSTEMIC MEDICATIONS

The parenteral antibiotic of choice in horses with suspected or confirmed sepsis is injectable K-penicillin (22,000 to 44,000 IU/kg IV 4 times daily) in combination with gentamicin (3.3 mg/kg IV twice daily or 6.6 mg/kg IV 4 times daily [see Table 3-5]). This combination results in very broad-spectrum antimicrobial coverage with excellent distribution to the orbit and globe. The combination is also excellent when emergency anesthesia and surgery are required, although K-penicillin is preferentially given as far in advance of anesthesia induction as possible to avoid complications from hypotension. When K-penicillin is unavailable, ampicillin sodium may be used in horses (20 to 50 mg/kg IV 3 to 4 times daily). The trihydrate form of ampicillin should not be used intravenously. Procaine penicillin requires less frequent administration, but the typical volume of injection (30 to 35 mL) requires distribution over at least two sites and is generally a poor choice for long-term use. Gentamicin has broad effects against gram-negative and some gram-positive bacteria. Dosing may be varied, with the high peak and low trough of once-daily dosing preferred in individuals with no contraindications (e.g., renal disease). Enrofloxacin (7.5 mg/kg every 24 hours) has been reported to have good ocular and presumably orbital penetration.[100]

For prophylactic antimicrobial therapy, less intensive therapy is usually adequate. Oral antibiotics that achieve good tissue concentrations include trimethoprim sulfonamide (15 to 20 mg/kg PO twice daily), which is moderately broad spectrum and readily tolerated, particularly for intermediate and long-term use. Oral doxycycline (10 mg/kg PO twice daily) is also well-tolerated, but use for orbital disease is not indicated unless sensitivity is confirmed. Doxycycline should not be administered intravenously in horses. Tetracycline is more broad spectrum and may be preferred in cases of orbital cellulitis. Caution should be used with intravenous use of tetracycline in horses to avoid anaphylaxis, and dilution in a moderate volume (100 to 500 mL) of saline has been recommended. All orally administered antibiotics in horses may result in diarrhea and bacterial overgrowth that requires veterinary attention. Clients should be advised to report if complications arise with their use.

Antibiotics against anaerobic bacteria are rather limited in horses, but metronidazole (15 mg/kg PO initial dose, then 7.5 mg/kg PO 4 times daily) is generally very well tolerated by oral administration. Use is reserved for confirmed or highly suspicious cases of cellulitis or where evidence of gas production is present. It may be used rectally in individuals with gastrointestinal intolerance.

SURGERY OF THE ORBIT

TARSORRHAPHY

Indications for tarsorrhaphy are facial nerve trauma (temporary or permanent), neuroparalytic keratitis, exophthalmos, lagophthalmos, keratoconjunctivitis sicca, and post ocular surgical intervention (i.e., protect the eye during recovery from general anesthesia). A variety of methods has been recommended, but multiple horizontal mattress sutures without the presence of a stent is preferred. The tarsorrhaphy suture enters the eyelid 3 to 5 mm from the margin, exits through the gray line of the meibomian gland orifices, and traverses the opposite eyelid in a symmetric manner (Fig. 3-32). Suture material of choice is a nonabsorbable 5-0 or 6-0, such as surgical nylon. If there is tension, a stent may be used on either side of the eyelid and may include use of rubber bands, sections of intravenous tubing, or a section of surgical drain material.

RETROBULBAR BLOCKADE

A retrobulbar block is highly recommended in any case of orbital surgery, especially where removal of the globe or evisceration is being performed. The block keeps the eye from moving during the procedure and provides analgesia during and after surgery. The procedure is outlined in detail in Chapter 1.

ORBITAL EXPLORATION

Orbital exploration is indicated to identify, sample, and/or remove masses of the equine orbit; to reduce fractures and reverse globe entrapment; to extract foreign bodies; and to investigate nonspecific causes of general orbital disease such as exophthalmos, nictitans prolapse, and generalized tissue displacement.[25,46,101,102] The decision to perform an orbital exploratory should not be undertaken lightly. It behooves the surgeon to consider the potential lesions to be encountered and the surgical manipulations and skills that may be required, and to assimilate as many diagnostic results as are available before anesthesia induction. Surgery of the orbit for exploratory purposes may be challenging and requires advance planning and a surgical text for reference. Also of value are an anatomy atlas and a skull to aid in three-dimensional mental reconstruction of the lesion, its access routes, and its removal. CT or MRI imaging is strongly recommended prior to any orbital procedure in the horse to fully determine the extent of the lesion preoperatively.[26,32] Minor procedures to remove an apparent anterior mass are seldom challenging, but resection and repositioning bone segments, restoring distorted anatomy, and extraction of embedded neoplastic masses while preserving a functional globe are challenging for any surgeon. Specific orthopedic instruments may be necessary to elevate the periosteum, to perform an orbitectomy, and to remove affected areas

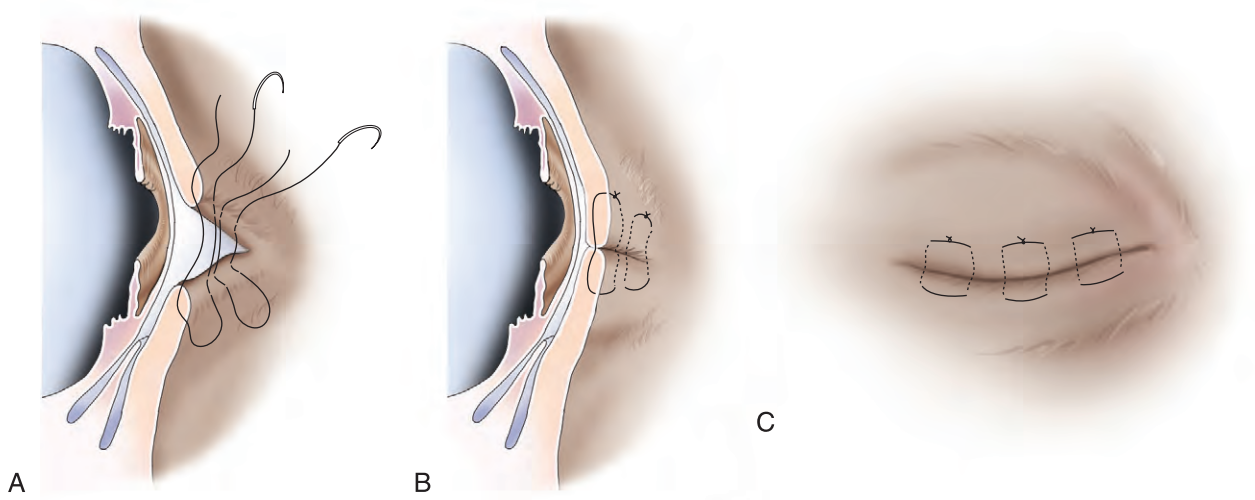


Figure 3-32. Temporary tarsorrhaphy for temporary protection of the cornea. The tarsorrhaphy horizontal mattress suture enters the eyelid 3 to 5 mm from the margin, exits through the gray line of the meibomian gland orifices, and traverses the opposite eyelid in a symmetric manner. Suture material of choice is a nonabsorbable 5-0 or 6-0, such as surgical nylon.

of bone. Ancillary equipment will frequently be necessary to control the pathology—for example, cryosurgery to limit the expansion or persistence of neoplastic cells. The most aggressive surgical resection is to elevate the periosteum in an attempt to remove the lesion in toto. This requires a meticulous surgical approach, careful dissection, and attention to preventing contamination of the surgical procedure. If the pathology has already breached the surgical containment, the risk of tumor recurrence or persisting infection is raised substantially.

Exploration of the equine orbit is rarely performed because of the complex nature of the anatomic structures, together with its infrequent indication. Typically when exophthalmos is present in an older horse, suggesting an intraorbital mass, imaging reveals the mass to be sufficiently large that surgical debulking is either not reasonable or would also require concurrent removal of the globe. This procedure is described as *exenteration* and is considered a radical reduction of the orbital bulk in an effort to extend a comfortable life (see later section).

Orbital exploration would be indicated in a younger individual to identify, locate, and remove a mass. Examples of suitable lesions would be parasitic cysts or granulomas, encapsulated orbital abscesses, foreign bodies, circumscribed neoplasia, cystic dilation of the nasolacrimal or salivary apparatus such as the zygomatic gland, or a restrictive mass encircling the optic cone and resulting in secondary ocular disease, glaucoma, and possibly blindness.

The approach to the orbit for exploration depends on the expected location of the mass. Extraconal masses displace the globe and assist in localization. This area should then be subjected to advanced imaging techniques such as CT, MRI, or even contrast radiography with air or a radiopaque fluid. Ultrasonography rarely is diagnostic and does not allow determination of the extent of the lesion. Diagnostic orbitotomy is uncommon and risks extensive anesthesia and surgical time and dissection, but it may be necessary if more advanced imaging is unavailable. All tissues removed should be examined by histopathology, tissue imprints (cytology), and culture as appropriate.

Access to the deeper orbit is problematic because of the complete bony orbit. A dorsal orbitotomy approach[80] was reported to remove retrobulbar neuroendocrine tumors in three horses. A curvilinear skin incision is made just lateral to the sagittal crest of the frontal and parietal bones, traveling laterally beyond the zygomatic process of the frontal bone. Retraction of the temporalis muscle attachments exposes the extraocular muscle cone ventrally deep within the orbit. As an alternative, the zygomatic process of the frontal bone may be resected in section by an oscillating bone saw (or osteotome) with appropriate caution to avoid severing the neurovascular bundle within the supraorbital foramen.[102] This step exposes the dorsolateral globe and orbital contents, and the operating window may be further extended by performing a lateral canthotomy. The skin incision is made parallel to the zygomatic process of the frontal bone, cautiously incising to avoid sectioning nerve fibers that enter the orbicularis oculi laterally. The periosteum is incised anteriorly and reflected off, preserving it to permit its closure at the conclusion of the procedure. The zygomatic process is removed in an elongate section sufficient to expose the area of interest, after predrilling 20-gauge holes for its subsequent reattachment. Stay sutures may be placed around ocular muscles to permit gentle retraction and dissection of the globe and cone from the mass. Culture and biopsy for histopathologic examination may be obtained. If the mass is to be removed in its entirety, cautious dissection should be performed to avoid inadvertent transection of the myriad vessels, nerves, and muscle attachments. Multiple layers of connective tissue are present in the orbit to maintain its precise alignment and function. Thus, prior to surgical intervention, it is worthwhile to precisely locate the mass within the orbit and determine whether it is intraconal, extraconal, or subperiosteal within the orbit. At the conclusion of the surgical procedure, the zygomatic process is repositioned and fixated with stainless steel surgical wire (20 gauge). Periosteal closure may be performed with simple interrupted absorbable suture in size 4-0 to 5-0. A subcutaneous closure is performed in like manner. The skin is reapposed with simple interrupted or cruciate nonabsorbable

sutures. If a canthotomy was performed, it is closed starting at the eyelid margin with a buried deep layer, and a skin layer that incorporates a figure-8 suture at the canthus. These sutures should be retained for 2 to 3 weeks to avoid subsequent dehiscence, because the site is mobile.

ORBITAL FRACTURE

Fractures of the orbital rim are a potentially globe-threatening disease that may result in displacement, impingement, functional restriction, or laceration of the globe. Hemorrhage and increased tissue volume may compress the globe or its vascular channels. Most commonly, the dorsal orbital rim is fractured and is often diagnosed by observation and palpation (Fig. 3-33; see Fig. 3-19). The fractured area may be quite painful, and care is indicated to avoid complicating the injury. Inferior orbital rim fractures may occur from blunt trauma due to polo balls or mallets, excessive disciplining, injuries in stalls, transportation, or pasture turnout. Fracture of the lacrimal bone threatens the integrity of the nasolacrimal duct. Fractures that are more extensive result from vehicular accidents and excess struggling in a panicked individual. If the injury involved rearing or falling over backwards, damage to the poll may entail fractures to the basioccipital and consequently basisphenoid bone in the inner orbit. This can result in blindness if it involves the sphenoid foramina, and probably epistaxis if the cranial fractures continue rostrally. Dissecting fracture is most at risk in individuals less than 5 years old, because the occipitosphenoid suture line remains incomplete until that time,[73] and concussive force separates preferentially along that line. This area is particularly hard to diagnose and image with radiographs but is readily apparent on CT. A complete neurologic examination may assist in determining the location of damage. When internal fractures are present, the demeanor and alertness of the patient are often reduced if the calvarium is traumatized and central nervous system damage occurs, which concurrently worsens the prognosis.

Imaging by radiography, and preferably CT, should be performed prior to initiating surgical intervention. Skyline views are helpful for the orbital rim but may be challenging to attain over the sinus (see Fig. 3-6). In fact, one study reported that digital palpation was better for diagnosis of orbital fractures than radiology.[103] Despite this, the extent of the fracture may be greater than anticipated from the imaged margins, and a complete evaluation of the injury is necessary before determining the ideal method of fixation. A CT scan is nearly always recommended when orbital fractures are present. The extent of the fractures and damage are readily visualized (Fig. 3-34).

When the ultimate cosmetic outcome is desired, closed fracture reduction is highly desirable. Under general anesthesia, zygomatic process fractures may be reduced by manipulation of the bone piece into position using a bone hook.[103] More

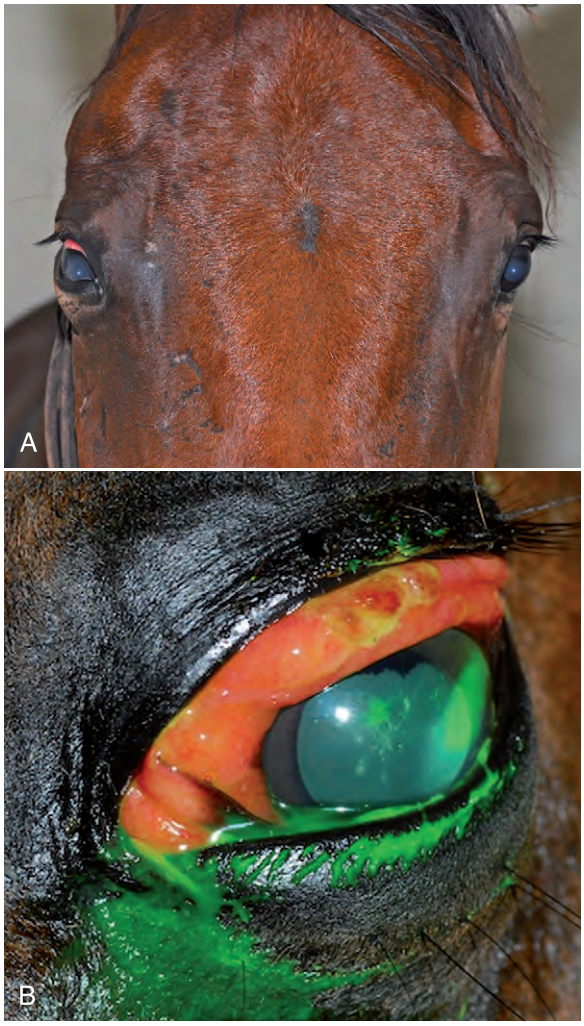


Figure 3-33. A, Horse with a depressed dorsal orbital rim fracture resulting in a ventral displacement of the globe. **B,** Horse with dorsal orbital rim fracture with resulting exophthalmos, severe conjunctival swelling, and exposure keratitis.

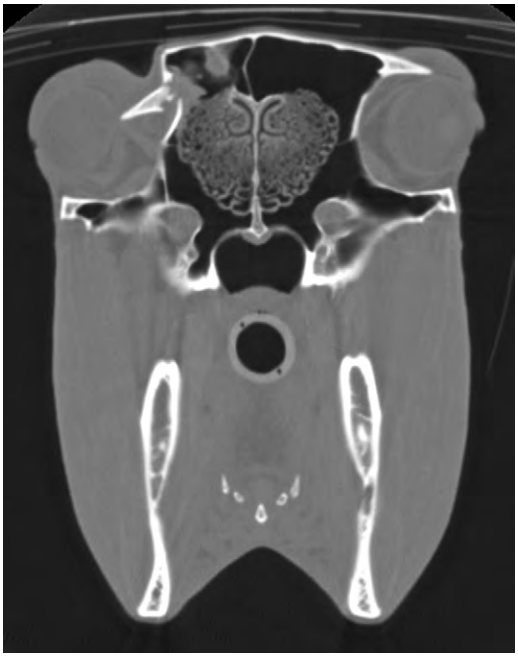


Figure 3-34. Transverse computed tomography (CT) of a horse with a displaced fracture of the dorsal orbital rim that is impinging on the globe. CT scans are the best imaging modality to determine the location of the fractures and extent of injury.

complex fractures of the dorsal orbital rim may be reduced with a malleable plate or bone plate.[104] If the fracture is repaired by open technique or if an implant is used, parenteral antibiotics are administered. Alignment of the orbital rim is attained more accurately if local tissue inflammation has been attenuated by systemic medications and local compression. Surgical intervention should be initiated early before callus formation becomes significant. Callus formation initiates very rapidly and may be well established at 7 to 10 days. Early stages of second-intention healing are typically advanced by 1 or 2 weeks.[101,103] Fractures of the orbital margin may immediately result in sequelae that require surgical intervention to prevent blinding and painful damage to the globe itself. Entrapment of the ocular muscles, venous stasis, unstable fragment edges, and laceration of blood vessels may necessitate surgical intervention to stabilize the orbit and globe by decompressing the orbit and removing or repositioning the displaced bones (Fig. 3-35).

Fractures of the skull's flat bones may be categorized as displaced or nondisplaced, and either open or closed. Closed nondisplaced fractures, together with some closed displaced fractures, are frequently permitted to heal by second intention. Depressed fractures may be realigned by drilling a 2- to 3-mm hole in the bone fragment and inserting angled surgical wire or an instrument to elevate the bone fragment into position. Frequently it is unnecessary to provide fixation when repositioned, but fixation with 20-gauge wire is appropriate if necessary. In most situations, cosmetic outcome is near perfect. Flat bones are likely to heal rapidly and pose little risk of complication if not exposed to further stress and extension of the fracture. Stall rest and limited athletic exercise are indicated, together with control of inflammation. Commonly, emphysema occurs, which may be monitored for stabilization and treated with parenteral antibiotics because of the open sinus. Fracture pieces may alter position from day to day despite the large bulk of the equine skull. Such motion does not necessarily imply an unstable fracture, but it should be monitored to ensure that the fragment lines are not progressing. Fractures of the flat bones adjacent to the orbital rim seldom jeopardize the globe. However, if the zygomatic or palatine is fractured, the orbital floor may capsize at the time of fracture, and the globe becomes ventrally displaced.

When surgical repair is indicated or the fracture is open, it should be approached with a curvilinear skin incision to provide adequate exposure adjacent to the site, with careful dissection to the location of the fracture. Acute open fractures should be clipped and surgically prepared and any necrotic or poorly viable skin and subcutaneous tissue removed. The exposed surfaces are flushed copiously with sterile saline or dilute povidone iodine, which may be administered via a pressure bag if desired, if appropriate measures to avoid further spread of contaminants are taken. Exposed bone should be débrided aggressively to ensure a healthy vascular supply.

Fractures that expose the periorbital sinuses may result in emphysema and epistaxis. Sinus fractures are considered open wounds and should be treated aggressively. If hemorrhage is substantial, prophylactic irrigation with saline (possibly with pressure bag) followed with antibiotic solution is appropriate. A drain may be placed if there is any evidence of infection (purulent exudate, cytologic evidence of bacteria or fungus). Alternatively, comprehensive parenteral antimicrobials and healing by second intention may be elected if displacement is minimal, because healing is typically rapid. Tetanus vaccination status should be evaluated, and tetanus antitoxin or toxoid administered as appropriate. The sinus egress should be verified, and if drainage is inadequate, the opening into the nasal cavity should be enhanced or an indwelling drain established. Microbial colonization of clotted hemorrhage within the sinus may lead to severe sinusitis.

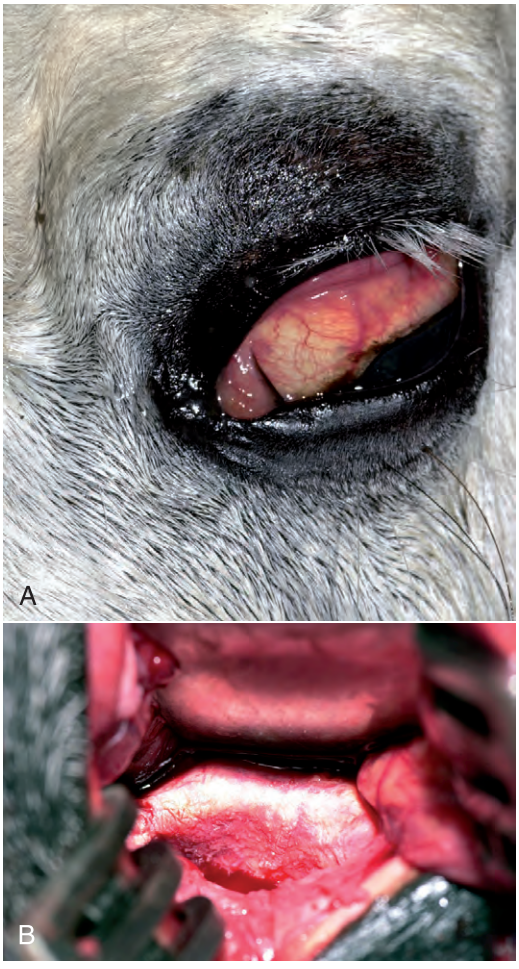


Figure 3-35. **A,** Orbital fracture resulting in ventral strabismus from bone fragments impinging on the globe and extraocular muscles. **B,** Ventral transconjunctival approach to the orbit for removal of bone fragments that are impinging on the extraocular muscles.

SOFT-TISSUE DAMAGE

Initial soft-tissue injuries should be treated aggressively with systemic antiinflammatory agents together with antibiotics if an open wound is present (see Table 3-4). Cold compresses and compression bandages limit tissue volume expansion immediately post injury, which permits more accurate evaluation and reconstruction. Thorough cleansing and minor débridement are an important component of first aid care, but if the orbit itself is open, caution is warranted to avoid introducing noxious fluids, cleansing agents, or petroleum-based products that may incite an aggressive inflammatory response.

Avulsion of ocular muscles may be repaired in the acute stages if local inflammation is adequately controlled. Alternatively, repair may be delayed by 1 to 2 weeks, during which antiinflammatory therapy is administered. The muscle may be avulsed completely or be strained and lose its mechanical leverage. If the injury is very chronic, an avulsed muscle becomes fibrotic and is too short and mechanically ineffective to reattach. Reattachment of the muscle should be performed with a suture pattern designed to resist tearing or shearing. Sutures are placed adjacent to the original insertion with absorbable material such as 5-0 polyglactin 910. If the muscle and tendon are still inserted but are strained, it may only be necessary to imbricate the weakened tendinous attachment to achieve more normal globe position and restore function. It is often necessary to overcorrect the positional defect at surgery because of the tendency for the suture to loosen during resolution of the inflammation. Exposure of orbit contents, which is predominantly fat, may be resected and the fascial layers reapposed over the surface before closing the conjunctival layer.

Eyelid repair may also be necessary to restore a functional margin without step defect and to minimize cicatricial sequelae in the conjunctiva. Minor damage to the nictitans free margin is common in extensive trauma, and options are either repair with buried sutures or resection. Exposed cartilage poses a minor threat to corneal abrasion. Nasolacrimal duct laceration may be the most challenging to repair functionally. If stricture results, a new drainage conduit may be created into the adjacent sinus. Surgical intervention in the eyelid is reviewed in detail in Chapter 4.

ENUCLEATION

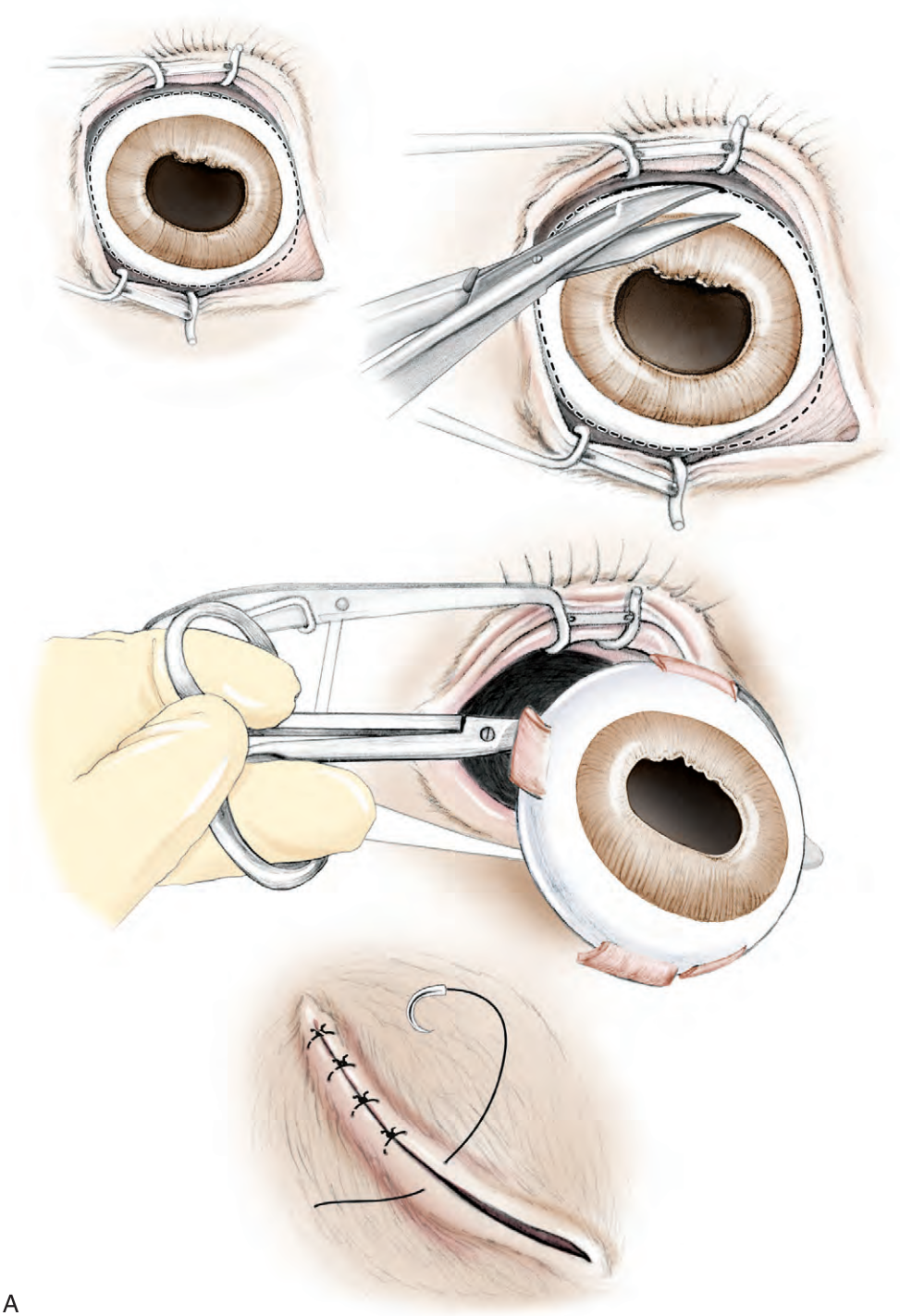
Enucleation is indicated for the removal of a painful, blind, deformed, or traumatized eye or where extensive neoplasia or infection renders survival of the globe unlikely or requires unreasonable duress for the patient. In some situations where only a single anesthesia is tolerable and the ipsilateral globe is visual, enucleation may be preferable to treatment of advanced disease. In individuals considered to be high-risk anesthesia candidates or who will not tolerate frequent medications, and for those where greater economic expenditure is not possible, removal of the globe is a rapid method to restore comfort and avoid further adverse sequelae. Enucleation may be the only humane intervention, but it is important to ensure that the anesthesia and postoperative recovery are not of greater risk than the discomfort of the presenting condition. Removal of an equine globe is a major undertaking, and it should rarely if ever be considered in a nonanesthetized individual,[105] and even then, only with appropriate preoperative planning, aggressive analgesia, sedation, restraint, and appropriate counseling of the client and assisting staff.

A brief candid discussion with the client about alternatives to enucleation is warranted before surgery. All alternatives to enucleation require ongoing maintenance care and have a greater incidence and spectrum of complications, as well as a larger initial and recurring financial investment. For the majority of horses, enucleation remains the most appropriate selection. However, while the client may not initially contemplate cosmetic alternatives, it should be offered to avoid the uncomfortable discussion later that another procedure would have been preferred if it had been made available. The only postoperative cosmetic alteration that can be performed is implantation of an orbital prosthesis beneath a closed palpebral fissure. Cosmetic alternatives to enucleation are detailed later in this chapter.

The techniques for enucleation have varied little in recent years, and the major approaches reflect the reason for removing the globe. If neoplasia or severe infection is present, the preferred technique is a closed transpalpebral method (Fig. 3-36). If the ocular disease is contained within the globe or does not threaten the orbit, a transconjunctival approach is simpler, more easily performed, and results in less surgical trauma (see Fig. 3-36). Postoperative pain and inflammation are also reduced, because fewer tissue planes are interrupted. Routine preparation includes general cleansing of the face, surgical clipping of a 1- to 2-inch margin around the eyelids (in preference to shaving), removal of the eyelashes and possibly the vibrissae, and performing a surgical scrub of the skin with baby shampoo, chlorhexidine, or Betadine scrub. Because of its epitheliotoxic effects, detergent is normally avoided on the globe, but it is not of concern in this procedure. The ocular surfaces may be cleansed with dilute povidone iodine and flushed with sterile saline. The head is typically positioned laterally, preferably with the nose elevated to level the orbit, and the surgeon seated on the dorsal side. Routine draping is performed to establish a sterile field. A retrobulbar block is recommended (see Chapter 1) to improve anesthetic stability and reduce postoperative discomfort and intraoperative hemorrhage. Local auriculopalpebral and sensory nerve blocks may also be performed, together with topical proparacaine and phenylephrine. Local anesthesia greatly reduces reliance on general anesthesia and has a more profound effect on pain awareness, thus permitting a generally lighter anesthesia plane.

The transconjunctival enucleation is initiated with placement of an eyelid speculum, and a short lateral canthotomy is performed (see Fig. 3-36). A complete peritomy is completed adjacent to the limbus. The extraocular muscles are identified and resected at the globe, permitting its free rotation. The retrobulbar attachments of the recti muscles are very extensive and are resected blindly. The optic nerve should never be clamped or ligated; instead, if necessary, the orbit may be temporarily packed with gauze and pressure applied to control bleeding. The nictitans may be removed concurrently with the globe or subsequently. To avoid subsequent dehiscence due to lacrimal secretions, it is imperative to not retain the nictitans within the orbit. In contrast, the lacrimal gland is rarely removed and typically somewhat difficult to identify. The orbital contents should always be inspected to ensure that no pathology remains. Capillary seepage is ubiquitous, but it should not preclude inspection of the orbit. Normal contents include moderate amounts of fat interspersed between fascial layers, the ocular muscles, and periorbitum. The orbit may be flushed with saline and temporarily packed with sterile gauze. The conjunctiva is separated from the eyelid and Tenon's capsule, and the eyelid margin is resected from lateral to medial. Care is exercised to ensure the medial canthus is completely excised, while avoiding the angularis oculi vein just below.

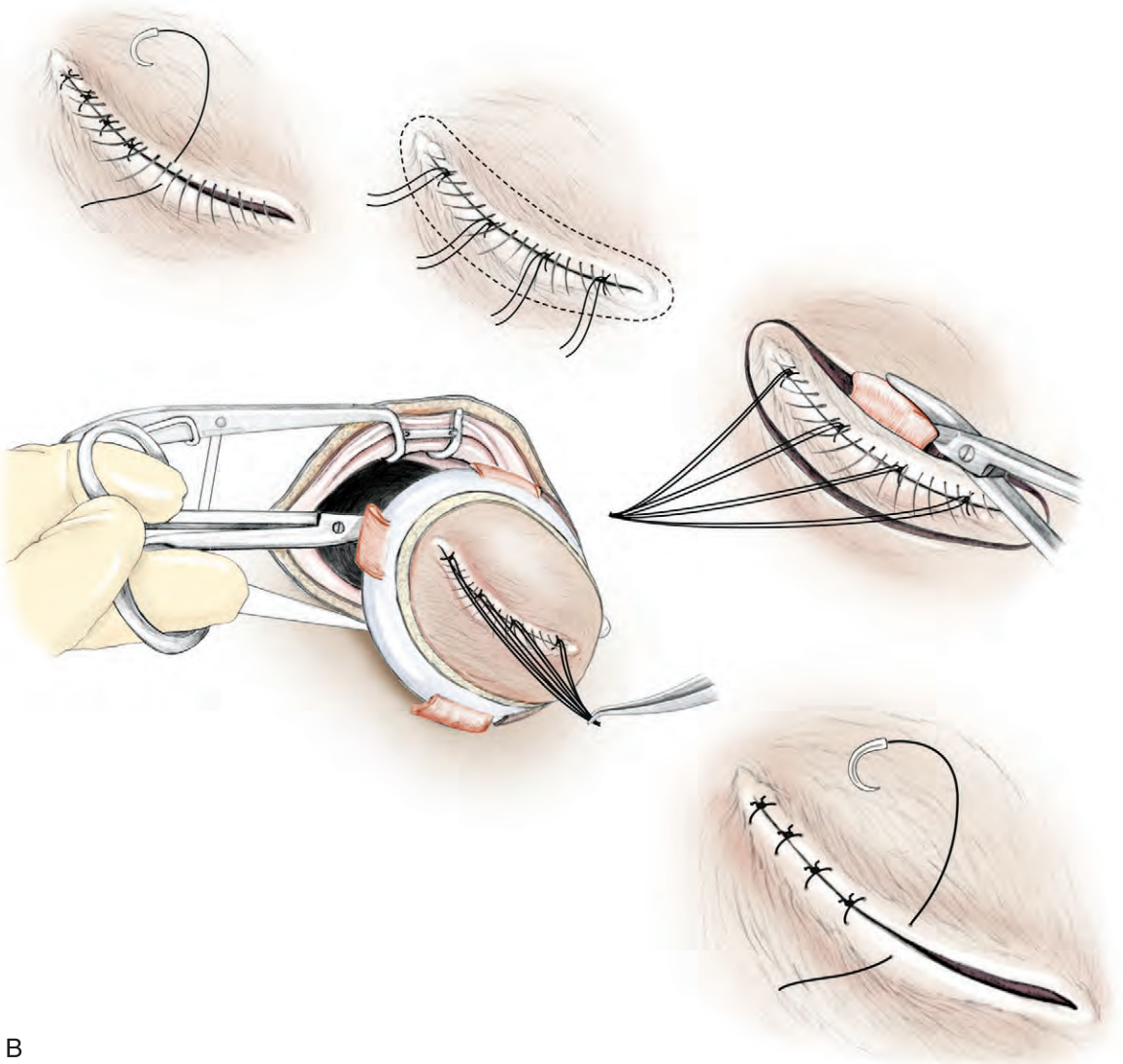
An intraorbital prosthesis may be placed to limit the appearance of a hollow orbit visible through the eyelids, although whether or not this actually improves the cosmetic appearance postoperatively is debatable (Fig. 3-37). Particular attention should be paid to removing any surgical powder on the pros-



A

Figure 3-36. A, Transconjunctival enucleation. A complete 360-degree conjunctival peritomy is completed adjacent to the limbus. Extraocular muscles are identified and resected at the globe, permitting its free rotation. The retrobulbar attachments of the retractor bulbi muscles are very extensive and are resected. The optic nerve is transected (but never clamped or ligated), and the globe is removed. The nictitans, eyelid margins, and conjunctiva are excised. The wound is closed in three layers (see text).

Continued



B

Figure 3-36, cont'd. B, Transpalpebral enucleation. The transpalpebral approach is preferred for removing septic globes and malignant neoplasia. Eyelid margins are temporarily tightly apposed with suture (2-0 nylon) in a continuous or interlocking pattern. An incision is made full thickness through the skin 5 to 7 mm from the eyelid margin to expose the subcutaneous tissues. Incision is extended to the periorbital margin, with care to avoid perforating the inner eyelid and contaminating the orbit with contents of the conjunctival fornix. Dissection is continued deeper to the fornix, and minor blunt dissection will rapidly free the globe from its surrounding tissue envelopes. The ocular muscles are resected, and the globe is removed. Closure is as described for transconjunctival enucleation.

thesis by rinsing or wiping it with saline or Betadine solution. It is aseptically introduced into the orbit. The prosthesis size should be selected to occupy the orbit and approximate the size of the globe removed, typically ranging from 40 to 50 mm in size. The contralateral globe may be measured prior to anesthesia for size comparison. The prosthesis may be fixed in position if desired with 2-0 or 3-0 nylon suture attaching it to the periosteum, or by incorporating it into a surgical meshwork in an interlocking pattern, taking shallow bites in the prosthesis to maximize stabilization. Some previous surgical descriptions recommend cutting the anterior face to a flat surface to avoid a prominent anterior curvature under the eyelid, although this would seem to be a desirable characteristic of the prosthesis. To avoid later migration of the prosthesis or nonabsorbable knots, dehiscence of the wound, or expulsion of the prosthesis, closure of surgical margins should include complete apposition of a layer between the prosthesis and the eyelid skin. The cosmetic outcome of placement of orbital prostheses is questionable, and complications such as dehiscence and draining tracts can occur if an orbital prosthesis is used (see Fig. 3-37). Fewer complications may occur with an integrated orbital implant, as described later with cosmetic prostheses, but use of these integrated implants has not been described after enucleation.

Closure is performed in several layers. If no orbital prosthesis is placed, the periorbitum may be partially approximated with an interlocking layer of 0 to 2-0 nylon in a continuous pattern. To ensure maximal apposition and closure, the surgical incision may need to be retracted to identify the incised margin

Figure 3-37. **A,** Intraorbital silicone prosthesis implanted into the orbit after enucleation of the left eye. **B,** Central dehiscence and draining tract 5 years after placement of a silicone intraorbital prosthesis after enucleation.

of the periorbitum if it has recoiled. It is important to avoid combining the periorbital and subcutaneous layers; they should be closed separately. The subcutaneous layers are closed with an absorbable suture of the surgeon's preference. Either polydioxanone or polyglactin 910 are suitable, in sizes of 2-0 to 4-0. The pattern may be interrupted, continuous, interlocking, or cruciate as desired, with the former two being most commonly used. Continuous sutures have a greater risk of dehiscence, although this is rarely a practical problem. The skin layer is closed with nonabsorbable sutures in a cruciate or interrupted pattern, using 3-0 nylon. As an alternative, if the patient is difficult to handle or to avoid suture removal, intradermal skin closure in a continuous pattern of 4-0 polyglactin 910 may be performed. Routine tetanus vaccine should be verified or be administered if the history is unknown. Tissue swelling is typically minimal at surgical conclusion but increases with recovery from anesthesia and increasing blood pressure. Pressure bandages may be applied or compresses used if the patient tolerates them, although the majority of cases do not require either.

The transpalpebral approach focuses on globe removal with constant separation of exposed surfaces from the orbital cavity (see Fig. 3-36). It is preferred for removing septic globes and malignant neoplasia. The eyelid margins are temporarily tightly apposed with suture (2-0 nylon) in a continuous or interlocking pattern. Allis tissue forceps may be placed on each knot end for identification and manipulation. An incision is made full thickness through the skin 5 to 7 mm from the eyelid margin to expose the subcutaneous tissues, which are bluntly dissected to divide the eyelid into dermal (retained) and tarsal (excised) layers. This is a potential space of embryologic derivation and readily separates. The division is extended to the periorbital margin, with care to avoid perforating the inner eyelid and contaminating the orbit with contents of the conjunctival fornix. The medial and lateral orbital ligaments are sharply severed with a surgical blade. Dissection through the reflections of the periorbitum/periosteum opens the orbital cavity deeper to the fornix, and minor blunt dissection will rapidly free the globe from its surrounding tissue envelopes. The ocular muscles are resected close to the globe, with limited visibility. The optic nerve should never be clamped or ligated; instead, if necessary, the orbit may be temporarily packed with gauze and pressure applied to control bleeding. The optic nerve is resected 1 to 2 cm posterior to the globe. Closure is as described earlier for transconjunctival enucleation.

Enucleation has a low incidence of complications (<5%). It is imperative to remove the nictitans, the eyelid margins, and the majority (if not all) of the conjunctiva; otherwise dehiscence is likely to occur, or distension of the orbit with mucoid or mucoserous debris will occur chronically. Removal of the lacrimal gland from the dorsolateral orbit appears unnecessary. It is rarely entirely removed, even when intended, because of its protected location. Complete resection of the medial canthus ensures that dehiscence and drainage do not occur at the site of a persistent mucocutaneous junction after suture removal or absorption. When this complication is observed, the surgical correction depends on differentiation of a persistent eyelid margin that may be removed and closed from a draining, possibly septic, tract into the orbit that requires orbital exploration, débridement, flushing, and closure. If the orbit may be septic, it should be débrided, extensively flushed with antibiotic solution, and a drain created through a stab wound ventral to the incision closure. The drain tubing is left in position until no further drainage occurs for 24 hours. Alternatively, gauze may be soaked in povidone iodine, rolled up, and placed in the orbit, passing through a stab incision and through a holding suture tied loosely in the skin. A section of gauze is removed (under sedation if needed) on a daily basis for 3 to 5 days or until the

drainage becomes clear. The stab incision heals by second intention.

EVISCERATION AND INTRASCLERAL PROSTHESIS

The most common indications for evisceration are a cosmetic alternative to enucleation for blind, painful eyes or globes that are beginning the process of phthisis bulbi. In general, intraocular neoplasia and septic processes should be considered a contraindication to retaining the scleral/corneal shell with implant placement. However, intrascleral prostheses (ISPs) have been placed in such cases, and with appropriate informed consent from the client, may not be an absolute contraindication.[106] Cosmetic alternatives that feature an artificial globe are available with the complete removal of the globe, but these require additional procedures to be performed at the time of first surgery (see later). All prostheses require routine maintenance and greater attention to cleanliness than enucleation. An ISP requires a single surgery but has a less cosmetic outcome and the potentially more serious complication of future corneal ulcers.

Consultation with a veterinary ophthalmologist should be performed prior to surgery for potential candidates for cosmetic globes. Most owners find an ISP to be preferable to enucleation or retention of a phthisical globe, but it is important to discuss the fact that corneal ulceration may occur postoperatively and still requires therapy. More poignantly, if stromal loss occurs and is progressive, a conjunctival flap or intensive medication will be required. If perforation occurs and fails to granulate rapidly, enucleation is required, but a prosthetic hydroxyapatite implant remains a final alternative.

It is pertinent to consider that the cornea will still be at risk of ulceration unless vascularization occurs. Preexisting corneal disease (traumatic or otherwise) increases the risk of complications post surgery, and an advancement conjunctival flap may be placed concurrently if the injury is near the limbus, such as a corneoscleral laceration.[107] If anticipated management/lifestyle changes make daily observation unlikely, then evisceration is not an appropriate surgical choice. Corneal health is somewhat compromised with the removal of aqueous humor, and an adequate tear film and eyelid coverage is important to prevent future disease. Globes with preexisting keratitis may also be regarded as high-risk candidates. Attempts to quantify tear production are warranted but may not be representative in light of concurrent trauma and pain.

Evisceration is the removal of the ocular contents with preservation of the ocular shell, comprising the cornea, sclera and its connective tissues, and conjunctiva. Surgical preparation is as for other intraocular surgery, with removal of eyelashes and fastidious surgical preparation of the skin. The cornea and conjunctival fornices are surgically prepared with dilute povidone iodine, which is adequately flushed with sterile saline. A brief sweep of the fornix may be performed with sterile cotton-tipped applicators to remove loose hairs, particularly from under the nictitans. Topical proparacaine and phenylephrine are applied several times. A self-adhesive drape is preferred to avoid any possible contamination of the intraocular space from the eyelid and skin hair. The conjunctiva and Tenon's capsule is deeply incised over 160 to 180 degrees parallel and 6 to 8 mm posterior to the limbus to completely expose sclera.[108] If the eye has had chronic uveitis, Tenon's capsule may be remarkably thickened, requiring deep incision and blunt dissection to expose sclera. The sclera is incised full thickness in a position to permit easy closure. A shorter perpendicular incision traveling caudally (to complete a T shape) may be made for improved exposure. Dexterity permits the scleral incision to be entirely completed without perforating the uveal tract. The uveal tract and ocular contents may then be removed by alternate rocking motions alternating between two non-toothed holding forceps. Alternatively, or if the tract ruptures, a lens loupe or probe may be used to undermine and remove the ocular contents. Caution is used to avoid damaging the corneal endothelium where possible. When the intraocular contents are removed and placed in formalin for histopathologic evaluation, the cavity is examined and débrided of remaining uvea. An intrascleral prosthesis is selected on the basis of corneal diameter, typically 1 to 2 mm larger than the corneal diameter of the ipsilateral or contralateral globe, approximately 36 to 40 mm for most adult horses. The prosthesis is cleaned of residual powder by rubbing it with a gauze moistened with dilute povidone iodine or sterile saline. The prosthesis is introduced, using caution to avoid touching the eyelids, and seated within the ocular tunics. Ability to appose the scleral margins is assessed, allowing accumulated hemorrhage to be expelled. The anterior surface of the prosthesis may be cut flat to reduce contact with the corneal endothelium, although this increases the likelihood of hemorrhage accumulating in this area, and its subsequent imbibition by the corneal stroma. At a later point, the heme breakdown products may result in a yellow-green corneal discoloration (Fig. 3-38). Closure of the sclera is performed with interrupted sutures of absorbable material such as 4-0 to 6-0 polyglactin 910. The margins are apposed without excess tightness because the globe is no longer fluid filled. The conjunctiva and Tenon's capsule are closed in one layer with absorbable suture in a continuous or interrupted pattern, ensuring that complete coverage of the scleral incision and suture is achieved with Tenon's capsule to avoid later dehiscence.

A partial temporary tarsorrhaphy is recommended postoperatively to reduce exposure and mechanical abrasion. The globe should be adequately lubricated, and routine postoperative therapy should include both topical and systemic antibiot-

Figure 3-38. Appearance of the cornea 5 days after evisceration of ocular contents and placement of an intraocular silicone prosthesis. There is corneal edema and ocular discoloration due to inflammation and resorbing blood products.

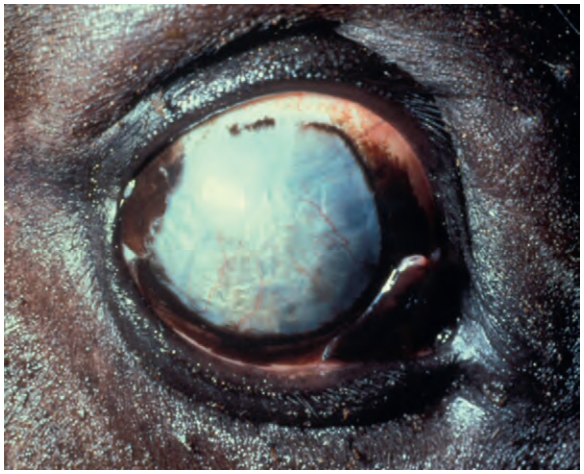


Figure 3-39. One year following evisceration of ocular contents and placement of an intraocular silicone prosthesis for treatment of chronic glaucoma. The cornea is extensively fibrotic and may become more cosmetic as the cornea pigments.

ics and systemic antiinflammatories. Increasing discharge or discomfort should prompt reexamination and fluorescein staining. Other than corneal ulceration, complications are uncommon but include endophthalmitis (septic or powder-induced), dehiscence of the surgical site if inadequately apposed, or if insufficient Tenon's capsule is incorporated, cellulitis from foreign-body response to surgical powder, and excessive periocular swelling if extensive dissection was performed. Histopathologic evidence of intraocular neoplasia or sepsis should prompt a discussion with the client about enucleation of the globe in toto with its prosthetic implant. Persistence of small amounts of uveal tissue does not appear to result in complications, but removal of the entire lens should be verified.

Most equine corneas vascularize and fibrose post surgery and may not be very cosmetic initially (Fig. 3-39). If pigmentation occurs, the cornea appears very cosmetic. Corneal tattooing has been described, although it is not universally satisfactory.[109] A cosmetic shell or a black contact lens can be fitted over the prosthesis in some horses to achieve a more cosmetic appearance.

EXENTERATION

The most aggressive orbital diseases are preferably treated by exenteration, which is the removal of all the orbital contents together with the periosteal lining. The intent with this procedure is to encapsulate the pathologic process within multiple natural tissue layers and remove them without contaminating the orbital cavity itself. Indications for exenteration are to control aggressive neoplasia, severe endophthalmitis, orbital cellulitis, or as a palliative measure to control rapidly expanding neoplasia without an attempt to cure. Exenteration may be performed after the failure of enucleation or other local surgical intervention, or as the first procedure for aggressive disease. Enucleation procedures may be expanded into exenteration if unexpected orbital contamination is identified, but the advantage of closed tissue layers is usually lost in a converted procedure. A thorough preoperative evaluation will permit the most appropriate procedure to be selected prior to commencing.

Routine surgical preparation is performed, with a larger area of clipping and prepping. The procedure is performed similarly to transpalpebral enucleation, ensuring preservation of the tissue layers intact. Dissection is performed along the orbital margin to remove as many concentric tissue layers as possible. Neoplastic involvement of the eyelid should be incorporated in the surgical plan as wider surgical margins. When the incision is beyond the level of the conjunctival fornix, dissection is continued close to the orbital margin to remove the tissue layers intact. The periosteum is preferably removed with this procedure if the pathologic process has reached that tissue boundary. A periosteal elevator is necessary. If the periosteum itself is penetrated, adjunctive treatment of the bone margin should be considered by removal with Rongeurs or osteotome. Subsequent adjunctive treatment, either with cryotherapy or potentially with radiotherapy implants such as iridium beads, can follow. The orbit should be flushed with dilute povidone iodine to decontaminate it. If septic endophthalmitis was present and the tissue layers were compromised, the orbit may be flushed with broad-spectrum antibiotics (see Table 3-5). Orbital evaluation is greatly facilitated if a preoperative retrobulbar block is placed with 1:100,000 epinephrine included. Ligation, hemostats, or cautery should be used as needed to permit a thorough evaluation.

A prosthetic implant is typically contraindicated by the pathology requiring the exenteration. However, if the globe and orbital contents are resected without contamination of the orbit, a meshwork of nonabsorbable suture material (2-0 or 3-0 nylon) may be placed across the orbit in an interlocking or continuous pattern to provide a flat surface for the dermis to rest upon, minimizing the tendency to exhibit a gaunt, hollow orbit post recovery. Often there is minimal periorbitum remaining, and the space is spanned with suture material only, which ultimately is likely to break down. Subcutaneous and skin closure are routine. Alternatively, a preformed mesh may be created to bridge the orbit, with a shallow convexity to resemble a globe behind closed eyelids. The prefabricated mesh is attached to the orbital margins.

After final closure of the skin layer, 10 to 20 mL of 0.5% bupivacaine may be aseptically injected transcutaneously to provide inexpensive short-term analgesia for up to 6 hours post recovery. This is useful in particular when a retrobulbar block was not performed prior to surgical exenteration.

If the orbit was contaminated during or prior to surgery, in addition to local lavage and antibiotics, a drain site should be created inferiorly; or less optimally, the incision should be maintained open postoperatively to permit drainage of exudate. The wound is managed to ensure drainage and granulation. The patient should be hospitalized and broad-spectrum systemic antibiotics administered. Granulation is typically well advanced by 7 days.

Complications of this procedure are predominantly incomplete removal of the neoplastic mass or infected tissue, allowing persistence of the pathologic process. Excessive swelling is common post exenteration because of the profound disturbance to the tissue layers and destruction of vascular beds. Every effort should be expended to ensure that inadvertent orbital contamination is avoided. More aggressive removal of blood clots and control of hemorrhage are necessary to identify the exact tissue boundaries.

RADICAL RESECTION OF EYELID SKIN AND GLOBE

A variation of these procedures has been described to permit closure of the orbit when large skin defects remain after neoplasm resection and globe removal.[110] In this procedure, the globe removal is performed routinely, and any neoplastic mass is excised with a 5- to 10-mm margin. If the skin margins are too widely separated to be apposed, a 10-mm osteotome is used to remove up to 75% of the dorsal and lateral bony orbital rim (the zygomatic process) to reduce the prominence of this landmark and permit closer approximation of the skin wounds. Cruciate sutures are placed in the skin margins, and tension is applied gradually at each site to close the defect. Releasing incisions 10 mm long are then positioned in a staggered pattern parallel and distant to the surgical wound to permit a meshlike expansion of the surface area. In many situations, this permits a near-complete closure over the orbit. In the most extreme circumstances, the orbit may still remain open. In such cases, the skin is apposed in the most practical and complete method possible, using tension-bearing sutures such as vertical mattress and near-far-far-near sutures; the remaining area is handled as a granulating open wound. Gauze packing of the orbit, protection of the surface, and topical disinfection are recommended. Systemic antibiotics are administered until a healthy granulation bed completely covers the internal orbit. Lavage is performed daily, initially with sterile saline, and after a healthy granulation bed is established in the orbit, continued with clean water. The authors reported excellent outcomes with diligent management and had no recurrences of the skin pathologies that were excised. Clients should be prepared for prolonged postoperative care and a gradual return to cosmetic appearance. Rotational skin flaps and grafts may be performed but are relatively high risk in the horse. Consultation with a surgeon is recommended to determine the most practical and effective option for each individual case.

COSMETIC CONFORMER AND HYDROXYAPATITE ORBITAL IMPLANTATION

An option for an improved cosmetic outcome when the globe must be removed is the use of ocular conformers placed over a prosthetic globe implant.[35] The primary candidates for such procedures are individuals for which the utmost cosmetic appearance is required, or for globes that have sustained injuries so substantial that repair is not possible. The cosmetic appearance is superior to the implantation of an intrascleral prosthesis, and when the initial surgical intervention is healed, the risk of implant expulsion is extremely low. In contrast, the intrascleral prosthesis has risk of corneal ulceration, infection, and dehiscence via corneal trauma and the potentially poor cosmetic appearance of an opaque and/or vascularized cornea.

The surgical procedure for hydroxyapatite-based conformers is performed similarly to the transconjunctival enucleation, but only the globe itself is removed. The extraocular muscles, conjunctival fornices, and other tissues within the orbit are carefully preserved. Cautious microsurgical techniques are necessary. Twenty-four hours prior to surgery, an immediately postmortem globe is acquired, and the sclera is dissected free and submersed in 100% ethanol. Before anesthesia induction, a 40-mm hydroxyapatite sphere prosthesis is soaked in cefazolin for 1 hour, and the donor sclera is thoroughly lavaged in sterile saline. The sphere is inserted into the sclera using releasing incisions, which are closed with polyglactin 910 (Fig. 3-40). A stay suture through the eyelid skin and conjunctiva is useful to demarcate the levator muscle and the extent of the conjunctival fornix dorsally. A deep peritomy is performed to expose the sclera, and each extraocular muscle is identified and sutured with 5-0 polyglactin 910 and transected at the globe. The retractor bulbi muscles and optic nerve are severed, and the globe is removed. Full-thickness incisions, 2 × 4 mm in size, are made in the donor sclera 1 cm from the posterior pole. The sclera-clad prosthesis is inserted into the orbit with the exposed coral facing posteriorly (the cornea having been removed). Each ocular muscle is inserted through the incision in apposition with the hydroxyapatite and sutured to the interior of the sclera. The oblique muscles are sutured to the sclera directly. Tenon's capsule and fascial layers are apposed across the anterior face of the implant, obscuring it. The peritomy edges are apposed to create a single large conjunctiva-lined fornix (Fig. 3-41). Antibiotic ointment is applied, and a generic plastic extrascleral conformer (prosthesis) is inserted between the eyelids and the conjunctival surface (Fig. 3-42). A compression bandage is placed and changed daily for 3 days. Routine postoperative antibiotics and antiinflammatories are administered. After the swelling has subsided, the tarsorrhaphy is removed, and the conjunctival fornix is lavaged and treated with topical antibiotics during extended hospitalization for 7 days. With appropriate healing, the patient may be discharged on topical antibiotics 3 times a day for 3 weeks and daily cleaning and repositioning of the conformer. At 4 weeks, the conformer is removed, and an impression is made to create a new device to correctly fill the fornix for the permanent conformer. This is usually done by an ocularist with experience making equine prostheses. Typically, several black prostheses are used routinely, and one is painted by an ocularist to match the original globe (Fig. 3-43). The individually hand-painted conformers are used only for short periods because of cost ($3000 to

Figure 3-40. Hydroxyapatite orbital implant and cosmetic corneal-scleral prosthesis. A hydroxyapatite sphere *(white)* is inserted into donor cadaver sclera and placed within the orbit following enucleation. Extraocular muscles are sutured to the donor sclera.

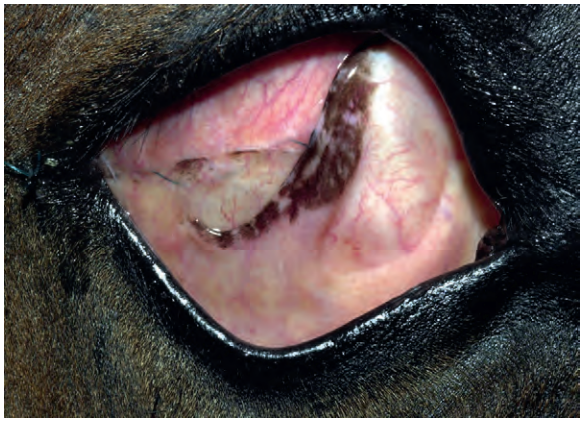


Figure 3-41. Hydroxyapatite orbital implant and cosmetic corneal-scleral prosthesis. The conjunctiva is apposed over the orbital implant to create a single, large, conjunctiva-lined fornix.

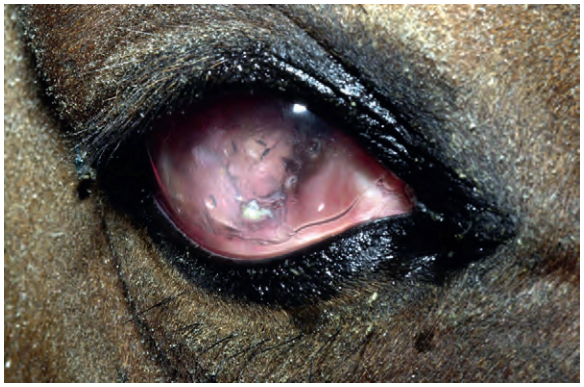


Figure 3-42. Hydroxyapatite orbital implant and cosmetic corneal-scleral prosthesis. Antibiotic ointment is applied, and a generic plastic extrascleral conformer (prosthesis) is inserted between the eyelids and the conjunctival surface during the healing of the orbit to prevent contracture of the eyelids.

$5000 USD). At the final fitting, any further adjustments in the conformer can be made. Ocular mobility with this procedure may be moderate to excellent depending on the positioning of the muscles, final prosthesis position, and the amount of tissue between the prosthesis and the conformer. The eyelid position and palpebral fissure size are determined at the time of surgery by the conformer, which should be placed continuously to ensure that no retraction occurs. If the conformer is cared for appropriately, the final outcome can be excellent (see Fig. 3-43, *C*). Potential complications of expulsion of the implant or infection are less common with hydroxyapatite, because its porosity encourages vascular ingrowth and permanent tissue attachment. Potential candidates should be aware that the attempt to increase cosmesis also risks additional complications, and that ongoing care of the conformer is necessary.[35]

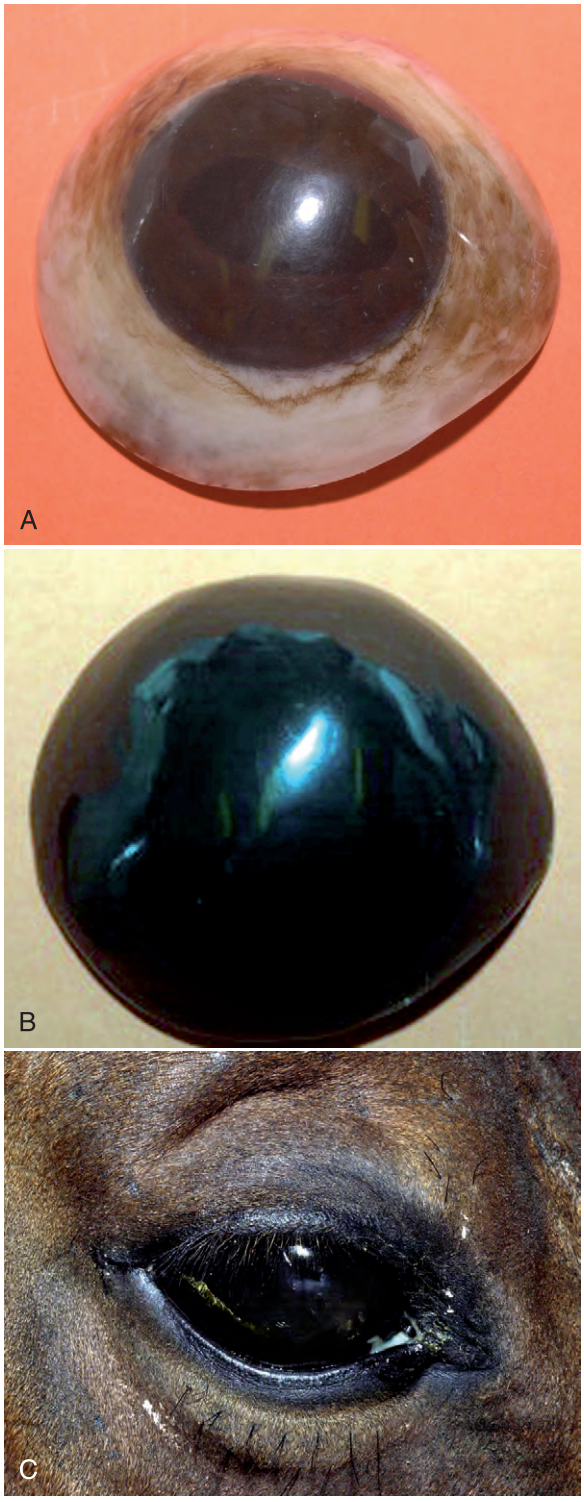


Figure 3-43. A to **C,** Hydroxyapatite orbital implant and cosmetic corneal-scleral prosthesis. The final corneal-scleral cosmetic prosthesis is made by an ocularist and can be made to appear like a normal eye **(A),** or can be black **(B).** With either cosmetic shell, the final appearance can be excellent **(C).**

RELATED SURGICAL PROCEDURES

TREPHINATION OF SINUSES

Trephination may be performed in the standing sedated or recumbent anesthetized horse, depending upon the indication and other procedures that must be performed. The maxillary

sinus is most commonly involved, because it is the largest and the common exit for the air-filled spaces of the equine skull. Primary indications are exploration, sample acquisition, flushing and drainage of sinusitis and solid masses, and repair of skull fractures. Trephination may be necessary to expose a fracture for repair, in which case it is considered an open contaminated site, because the sinuses communicate via the maxillary sinus to the nasal cavity. When sinusitis is diagnosed radiographically or clinically, samples are necessary for culture and cytology as well as to remove solid material, flush the sinus, and potentially establish drainage. Large volumes of hemorrhage should be flushed to prevent bacterial colonization.[103] Draining tracts, although rare, may develop through the orbit and skin. Inferior drainage should be established and the tract treated as a contaminated wound.

The major ocular significance of trephination of the maxillary sinus is the potential puncture and destruction of the nasolacrimal duct (NLD) or infraorbital nerve. The trephination should be performed dorsal to the facial crest and ventral to the line connecting the medial canthus and the infraorbital foramen. The trephination site should center within this area. Alternatively, if greater access is required, a skin and bone flap may be created under general anesthesia to flush the sinus and establish drainage.[74] The entire area described is used to create the flap, which opens the caudal maxillary sinus.[70,74] If the incision is made too dorsal, the nasolacrimal duct may be exposed or perforated; if damaged, it is likely to be difficult to repair. Attempts at repair may be made by cannulating the duct with a flexible retention stylette and realigning the sectioned area across the incision. Sutures should be placed parallel to the long axis of the duct. However, obstruction is likely, and if epiphora results, a canaliculorhinostomy may be required to establish internal drainage (see earlier). Trephination of the frontal sinus is less commonly performed and is of minor threat to the orbit unless a fracture line extends laterally. A bone flap centered on the midline between the orbits may be performed for greater access.

DENTAL SURGERY

As mentioned earlier in this chapter, dental disease seldom has direct impact on the equine orbit. The last premolar and first three molars arise in the maxillary sinus, and the last molar is adjacent to the sphenopalatine sinus. Dental disease may result in sinusitis that secondarily affects the orbit, and the caudal cheek teeth may establish tracts from infected tooth roots that abscess. Spontaneous tracts and fistulas may be identified in the retrobulbar area. Extraction of molars may be challenging, and complications from that extraction may ultimately impact the orbit. Complicated surgical treatment of dental misalignment is attempted uncommonly but may place the orbit at risk of sequelae. Surgical correction of prognathism in older individuals has been performed by wiring the maxilla; the resulting tissue planes may induce cellulitis or sepsis that secondarily involves the orbit. Similarly, implantation of orthopedic plates and screws may result in secondary exophthalmos or lagophthalmos of the globe. Nasolacrimal duct obstruction may also result from the original fracture or attempts at fixation.[111]

FUTURE RESEARCH

Advancement of imaging modalities will greatly improve our ability to identify, categorize, and diagnose equine orbital disease and, one hopes, concurrently result in retaining both the globe and vision. Advances in CT technology and use, for example, have made older imaging modalities such as routine radiology nearly obsolete for imaging orbital disease. New pathologic conditions of the equine orbit will likely be identified in the future as a result of advances in imaging, an increasing population of geriatric horses, and greater expectations of the horse-owning public. Improvements in medical and surgical therapy for sinus and orbital neoplasia will ultimately improve the short and midterm outcome of such cases. Improved staging of orbital neoplasia may greatly enhance selecting cases for therapy and the number of visual and comfortable eyes that may be maintained. Further improvements in implant materials will generate new cosmetic procedures for individuals with painful or severely damaged globes.

Large, multicentered studies of orbital disease such as fractures, neoplasia, and infections are needed to better understand the causes, treatment, and outcome of orbital disease in the horse. Other than a few isolated examples, these studies are nonexistent in the literature.

Acknowledgment

The author acknowledges and appreciates the work of Tim J. Cutler, who authored this chapter in the previous edition. The author would also like to thank Beth Salmon for her review of this chapter and Dr. Richard McMullen for assistance in the acquisition of images.

References

1. Evans KE, McGreevy PD: Conformation of the equine skull: a morphometric study, Anat Histol Embryol 35:221–227, 2006.
2. Farrall H, Handscombe M: Equine vision, Equine Vet J 31:354–355, 1999.
3. Samuelson D: Ophthalmic anatomy. In Gelatt KN, editor: Veterinary ophthalmology, ed 3, Baltimore, 1999, Lippincott Williams & Wilkins, pp 31–150.
4. Wilkins P: Use of an infraorbital nerve block in the diagnosis of headshaking, Proc Am Assoc Eq Pract 43:156–157, 1997.
5. Mair TS: Assessment of bilateral infra-orbital nerve blockade and bilateral infra-orbital neurectomy in the investigation and treatment of idiopathic headshaking, Equine Vet J 31:262–264, 1999.
6. Gilger BC, Reeves KA, Salmon JH: Ocular parameters related to drug delivery in the canine and equine eye: aqueous and vitreous humor volume and scleral surface area and thickness, Vet Ophthalmol 8:265–269, 2005.
7. Ramsey DT, Hauptman JG, Petersen-Jones SM: Corneal thickness, intraocular pressure, and optical corneal diameter in Rocky Mountain horses with cornea globosa or clinically normal corneas, Am J Vet Res 60:1317–1321, 1999.
8. van der Woerdt A, Gilger BC, Wilkie DA, et al: Effect of auriculopalpebral nerve block and intravenous administration of xylazine on intraocular pressure and corneal thickness in horses, Am J Vet Res 56:155–158, 1995.

9. Andrew SE, Willis AM, Anderson DE: Density of corneal endothelial cells, corneal thickness, and corneal diameters in normal eyes of llamas and alpacas, Am J Vet Res 63:326–329, 2002.
10. Plummer CE, Ramsey DT, Hauptman JG: Assessment of corneal thickness, intraocular pressure, optical corneal diameter, and axial globe dimensions in Miniature horses, Am J Vet Res 64:661–665, 2003.
11. Simoens P, Muylle S, Lauwers H: Anatomy of the ocular arteries in the horse, Equine Vet J 28:360–367, 1996.
12. van Maanen C, Klein WR, Dik KJ, et al: Three cases of carcinoid in the equine nasal cavity and maxillary sinuses: histologic and immunohistochemical features, Vet Pathol 33:92–95, 1996.
13. Scott EA, Duncan JR, McCormack JE: Cryptococcosis involving the postorbital area and frontal sinus in a horse, J Am Vet Med Assoc 165:626–627, 1974.
14. Modransky P, Welker B, Pickett JP: Management of facial injuries, Vet Clin North Am Equine Pract 5:665–682, 1989.
15. Mason BJ: Spindle-cell sarcoma of the equine para-nasal sinuses and nasal chamber, Vet Rec 96:287–288, 1975.
16. Hill FW, Moulton JE, Schiff PH: Exophthalmos in a horse resulting from an adenocarcinoma of the frontal sinus, J S Afr Vet Assoc 60:104–105, 1989.
17. Barnett KC, Blunden AS, Dyson SJ, et al: Blindness, optic atrophy and sinusitis in the horse, Vet Ophthalmol 11(Suppl 1):20–26, 2008.
18. Latimer CA, Wyman M, Diesem CD, et al: Radiographic and gross anatomy of the nasolacrimal duct of the horse, Am J Vet Res 45:451–458, 1984.
19. Freestone JF, Glaze MB, Pechman R, et al: Ultrasonic identification of an orbital tumor in a horse, Eq Vet J 21:135–136, 1989.
20. Scotty NC, Cutler TJ, Brooks DE, et al: Diagnostic ultrasonography of equine lens and posterior segment abnormalities, Vet Ophthalmol 7:127–139, 2004.
21. Brooks D. Orbit. In Auer J, editor: Equine surgery, Philadelphia, 1992, WB Saunders, pp 654–666.
22. Williams J, Wilkie D: Ultrasonography of the eye, Comp Contin Educ Pract Vet 18:667–677, 1996.
23. Barbee D: Computed tomography in horses, Vet Radiol Ultrasound 28:144–151, 1987.
24. Tucker RL, Farrell E: Computed tomography and magnetic resonance imaging of the equine head, Vet Clin North Am Equine Pract 17:131–144, vii, 2001.
25. Colitz CM, Gilger BC, Davidson CP, et al: Orbital fibroma in a horse, Vet Ophthalmol 3:213–216, 2000.
26. Miesner T, Wilkie D, Gemensky-Metzler A, et al: Extra-adrenal paraganglioma of the equine orbit: six cases, Vet Ophthalmol 12:263–268, 2009.
27. Witzel DA, Smith EL, Wilson RD, et al: Congenital stationary night blindness: an animal model, Invest Ophthalmol Vis Sci 17:788–795, 1978.
28. Joyce JR, Witzel DA: Equine night blindness, J Am Vet Med Assoc 170:878, 880, 1977.
29. Lavach JD: Large animal ophthalmology, St. Louis, 1990, The CV Mosby Company, pp 1–395.
30. Green SL, Little CB, Baird JD, et al: Tetanus in the horse: a review of 20 cases (1970 to 1990), J Vet Intern Med 8:128–132, 1994.
31. Newton SA: Suspected bacterial meningoencephalitis in two adult horses, Vet Rec 142:665–669, 1998.
32. Davis JL, Gilger BC, Spaulding K, et al: Nasal adenocarcinoma with diffuse metastases involving the orbit, cerebrum, and multiple cranial nerves in a horse, J Am Vet Med Assoc 221:1420, 1460–1463, 2002.
33. Mayhew I. Large animal neurology, Philadelphia, 1989, Lea & Febiger, pp 179–192.
34. Bianchi M: Fat cell size in various body region. A statistical analysis in *Equus caballus*, Anat Anz 169:351–366, 1989.
35. Gilger BC, Pizzirani S, Johnston LC, et al: Use of a hydroxyapatite orbital implant in a cosmetic corneoscleral prosthesis after enucleation in a horse, J Am Vet Med Assoc 222:316, 343–345, 2003.
36. Ramsey DT, Ewart SL, Render JA, et al: Congenital ocular abnormalities of Rocky Mountain horses, Vet Ophthalmol 2:47–59, 1999.
37. Matthews A: Nonulcerative keratopathies in the horse, Eq Vet Educ 12:271–278, 2000.
38. Garner A, Griffiths P: Bilateral congenital ocular defects in a foal, Br J Ophthalmol 53:513–517, 1969.
39. Priester WA: Congenital ocular defects in cattle, horses, cats, and dogs, J Am Vet Med Assoc 160:1504–1511, 1972.
40. Munroe GA, Barnett KC: Congenital ocular disease in the foal, Vet Clin North Am Large Anim Pract 6:519–537, 1984.
41. Latimer CA, Wyman M: Neonatal ophthalmology, Vet Clin North Am Equine Pract 1:235–259, 1985.
42. Schutte JG, van den Ingh TS: Microphthalmia, brachygnathia superior, and palatocheiloschisis in a foal associated with griseofulvin administration to the mare during early pregnancy, Vet Q 19:58–60, 1997.
43. Williams DL, Barnett KC: Bilateral optic disc colobomas and microphthalmos in a thoroughbred horse, Vet Rec 132:101–103, 1993.
44. Roberts SM: Congenital ocular anomalies, Vet Clin North Am Equine Pract 8:459–478, 1992.
45. Grant B, Slatter DH, Dunlap JS: *Thelazia* sp. (Nematoda) and dermoid cysts in a horse with torticollis, Vet Med Small Anim Clin 68:62–64, 1973.
46. Munoz E, Leiva M, Naranjo C, et al: Retrobulbar dermoid cyst in the horse: a case report, Vet Ophthalmol 10:394–397, 2007.
47. McEntee M, Summers BA, de Lahunta A, et al: Meningocerebral hemangiomatosis resembling Sturge-Weber disease in a horse, Acta Neuropathol (Berl) 74:405–410, 1987.
48. Chmielewski NT, Brooks DE, Smith PJ, et al: Visual outcome and ocular survival following iris prolapse in the horse: a review of 32 cases, Equine Vet J 29:31–39, 1997.
49. Gelatt KN: Herniation of orbital fat in a colt, Vet Med Small Anim Clin 65:146, 1970.
50. Bedford PGC, Barnett KC, Boydell P, et al: Partial prolapse of the anteromedial corpus adiposum in the horse, Eq Vet J 10:2–4, 1990.
51. Vestre WA, Steckel RR: Episcleral prolapse of orbital fat in the horse, Eq Pract 5:135–137, 1983.
52. Munroe G, Belgrave J: Surgical repair of an episcleral prolapse of orbital fat in a foal, Equine Vet J 20:131, 1988.
53. Roberts MC, Sutton RH, Lovell DK: A protracted case of cryptococcal nasal granuloma in a stallion, Aust Vet J 57:287–291, 1981.
54. Hubert J, Williams J, Hamilton HL, et al: What is your diagnosis? Chronic retrobulbar abscess in a horse, J Am Vet Med Assoc 209:1703–1704, 1996.
55. van den Top J, Shaashma I, Boswinkel M, et al: A retrobulbar abscess as an uncommon cause of exophthalmos in a horse, Eq Vet Educ 19:579–583, 2007.
56. Zamos DT, Schumacher J, Loy JK: Nasopharyngeal conidiobolomycosis in a horse, J Am Vet Med Assoc 208:100–101, 1996.
57. Barnett KC, Cottrell BD, Rest JR: Retrobulbar hydatid cyst in the horse, Equine Vet J 20:136–138, 1988.
58. Walde I, Prosl H: [*Strongylus edentatus* as the cause of subconjunctional phlegmon and granuloma formation in the horse], Tierarztl Prax 4:493–496, 1976.
59. Pearce SG, Boure LP, Taylor JA, et al: Treatment of a granuloma caused by *Halicephalobus gingivalis* in a horse, J Am Vet Med Assoc 219:1708, 1735–1738, 2001.
60. Isaza R, Schiller CA, Stover J, et al: *Halicephalobus gingivalis* (Nematoda) infection in a Grevy's zebra *(Equus grevyi)*, J Zoo Wildl Med 31:77–81, 2000.
61. Rames DS, Miller DK, Barthel R, et al: Ocular *Halicephalobus* (syn. Micronema) deletrix in a horse, Vet Pathol 32:540–542, 1995.
62. Kinde H, Mathews M, Ash L, et al: *Halicephalobus gingivalis (H. deletrix)* infection in two horses in southern California, J Vet Diagn Invest 12:162–165, 2000.
63. Akhan O, Bilgic S, Akata D, et al: Percutaneous treatment of an orbital hydatid cyst: a new therapeutic approach, Am J Ophthalmol 125:877–879, 1998.
64. Step DL, Divers TJ, Cooper B, et al: Severe masseter myonecrosis in a horse, J Am Vet Med Assoc 198:117–119, 1991.
65. Trotter G: Paranasal sinuses, Vet Clin North Am Equine Pract 1:153–169, 1993.
66. Brooks DE: Equine ophthalmology. In Gelatt KN, editor: Veterinary ophthalmology, Philadelphia, 1999, Lippincott Williams & Wilkins, pp 1053–1116.
67. Jacobs D, Galetta S: Diagnosis and management of orbital pseudotumor, Curr Opin Ophthalmol 13:347–351, 2002.
68. Miller SA, van der Woerdt A, Bartick TE: Retrobulbar pseudotumor of the orbit in a cat, J Am Vet Med Assoc 216:345, 356–358, 2000.
69. Weber AL, Romo LV, Sabates NR: Pseudotumor of the orbit. Clinical, pathologic, and radiologic evaluation, Radiol Clin North Am 37:151–168, xi, 1999.

70. Nickels F: Nasal passages and paranasal sinuses. In Auer J, Stick J, editors: Equine surgery, Philadelphia, 2006, WB Saunders, pp 533–544.
71. Kanda T, Hikasa Y, Naota M, et al: Exophthalmos caused by chronic sinusitis in a horse: a case of exophthalmos caused by sinusitis, J Eq Vet Sci 21:539–541, 2007.
72. Annear MJ, Gemensky-Metzler AJ, Elce YA, et al: Exophthalmus secondary to a sinonasal cyst in a horse, J Am Vet Med Assoc 233:285–288, 2008.
73. Butler J, Colles C, Dyson S, et al: Clinical radiology of the horse, Ames, IA, 1993, Blackwell Scientific.
74. Freeman DE, Orsini PG, Ross MW, et al: A large frontonasal bone flap for sinus surgery in the horse, Vet Surg 19:122–130, 1990.
75. Dixon PM, Head KW: Equine nasal and paranasal sinus tumours: part 2: a contribution of 28 case reports, Vet J 157:279–294, 1999.
76. Head KW, Dixon PM: Equine nasal and paranasal sinus tumours. Part 1: review of the literature and tumour classification, Vet J 157:261–278, 1999.
77. Veraa S, Dijkman R, Klein W, et al: Computed tomography in the diagnosis of malignant sinonasal tumours in three horses, Eq Vet Educ 21:284–288, 2009.
78. Kreeger J, Templer A, Tumquist S, et al: Paranasal meningioma in a horse, J Vet Diagn Invest 14:322–325, 2002.
79. Scotty NC, Ford M, Williams F, 3rd, et al: Exophthalmia associated with paranasal sinus osteoma in a Quarterhorse mare, J Vet Diagn Invest 16:155–160, 2004.
80. Basher AW, Severin GA, Chavkin MJ, et al: Orbital neuroendocrine tumors in three horses, J Am Vet Med Assoc 210:668–671, 1997.
81. Matiasek K, Cronau M, Schmahl W, et al: Imaging features and decision making in retrobulbar neuroendocrine tumours in horses—case report and review of literature, J Vet Med 54:302–306, 2007.
82. Goodhead A, Venter I, Nesbit J: Retrobulbar extra-adrenal paraganglioma in a horse and its surgical removal by orbitotomy, Vet Comp Ophthalmol 7:96–100, 1997.
83. Rebhun WC, Del Piero F: Ocular lesions in horses with lymphosarcoma: 21 cases (1977–1997), J Am Vet Med Assoc 212:852–854, 1998.
84. Rebhun WC: Diseases of the ocular system. In Colahan P, Mayhew I, Merritt A, editors: Equine medicine and surgery, Goleta, CA, 1991, American Veterinary Publications, p 1083.
85. Bistner S, Campbell RJ, Shaw D, et al: Neuroepithelial tumor of the optic nerve in a horse, Cornell Vet 73:30–40, 1983.
86. Baptiste KE, Grahn BH: Equine orbital neoplasia: a review of 10 cases (1983–1998), Can Vet J 41:291–295, 2000.
87. Eagle RC, Jr, Font RL, Swerczek TW: Malignant medulloepithelioma of the optic nerve in a horse, Vet Pathol 15:488–494, 1978.
88. Lavach JD, Severin GA: Neoplasia of the equine eye, adnexa, and orbit: a review of 68 cases, J Am Vet Med Assoc 170:202–203, 1977.
89. Ramirez S, Tucker RL: Ophthalmic imaging, Vet Clin North Am Equine Pract 20:441–457, 2004.
90. Moore CP, Collins BK, Linton LL, et al: Conjunctival malignant melanoma in a horse, Vet Ophthalmol 3:201–206, 2000.
91. Ramadan RO: Primary ocular melanoma in a young horse, Equine Vet J 7:49–50, 1975.
92. Bolton JR, Lees MJ, Robinson WF, et al: Ocular neoplasms of vascular origin in the horse, Equine Vet J Suppl 73–75, 1990.
93. Bischofberger A, Konar M, Posthaus H, et al: Ocular angiosarcoma in a pony—MRI and histopathological appearance, Eq Vet Educ 20:340–347, 2008.
94. Hong C, Van Meter P, Latimer C: Malignant rhabdoid tumour in the orbit of a horse, J Comp Pathol 121:197–201, 1999.
95. Ueda Y, Senba H, Nishimura T, et al: Ocular medulloepithelioma in a thoroughbred, Equine Vet J 25:558–561, 1993.
96. Hayes H, Priester W, Pendergrass T: Occurrence of nervous-tissue tumors in cattle, horses, cats and dogs, Int J Cancer 15:39–47, 1975.
97. Hardy J, Robertson JT, Wilkie DA: Ischemic optic neuropathy and blindness after arterial occlusion for treatment of guttural pouch mycosis in two horses, J Am Vet Med Assoc 196:1631–1634, 1990.
98. Leveille R, Hardy J, Robertson JT, et al: Transarterial coil embolization of the internal and external carotid and maxillary arteries for prevention of hemorrhage from guttural pouch mycosis in horses, Vet Surg 29:389–397, 2000.
99. Hatziolos BC, Sass B, Albert TF, et al: Ocular changes in a horse with gutturomycosis, J Am Vet Med Assoc 167:51–54, 1975.
100. Divers TJ, Irby NL, Mohammed HO, et al: Ocular penetration of intravenously administered enrofloxacin in the horse, Equine Vet J 40:167–170, 2008.
101. Blogg JR, Stanley RG, Phillip CJ: Skull and orbital blow-out fractures in a horse, Equine Vet J Suppl 5–7, 1990.
102. Koch D, Leitch M, Beech L: Orbital surgery in 2 horses, Vet Surg 9:61, 1980.
103. Caron JP, Barber SM, Bailey JV, et al: Periorbital skull fractures in five horses, J Am Vet Med Assoc 188:280–284, 1986.
104. Brooks DE: Ocular emergencies and trauma. In Auer J, editor: Equine surgery, Philadelphia, 1992, WB Saunders, pp 666–667.
105. Robertson S: Standing sedation and pain management in the horse, Vet Clin N Am Eq Pract 20:485–497, 2004.
106. McLaughlin SA, Ramsey DT, Lindley DM, et al: Intraocular silicone prosthesis implantation in eyes of dogs and a cat with intraocular neoplasia: nine cases (1983–1994), J Am Vet Med Assoc 207:1441–1443, 1995.
107. Riggs C, Whitley RD: Intraocular silicone prostheses in a dog and a horse with corneal lacerations, J Am Vet Med Assoc 196:617–619, 1990.
108. Meek LA: Intraocular silicone prosthesis in a horse, J Am Vet Med Assoc 193:343–345, 1988.
109. Michau T, Gilger BC: Ocular cosmesis in the horse, Vet Clin N Am Eq Pract 20:467–484, 2004.
110. Beard WL, Wilkie DA: Partial orbital rim resection, mesh skin expansion, and second intention healing combined with enucleation or exenteration for extensive periocular tumors in horses, Vet Ophthalmol 5:23–28, 2002.
111. McIlnay TR, Miller SM, Dugan SJ: Use of canaliculorhinostomy for repair of nasolacrimal duct obstruction in a horse, J Am Vet Med Assoc 218:1271, 1323–1324, 2001.
112. Schaaf KL, Kannegieter NJ, Lovell DK: Calcified tumours of the paranasal sinuses in three horses, Aust Vet J 85:454–458, 2007.
113. Dopke C, Grone A, von Borstel M, et al: Metastatic esthesioneuroblastoma in a horse, J Comp Pathol 132:218–222, 2005.

Chapter 4

Equine Ocular Adnexal and Nasolacrimal Disease

Elizabeth A. Giuliano

Equine ocular disease affecting the adnexa (i.e., appendages of the globe, including the superior, inferior, and third eyelid) and nasolacrimal system is commonly encountered in veterinary practice. When normal eyelid function is permanently damaged, the health of the globe is often compromised, and vision may be lost. The importance of accurate, prompt diagnosis and treatment to restore/preserve normal anatomic function to both the eyelids and nasolacrimal system should not be underestimated. This chapter will review those diseases commonly affecting the equine adnexa and nasolacrimal system, with the aim to provide diagnostic and therapeutic approaches to treatment.

CLINICAL ANATOMY AND PHYSIOLOGY

EYELIDS

Equine eyelids conform to the same basic anatomy of other domestic animals. The three basic layers of the superior and inferior eyelids from external to internal are (1) the skin with its haired and associated sebaceous glands; (2) a musculofibrous layer consisting of muscle, connective tissue, and tarsal plate; and (3) the palpebral conjunctiva.[1] The eyelids are critical to ocular health in a number of ways. The blink reflex in response to tactile, chemical, or thermal stimuli of the skin, vibrissae, cilia, conjunctiva, or cornea serves to protect the eye. Reflex blinking (and tearing) also helps remove any foreign particulate matter from the eye. The eyelids produce portions of the preocular tear film (e.g., meibomian glands produce lipid, conjunctival goblet cells produce mucin) and facilitate tear distribution across, and clearance from, the corneal surface. Finally, the eyelids regulate the amount of light that enters the eye.

On the skin surface, the equine eye has three types of hair: vibrissae, cilia, and dermal hair (Fig. 4-1). Typically, two to four vibrissae are present 2 to 3 cm dorsal to the medal canthus and 8 to 10 vibrissae emerge approximately 1 cm ventral to the inferior eyelid and run parallel to the interpalpebral fissure. The function of these relatively stiff hairs is to provide tactile stimuli via cranial nerve (CN) V; touching the vibrissae will usually prompt eyelid closure and therefore should be avoided during the ocular examination. Eyelid cilia originate just exter-

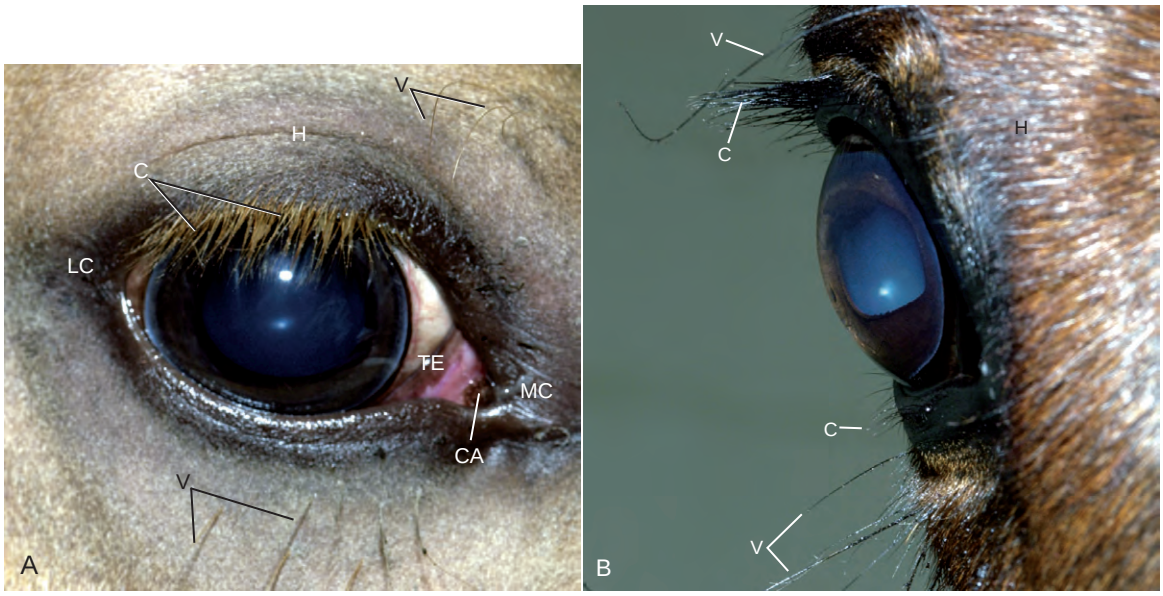


Figure 4-1. **A,** Equine eye as examined from the side of the horse. **B,** Front view. Three types of hair are present on the equine eyelids, including vibrissae *(V)*, cilia *(C)*, and dermal hair *(H)*. Medial *(MC)* and lateral canthus *(LC)* and lacrimal caruncle *(CA)*. Third eyelid *(TE)*.

nal to the opening of the meibomian glands on the palpebral margin and may be associated with other modified skin glands (e.g., glands similar to those of Zeis and Moll). Equine eyelid cilia are large and numerous on the superior eyelid but few or absent on the inferior eyelid (see Fig. 4-1).[2] Eyelid cilia primarily function to protect the cornea, shield the eye from light, and provide tactile sensory input. Fine, soft dermal hairs cover the eyelid surface in variable degrees of density. The area within 0.5 mm of the eyelid margin generally has few dermal hairs.

The tarsus or tarsal plate is a narrow, dense layer of connective tissue located between the palpebral conjunctiva and the eyelid skin surface. Both superior and inferior eyelids possess a tarsal plate, but it is more fully developed in the superior eyelid. The tarsi provide structure and rigidity to the eyelids.[3] Horses possess a well-defined orbitopalpebral sulcus, most evident in the superior eyelid (Fig. 4-2).[1] This sulcus forms a fold of skin that delineates the eyelid into an orbital portion and a tarsal portion. The orbital portion lies between the dorsal margin of the bony orbit and the globe, and the tarsal portion overlies the globe itself. Traumatic superior eyelid lacerations are often observed to tear along this sulcus and necessitate meticulous surgical repair.

The tarsal, or meibomian, glands are a row of well-developed sebaceous eyelid glands (Fig. 4-3). Meibomian glands are arranged in a single row running parallel to the lid margins and are embedded within the tarsal plate. The glands open directly onto the eyelid margins in a row of evenly spaced orifices collectively known as the *gray line*, an important surgical landmark. The meibomian glands secrete the lipid layer of the precorneal tear film. Other glandular structures in the equine eyelid (see Fig. 4-3) include sebaceous glands associated with cilia (i.e., Zeis-like glands) and modified sweat glands (i.e., Moll-like or ciliary glands).[3-5]

The eyelids are well vascularized via longitudinal vessels that run parallel to the eyelid margins and originate from the malar, superficial temporal, and ventral palpebral arteries.[3,4]

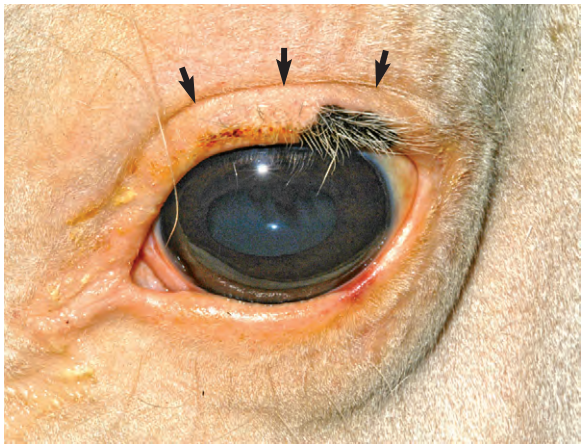


Figure 4-2. Prominent orbitopalpebral sulcus (skin fold) of the superior eyelid *(arrows)* delineating the orbital portion (above the skin fold) and tarsal portion (below the skin fold) of the eyelid.

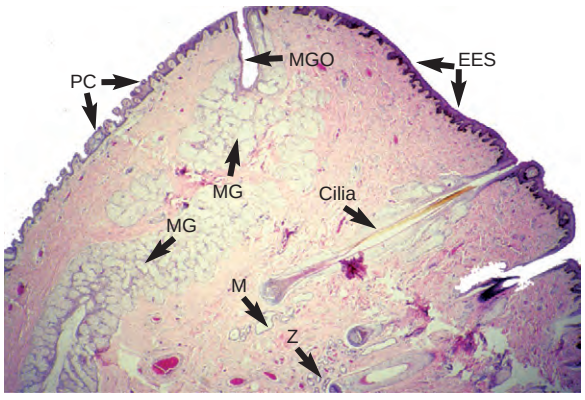


Figure 4-3. Histologic cross-section of the upper-eyelid margin (×40). The meibomian gland orifice *(MGO)* is the location of the mucocutaneous junction between the palpebral conjunctiva *(PC)* and the external eyelid skin *(EES)*. The meibomian gland *(MG)* is a large sebaceous gland. Sebaceous glands of Zeiss *(Z)* are adjacent to cilia and apocrine glands of Moll *(M)* are deep to the cilia.

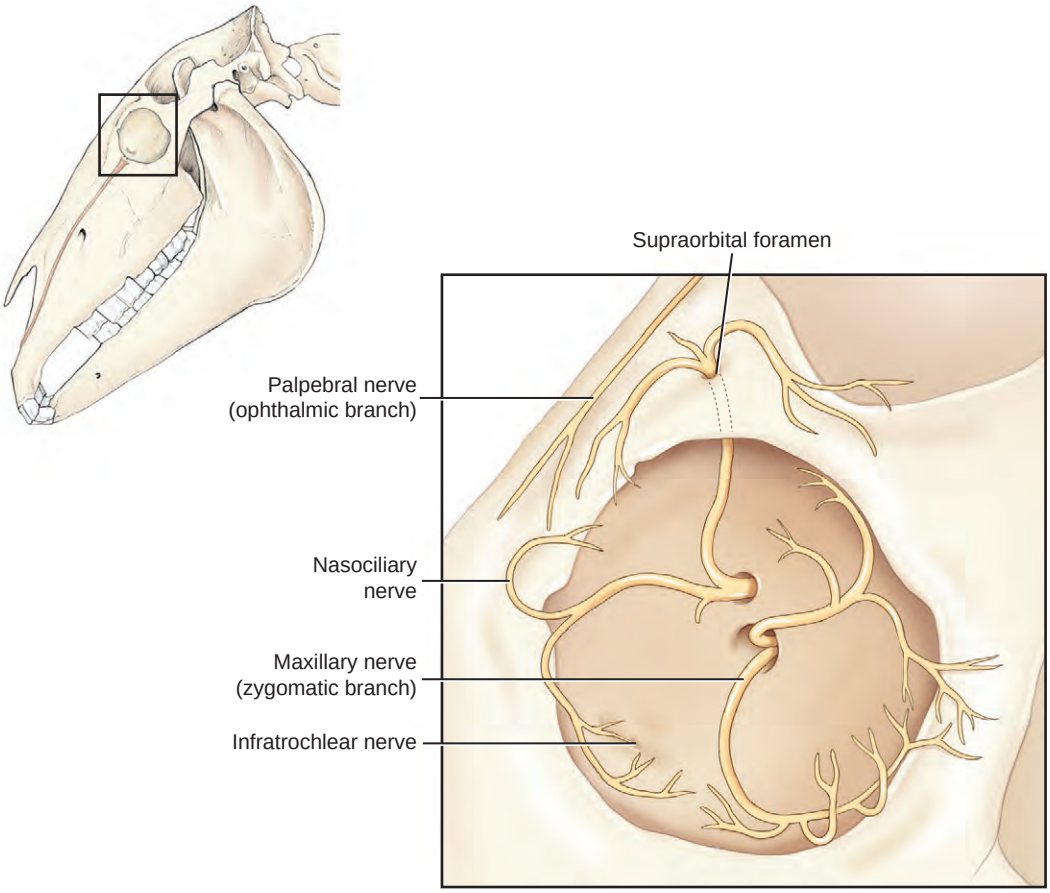


Figure 4-4. Schematic representation of equine eyelid innervation. Motor innervation to the eyelids is provided by cranial nerve (CN) III and CN VI. Sensory innervation to all equine periocular regions arises from CN V.

The excellent blood supply provides good healing of the eyelids after surgery or traumatic laceration. The eyelids have substantial lymphatic drainage, primarily to ipsilateral parotid and mandibular lymph nodes. This anatomic feature is of clinical significance in periocular neoplasia, especially squamous cell carcinoma, because the primary site of metastasis is to these draining lymph nodes.[6]

Eyelid musculature, innervation, function, and clinical descriptions of periocular motor and sensory nerve blocks have been reviewed in Chapter 1. Briefly, motor innervation to the eyelids is from CN III (the oculomotor nerve) and CN VII (the facial nerve). Sensory innervation to all aspects of the equine eyelid is from CN V (the ophthalmic branch of the trigeminal nerve) (Fig. 4-4). The muscles of the eyelids consist of the levator anguli oculi medialis, levator palpebrae superioris, frontalis, orbicularis oculi, retractor anguli oculi, malaris, and Müller's muscle (Fig. 4-5).[1] The orbicularis oculi muscle, innervated by the palpebral branch of CN VII, surrounds the palpebral fissure to form a sphincter that closes the eyelids. The levator palpebrae superioris, innervated by CN III, originates in the posterior orbit, inserts into fibers of the orbicularis oculi muscle of the upper eyelid, and acts to elevate the upper eyelid. The malaris muscle, innervated by a branch of CN VII, attaches to the orbicularis oculi fibers of the lower eyelid and functions to lower the inferior eyelid. Müller's muscle is smooth muscle innervated by the sympathetic nervous system. It is oriented perpendicular to the eyelid margin and provides the "tone"

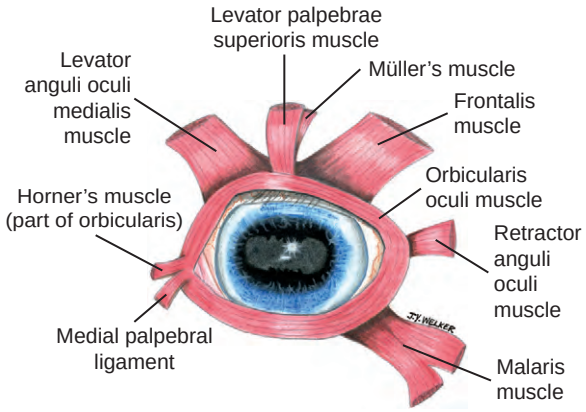


Figure 4-5. Muscles of the equine eyelid. (Courtesy Dr. Jeanie Y. Welker.)

to the tarsus. Loss of sympathetic tone to Müller's muscle occurs in Horner's syndrome and results in upper-eyelid ptosis.[7-9] Other muscles that control equine eyelid movement include the retractor anguli muscle that retracts and anchors the lateral canthus and the levator anguli oculi medialis and frontalis muscles that provide slight elevation of the upper eyelid (Table 4-1).

In the adult healthy horse, the palpebral fissure is open approximately 36 to 51 mm (mean of 43.5 mm) in the horizon-

Table 4-1 | **Equine Eyelid Muscles: Innervation and Function**

MUSCLE	INNERVATION	FUNCTION
Orbicularis oculi	CN VII (Facial)	Eyelid closure
Levator palpebrae superioris	CN III (Oculomotor)	Elevate the superior eyelid
Malaris	CN VII (Facial)	Depress the inferior eyelid
Müller's	Sympathetic	Elevate the superior eyelid
Retractor anguli oculi	CN VII (Facial)	Lengthen palpebral fissure
Levator anguli oculi medialis	CN VII (Facial)	Lengthen and elevate medial canthus
Frontalis	CN VII (Facial)	Elevate the superior eyelid

CN, Cranial nerve.

tal plane (temporal to nasal) and approximately 25 mm at its widest vertical dimension.[10] The lateral canthus denotes the region where the superior and inferior eyelids adjoin temporally, and the medial canthus is where the superior and inferior eyelids meet nasally (see Fig. 4-1). Structure of the equine eyelids is maintained not only by the palpebral muscles but also by palpebral ligaments. The medial canthal (palpebral) ligament is a firm, ligamentous band anchoring the medial canthus to the dense periorbital fascia and the periosteum of the medial orbital rim (see Fig. 4-5). The lacrimal sac lies just deep and ventral to this ligament. The anguli oculi vein runs just medial to the lacrimal sac. The lateral canthal (palpebral) ligament is formed by the junction of the temporal extremities of the superior and inferior eyelid tarsal plates and serves to anchor the lateral canthus to the lateral margin of the orbit. Normal eyelid position is necessary for adequate drainage of the tear film. Closure of the lids occurs from lateral (temporal) to medial (nasal). Normal eyelid closure distributes the preocular tear film over the corneal surface and mechanically facilitates tear drainage out the nasolacrimal outflow tract.

The lacrimal caruncle lies deep to the medial canthus and external to the third eyelid (see Fig. 4-1). This structure varies somewhat in size among horses and may contain modified sebaceous and sweat glands. If enlarged, the lacrimal caruncle may protrude and prevent the eyelids from conforming as well to the medial aspect of the cornea compared to the lateral aspect.[2] Conjunctiva, a nonkeratinized squamous epithelium, lines the inner aspect of the superior and inferior eyelids (i.e., palpebral conjunctiva) (see Fig. 4-3).

The third eyelid, or nictitating membrane (see Fig. 4-1), originates in the ventromedial aspect of the orbit and moves passively in the dorsolateral direction with retropulsion of the globe or as the globe is retracted during blinking. The third eyelid is covered with conjunctiva that is richly endowed with goblet cells. A T-shaped cartilage lies within the body of the third eyelid and conforms to the corneal curvature of the globe. The cartilage provides structural support along the leading margin of the third eyelid via a horizontal "arm" and through the center of the third eyelid by its vertical component (Fig. 4-6). The base of the third eyelid contains a lacrimal gland (tubuloacinar) that produces a portion of the aqueous component of the tear film (see Fig. 4-6).[11] A large fat pad lies ventral to the gland of the third eyelid.[4]

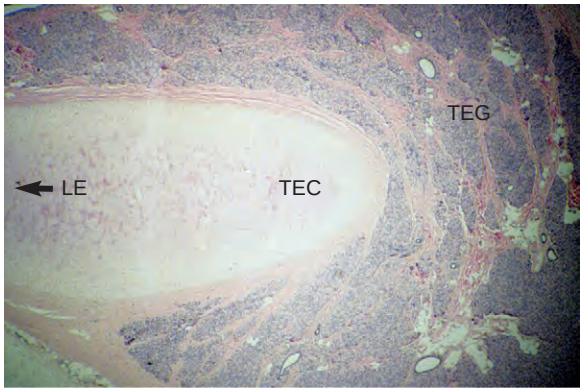


Figure 4-6. Photograph of the cross-sectional anatomy of the base of the third eyelid (×40). The third eyelid cartilage *(TEC)* runs through the center of the structure with the third eyelid gland *(TEG)*, surrounding the base of the third eyelid. The leading edge *(LE)* of the third eyelid is in the direction of the arrow.

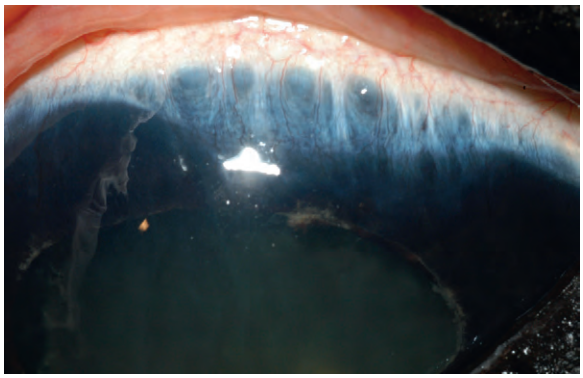


Figure 4-7. Prominent equine conjunctival lymphoid follicles visualized as rounded, relucent nodules at the superior limbus in this patient.

CONJUNCTIVA

Conjunctiva is composed of nonkeratinized stratified columnar cells that are continuous with the corneal epithelium. The conjunctiva consists of three primary anatomic regions that are contiguous with each other: the palpebral conjunctiva, the bulbar conjunctiva, and the fornix. The palpebral conjunctiva lines the superior and inferior eyelids (see Fig. 4-3). The bulbar conjunctiva covers the anterior aspect of the globe to the limbus. The conjunctival fornix (superiorly) and cul-de-sac (inferiorly) are the junctions between those areas where the superior and inferior palpebral and bulbar conjunctiva meet, respectively.[4,12] In the adult horse, the fornix (dorsally) is located approximately 3 cm from the limbus, while the cul-de-sac (ventrally) is approximately 2.5 cm from the limbus.[4] Conjunctiva also covers the anterior and posterior surfaces of the third eyelid. Conjunctiva is richly vascularized, variably pigmented (especially the bulbar conjunctiva), and has many goblet cells that contribute to the preocular tear film.[13] In horses, it is common to visualize aggregates of lymphoid follicles located perilimbally (Fig. 4-7). Likely, these lymphoid follicles represent part of the equine conjunctiva-associated lymphatic tissue (CALT) that has been shown to be integral to the ocular immune response in other species.[14-17]

NASOLACRIMAL SYSTEM

The nasolacrimal system of the horse comprises both secretory and drainage portions. The lacrimal gland, a tubuloacinar gland, is located dorsolateral to the globe and has 3 to 5 ductules that transport lacrimal fluid from the gland to the dorsal conjunctival fornix.[3] The gland of the third eyelid surrounds the base of the cartilage of the nictitans. The percentage of aqueous tears produced by the gland of the third eyelid in horses is not known; however, one study found that horses with surgically resected third eyelids did not have differences in basal (tested via Schirmer tear test II) or reflex (tested via Schirmer tear test I) tear production compared to normal horses.[18] In general, tear production in horses is robust, and copious reflex tearing can occur in response to ocular irritation or pain. Very few cases of keratoconjunctivitis sicca in horses have been reported in the veterinary literature.[19-22]

The nasolacrimal drainage apparatus of the horse may become obstructed due to a foreign body, calcification, dentition abnormalities, inflammation/infection, or neoplastic processes.[2,23,24] The eyelid lacrimal puncta are oval openings, approximately 2 mm in diameter and located 8 to 9 mm lateral to the medial canthus of the superior and inferior eyelids.[25] Through these puncta, lacrimal fluid enters the canaliculi, 3- to 4-mm diameter tubes that join to form the main nasolacrimal duct (Fig. 4-8). The equine nasolacrimal "sac" is much less developed than in human beings and anatomically represents only a slight dilation of the outflow tract where the two upper and lower canaliculi join.[25] The nasolacrimal duct continues distally 7 to 8 cm within the osseous lacrimal canal of the lacrimal and maxillary bones (Fig. 4-9).[25] The duct narrows slightly immediately prior to its exit from the lacrimal canal of the maxilla bone (see Figs. 4-8 and 4-9). Externally, the course of nasolacrimal duct through the maxillary bone follows a line from the medial canthus to the infratrochlear foramen.[25] The duct then courses in the submucosa along the nasal wall of the lateral aspect of the middle meatus, then dips ventrally as it courses in the ventral nasal fold. The duct curves laterally over the basal process of the incisive bone to open at a 3- to 4-mm, oval nasolacrimal orifice on the ventral floor of the nasal vestibule (Fig. 4-10).[25] Two or more nasolacrimal openings are very common in the nasal vestibule of horses. The total length of the nasolacrimal duct is approximately 24 to 30 cm long in the average adult horse.[4]

Figure 4-8. Methyl methacrylate cast of the right nasolacrimal duct. *A,* Lacrimal canaliculus. *B,* Lacrimal sac. *C,* Narrowing of nasolacrimal duct at the exit from the lacrimal canal. *D,* Flattening of the duct by cartilage plate in the sigmoid cartilage. (Photographs courtesy Dr. Clair Latimer. From Latimer CA, Wyman M, Diesem CD, et al: Radiographic and gross anatomy of the nasolacrimal duct of the horse, J Am Vet Med Assoc 45:451–458, 1984.)

ECONOMIC IMPACT OF OCULAR ADNEXAL DISEASE ON THE EQUINE INDUSTRY

Eyelid and nasolacrimal diseases are among the most common ocular diseases in horses. According to a U.S. Department of Agriculture 1998 study, the overall prevalence rate for eye

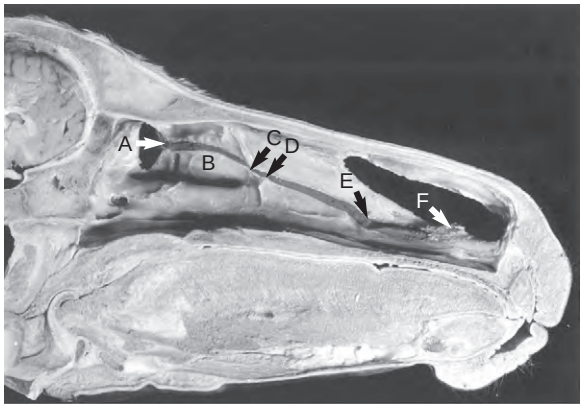


Figure 4-9. Methyl methacrylate cast of left nasolacrimal duct in a horse, with the medial bony orbit and medial wall of the lacrimal canal removed. *A,* Lacrimal sac. *B,* Duct within the lacrimal canal. *C,* Narrowing of nasolacrimal duct at the exit from the lacrimal canal. *D,* Exit of the duct from the lacrimal canal. *E,* Duct pressed laterally by cartilaginous plate in alar fold. *F,* Duct within basal fold. (Photographs courtesy Dr. Clair Latimer. From Latimer CA, Wyman M, Diesem CD, et al: Radiographic and gross anatomy of the nasolacrimal duct of the horse, J Am Vet Med Assoc 45:451–458, 1984.)

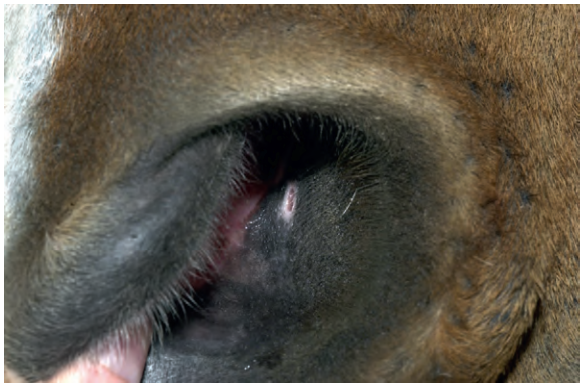


Figure 4-10. Nasal puncta of the nasolacrimal duct are 3- to 4-mm, oval orifices on the ventral floor of the nasal vestibule.

diseases was 7.4% in horses older than 6 months of age.[26] Although this study did not differentiate among ocular problems, eyelid and nasolacrimal diseases likely constitute a large majority of these cases. For example, eyelid disease is the second most common presenting complaint of horses presented to the Veterinary Medical Teaching Hospital at the University of Missouri. It is reasonable to conclude that equine adnexal disease has a substantial economic impact on the equine industry in general.

CONGENITAL OCULAR ADNEXAL DISEASE

ENTROPION

Entropion, or turning in of the eyelid margins, is the most common ocular abnormality in foals (Fig. 4-11).[27,28] Most commonly, the inferior temporal eyelid is affected, but both eyelids may be entropic. The most common cause of entropion in foals is secondary to loss of orbital fat (cachexia) or dehydration due to systemic illness or maladjustment. The loss of orbital contents results in globe retraction, thus allowing the eyelids to roll inward. The in-turned eyelids will result in corneal irritation and possibly ulceration from mechanical abrasion by the cilia and/or skin hair. Ocular discomfort from the anatomic component of entropion results in spastic entropion, where the globe retracts secondary to pain, further exacerbating the degree of entropion already present.

DIFFERENTIAL DIAGNOSIS

The most common cause of entropion in neonatal foals is systemic disease or maladjustment, as previously stated. However, some horses may be genetically predisposed, such as Thoroughbreds[29] and Quarter Horses.[2] The mode of inheritance or prevalence of this eyelid defect is not known. Other causes of entropion include microphthalmia, eyelid trauma, scarring (cicatricial entropion), or any disease causing prolonged blepharospasm.[2,30,31] Entropion in foals must be differentiated from other congenital eyelid abnormalities such as ankyloblepharon, coloboma, dermoids, and cilia abnormalities (Table 4-2).

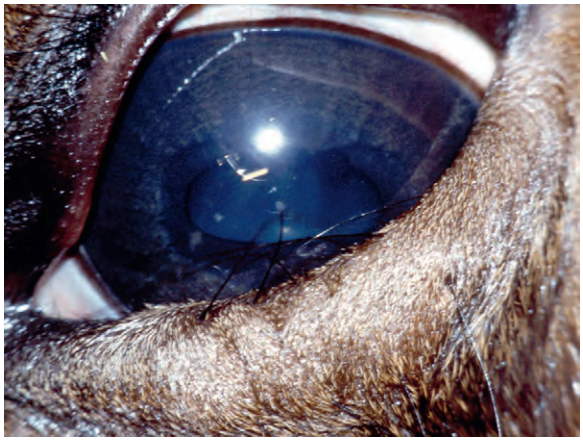


Figure 4-11. Entropion secondary to enophthalmos in a foal with neonatal maladjustment syndrome. (Photograph courtesy Dr. Riccardo Stoppini.)

TREATMENT

The goal of treatment for entropion is to correct the abnormal inversion of the eyelids and facilitate healing of concurrent conjunctivitis or keratitis. This therapeutic aim may be accomplished in a variety of ways. Most commonly, only a temporary tarsorrhaphy need be performed to correct the entropion while the foal is treated for any underlying systemic disease. Once the foal recovers from systemic illness, normal orbital structures/content should reestablish eyelid support and position. In rare instances, the entropion persists, and permanent surgical repair is required. In these foals, permanent repair of the eyelid should be delayed as long as possible, taking care to prevent corneal damage in the interim, because the rapid rate of head growth may result in facial changes (e.g., ectropion) and poor cosmetic results.

Medical therapy for entropion consists most commonly of corneal protection using frequent (every 4 to 6 hours) application of topical ophthalmic ointment on the affected eyes and appropriate therapy for any underlying systemic illness. Benign ophthalmic lubricating ointment (applied in conjunction with temporary tacking sutures [see next section]) is often sufficient, providing no corneal ulceration is present. If ulcerative keratitis is present, appropriate management for corneal ulcer and secondary uveitis should be instituted. Systemic nonsteroidal medications and topical atropine should be used with caution in these sick foals. Ophthalmic preparations containing steroids should be avoided. The recumbent nature of sick foals will predispose them to corneal ulceration even if fluorescein stain is negative at initial presentation to the veterinarian. Various materials have been reported for use to correct entropion. Substances including saline, penicillin G, silicone, hyaluronic acid, and liquid paraffin have been injected into eyelid margins to cause temporary eversion.[4] Although these materials may be effective, the need for repeated injections, eyelid inflammation, and the potential for scarring make this technique undesirable.

Temporary surgical repair of the entropion is almost always needed to correct both the anatomic and spastic components (i.e., entropion→ corneal irritation→ blepharospasm and globe retraction→ further exacerbation of entropion→ etc.). Temporary surgical repair allows the cornea to heal without mechani-

Table 4-2 | **Congenital Eyelid Abnormalities in Horses**

ABNORMALITY[4,27,28,30-34]	APPEARANCE	ASSOCIATED DEFECTS	BREEDS
Ankyloblepharon	Adhesion of the eyelid margins (superior and/or inferior) after birth	Microphthalmos	
Eyelid coloboma	Full-thickness absence of the eyelid margin	Corneal or conjunctival defects or ocular colobomas	
Entropion	Turning in of the eyelid margin	Corneal ulceration, enophthalmos, neonatal maladjustment syndrome	Quarter Horse Thoroughbred
Dermoid	Normal skin in an abnormal location	Conjunctival, corneal, or third eyelid dermoids	

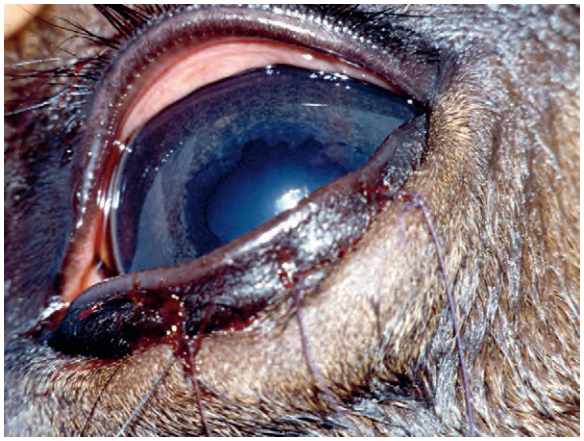


Figure 4-12. Temporary tacking sutures to roll out the eyelid margin in the foal with entropion in Fig. 4-11. (Photograph courtesy Dr. Riccardo Stoppini.)

cal irritation and does not carry with it the risk of permanent eyelid disfigurement from overcorrection. Temporary entropion repair is typically achieved with the foal sedated and placement of everting (tacking) sutures in a vertical mattress simple interrupted pattern. Nonabsorbable 4-0 to 5-0 monofilament suture is recommended. Silk has excellent knot security and can be used but may result in mild to moderate eyelid tissue reaction. When placing temporary tacking sutures, the "law of bisection" is recommended such that the first suture is passed in the center of the entropic eyelid, beginning 1 to 2 mm away from the eyelid margin perpendicular to the eyelid. The clinician should take care to avoid passing the suture through the eyelid margin, as sutures may be torn out, resulting in a large eyelid defect. Next, an additional bite of skin ventral to the original bite is taken. The distance between the two suture bites will determine the amount of eyelid eversion achieved once the vertical mattress suture is securely tied. If, for example, a large eversion/imbrication is necessary to correct the entropic eyelid, a 1- to 2-cm distance between the dorsal and ventral bites of the vertical mattress suture may be required. Additional sutures are placed in an identical fashion adjacent (usually 5 mm between sutures) to the central suture (Fig. 4-12). The number of sutures required will depend on the length of entropic eyelid. Knots should be secured with four throws, and the suture end nearest to the cornea should be cut short while the opposite end left longer to facilitate suture removal. Applying a drop of cyanoacrylic adhesive to the knots will help ensure that they will stay in place on the eyelid skin. After temporary tacking has been performed, elicit a palpebral reflex to ensure that the foal can blink normally. If the foal is lagophthalmic (e.g., unable to close the eyelids completely) after temporary tacking, removal of one or more sutures may be necessary to prevent exposure keratitis. Sutures typically remain in place for 2 to 4 weeks in most foals.

PERMANENT SURGICAL REPAIR FOR ENTROPION

Permanent correction of entropion should only be performed after several attempts at temporary correction in foals. If the foal regains health and grows normally but entropion persists, permanent surgical repair is required. If definitive surgical repair is performed prematurely (i.e., with loss of orbital fat still present) the foal may be overcorrected, and iatrogenic ectropion will result.

The most common surgical procedure for entropion involves an elliptical skin excision known as a *Hotz-Celsus procedure* (Fig. 4-13). This surgical procedure permanently everts the eyelid margin by removing a segment of skin equal to the amount of skin that is entropic. Some practical tips to help ensure success with a simple Hotz-Celsus include the following:

- The initial skin incision should be made close to the lid margin no more than 2 to 3 mm from the edge of the eyelid, at the haired/nonhaired junction, using a scalpel (e.g., #15 Bard-Parker blade).
- Use of a Jaeger lid plate (or a sterile tongue depressor coated with sterile lubricant ointment) will help support the eyelid and facilitate an accurate incision.
- Be certain to extend the incision parallel to the lid margin for the entire length of the affected area.
- The second incision should be made distal and relatively parallel to the first, tapering the ends to meet the first incision and incorporating enough eyelid tissue in the final ellipse to correct the entropion (see Fig. 4-13).
- Gently elevate one end of the incised tissue with fine-toothed forceps, and excise the outlined skin and subcutaneous tissue with small scissors (e.g., Stevens tenotomy scissors) (Fig. 4-14).
- Close the wound with 4-0 to 6-0 monofilament nonabsorbable suture in a simple interrupted pattern spaced at 2 to 3 mm intervals. To ensure an even closure without dog ears, apply the "law of bisection."
- Cut the suture end nearer the lid margin close to the knot to avoid corneal irritation, but leave the distal end longer to aid removal.
- At the conclusion of surgery while the horse is still anesthetized, be certain you can visualize the eyelid margin without manipulating the lid.
- Postoperatively, an equine eye cup may be used to prevent the horse from rubbing at the eye if necessary. Appropriate medical management for any concurrent corneal ulceration should be instituted (see Chapter 5), and sutures should be removed in 10 to 14 days (Fig. 4-15).

OTHER CONGENITAL DISEASES OF THE ADNEXA

Congenital adnexal diseases including ankyloblepharon, eyelid agenesis (Fig. 4-16), coloboma, dermoids (Fig. 4-17), and cilia abnormalities have been reported.[4,27,28,30,32-34] Features of these conditions are listed in Table 4-2. Congenital ankyloblepharon, or fusion of the eyelids together, after birth is not normal in foals, since horses have fully developed adnexa at birth.[4] Separation of the eyelids should be attempted first manually, then using blunt dissection starting at the medial canthus.[32] Occasionally, foals will present blind with significant congenital ophthalmic disease that affects both the adnexa and the globe (Fig. 4-18).[35]

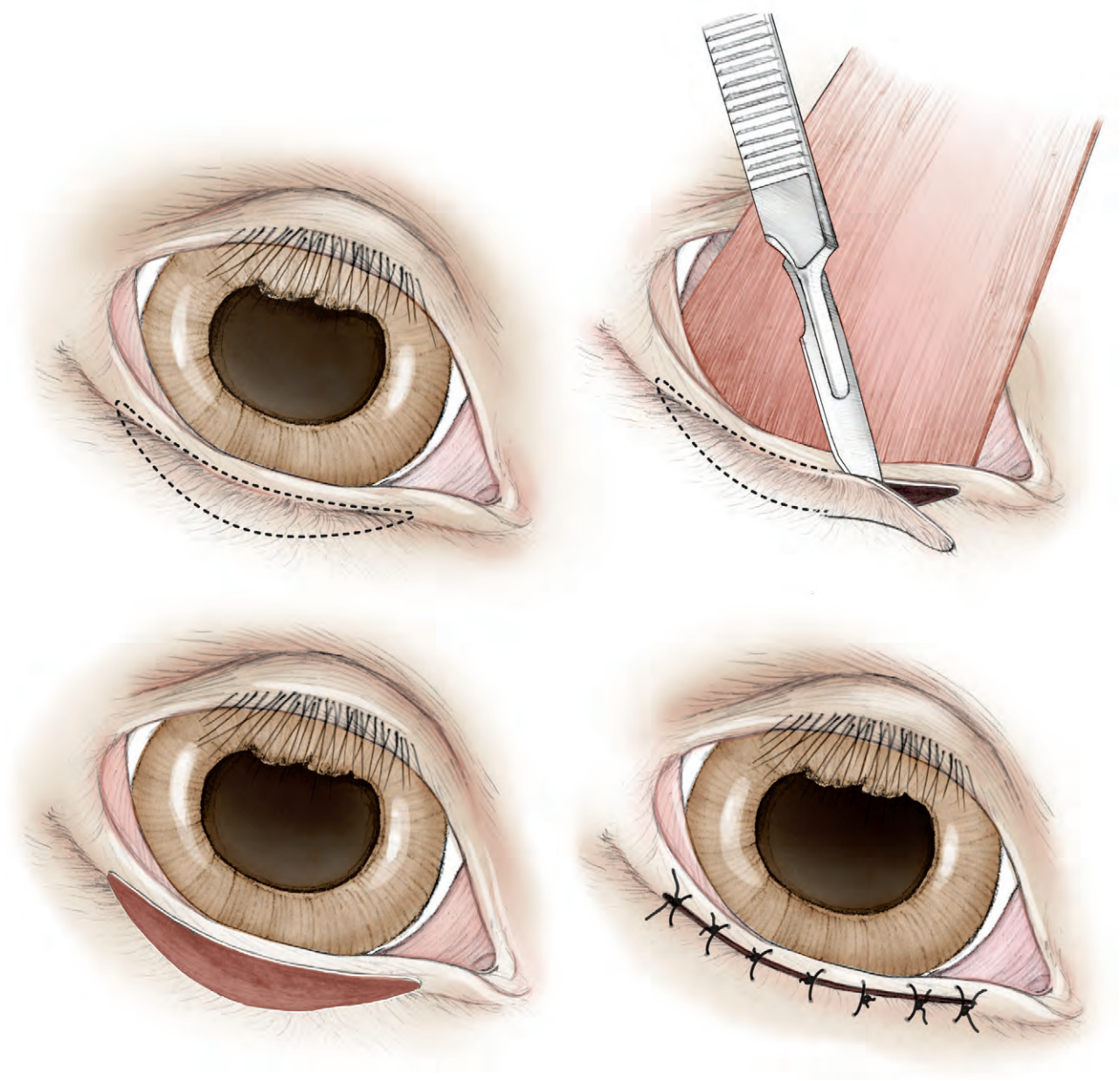


Figure 4-13. Hotz-Celsus entropion repair.

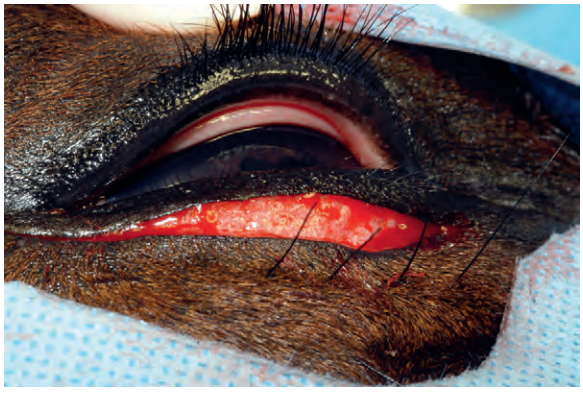


Figure 4-14. Horse undergoing Hotz-Celsus surgical repair for entropion.

Figure 4-15. Same patient as in Fig. 4-14, 2 weeks postoperatively at suture removal.

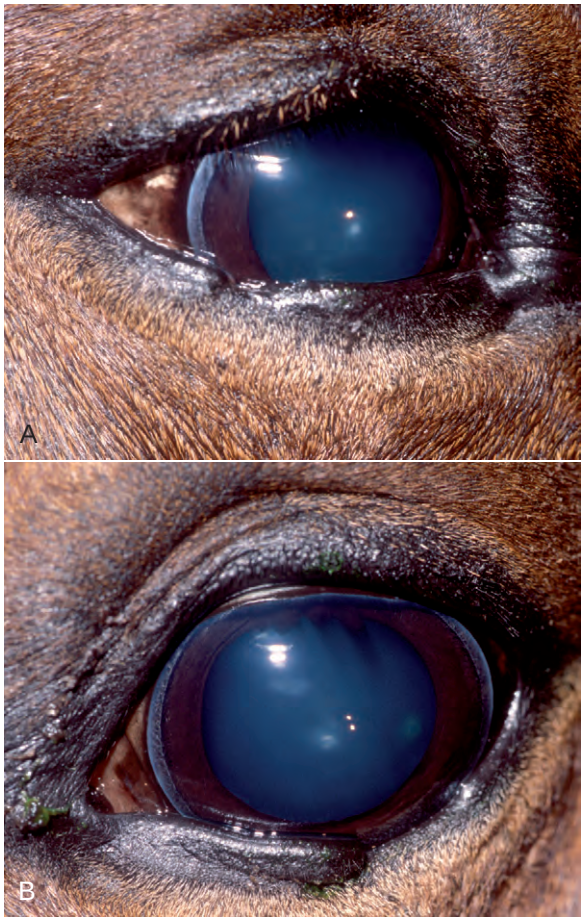


Figure 4-16. Inferior eyelid agenesis in a foal. **A,** Right eye (OD). **B,** Left eye (OS).

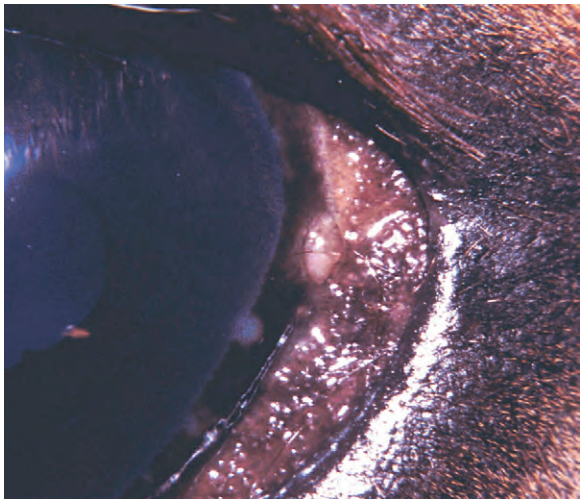


Figure 4-17. Conjunctival dermoid in a young horse. (Photograph courtesy Dr. Riccardo Stoppini.)

CONGENITAL DISEASES OF THE NASOLACRIMAL SYSTEM

EPIPHORA

Epiphora, or overflow of tears, can occur from excessive lacrimation due to ocular irritation, an eyelid abnormality (e.g., entropion), or obstruction of the nasolacrimal duct. Obstructions of the nasolacrimal duct occur as a result of, or develop secondary to, bacterial infections (i.e., dacryocystitis) and are associated with profound mucopurulent discharge (Fig. 4-19). Congenital deficiency in tear production or keratoconjunctivitis sicca (KCS) has not been reported in horses but may occur. In fact, spontaneous development of KCS in horses, in general, is very uncommon, and the KCS that has been reported is typically secondary to trauma or other inflammatory disorders or endocrinopathies.[19-22]

NASOLACRIMAL DUCT ATRESIA

The most common congenital anomaly of the nasolacrimal duct is nasolacrimal duct atresia.[4,27,30,32-34] The most common defect is an imperforate nasal punctum, although eyelid punctal atresia or incomplete formation of the duct can occur anywhere along

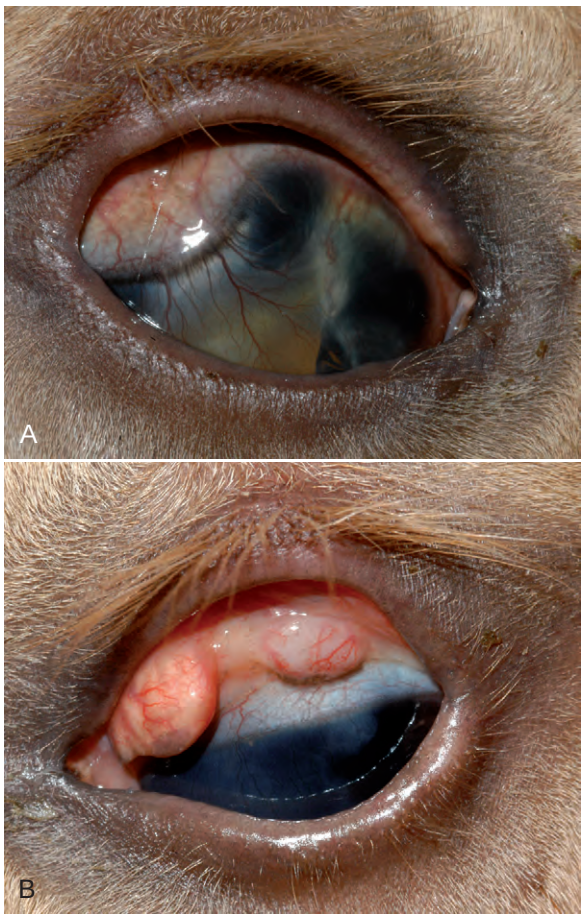


Figure 4-18. Four-day-old foal euthanized due to blindness. Ophthalmic examination and histopathology revealed congenital bilateral microphthalmia and anterior segment dysgenesis (Peter's anomaly) with persistent hyperplasic primary vitreous. **A,** Right eye. **B,** Left eye.

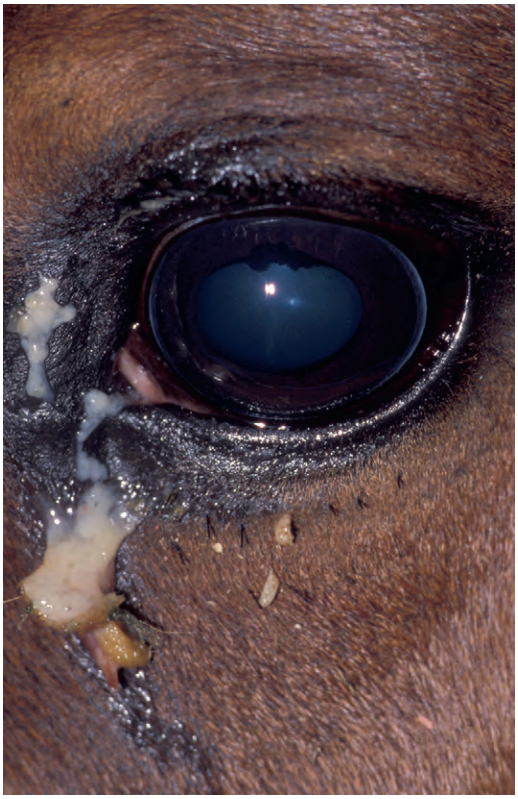


Figure 4-19. A 2½-year-old Quarter Horse with a 20-month history of copious mucopurulent discharge from the left eye. Diagnostic testing confirmed imperforate left nasolacrimal duct punctum.

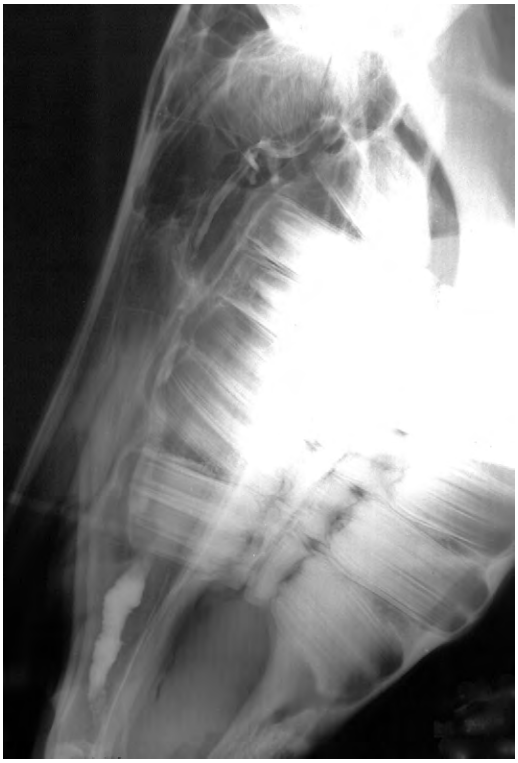


Figure 4-20. Contrast dacryocystorhinography (DCR) of the horse in Fig. 4-19, revealing irregularities in nasolacrimal duct lumen diameter along the length of the lacrimal duct, with the greatest dilation at the distal end. These findings were consistent with permanent occlusion, chronic inflammation, and subsequent dilation of the nasolacrimal duct.

its course (see Figs. 4-8 and 4-9). Mild to moderate unilateral or bilateral epiphora is initially observed, but by 4 to 6 months of age, the predominant clinical sign is severe mucopurulent ocular discharge (see Fig. 4-19) due to the development of secondary bacterial dacryocystitis. Diagnosis is made by direct observation of the nasal vestibule (i.e., lack of punctal openings) and inability to irrigate the nasolacrimal system from the eyelid puncta. Also, swelling of the nasal epithelium distally, near the area of normal punctal opening, may also suggest atresia.[4,36,37] Rarely, eyelid punctal atresia may occur, resulting in failure of nasolacrimal irrigation (retrograde) and conjunctival swelling.[30]

DIFFERENTIAL DIAGNOSIS

It is important to differentiate acquired obstructive diseases of the nasolacrimal duct from true atresia. Acquired obstructions generally have open, visible punctal openings (see Fig. 4-10) but an inability to irrigate the nasolacrimal system. Because nearly all cases of nasolacrimal punctal atresia (either eyelid or nasal) have secondary dacryocystitis, bacterial culture and sensitivity should be submitted to appropriately manage concurrent infection. Contrast radiography (e.g., dacryocystorhinography [DCR]; see Chapter 1 for description of the technique) can be very helpful in determining the exact location of the obstruction (Fig. 4-20). A diagnostic DCR may help determine the type of surgery that may be needed (i.e., incision of duct and stent placement versus dacryocystorhinotomy/sinostomy) and the long-term prognosis.[38]

TREATMENT

Treatment of nasolacrimal atresia consists of relieving the obstruction by creating a new opening (whether proximally or distally), treating the secondary bacterial infection, and preventing reobstruction.[24] Topical and/or systemic antibiotics may result in a temporary improvement in clinical signs. However, unless the obstruction is relieved, the infection and clinical signs will quickly return, so definitive surgical intervention is most frequently required for long-term successful resolution of epiphora or mucopurulent discharge. After surgery, topical ophthalmic drops are used to help address concurrent secondary dacryorhinocystitis. Drops are preferred over ointment because they travel the length of the nasolacrimal duct much more effectively.

For optimal results, surgical opening of obstructed or atretic puncta is always required, unless the nasolacrimal duct is agenic. Preoperative determination of the location(s) of the obstruction is critical for success. Usually the obstruction is just at the opening to the nasal puncta, and creating a new opening at the site is curative. Preoperatively determining the location of the obstruction(s) can be difficult. Careful physical examination (i.e., search carefully for submucosal swelling), dacryocystorhinography (see Fig. 4-20), and possibly advanced imaging (e.g., computed tomography) can accurately delineate the specific obstructive location. With the horse heavily sedated or anesthetized, an attempt can be made manually to locate and open a presumed distal atretic puncta. A 5 Fr male Silastic or plastic urinary catheter (with or without wire stent) is threaded

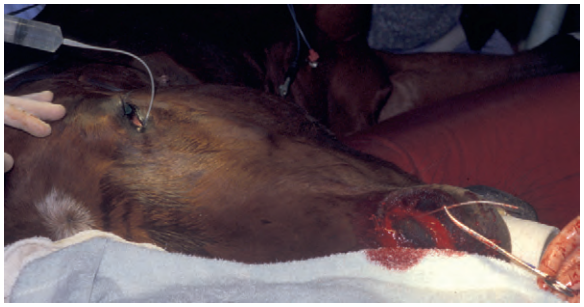


Figure 4-21. Horse in Fig. 4-19 under general anesthesia. A 5 Fr closed-ended urinary catheter was threaded rostrally from the inferior lacrimal punctum to the blind end of the lacrimal duct. The cannula was digitally palpated through the wall of the nasal meatus, and large curved scissors were used to create a distal nasolacrimal duct opening. The catheter was advanced through the nasolacrimal duct to exit through the newly created nasal punctum. Copious hemorrhage is to be expected with this surgery.

normograde (from proximal to distal) through the dorsal canaliculi into the nasolacrimal duct. The catheter is advanced until resistance is encountered. The catheter should not be forced ventrally if resistance is encountered, because severe hemorrhage may develop.[39] If it is only the nasal puncta that is occluded, the tip of the catheter will be palpable under the nasal mucosa. Occasionally, the duct terminates proximal to the normal puncta site, and careful palpation along the course of the nasolacrimal duct is needed to locate the catheter tip. An incision is made over the catheter through the nasal mucosa, and the catheter is pulled through the nares (Fig. 4-21). Profound hemorrhage from the incision through the nasal mucosa is common, therefore only a single bold cut should be made, or electrocautery on "cut" mode can be used to make the incision/opening. To recreate a punctal opening, the Silastic tubing is sutured in place for 4 to 6 weeks (Fig. 4-22). After surgery, topical and systemic antibiotics should be given according to culture and antimicrobial susceptibility results; however, frequently the choice is topical triple antibiotic solution (every 8 hours). Oral antibiotic and antiinflammatory therapy in horses should be used judiciously and for as minimal duration as possible. (Please see the discussion on general therapeutic strategies with adnexal disease in this chapter.) Once the nasolacrimal tube is removed after 4 to 6 weeks, a positive Jones test should be observed—that is, fluorescein stain applied to the ocular surface on the affected side should be visualized at the nares, confirming patency of the nasolacrimal outflow tract (Fig. 4-23).

Figure 4-22. Horse in Fig. 4-19 5 days after undergoing surgery to correct distal nasolacrimal duct atresia. A 5 Fr closed-ended male urinary catheter is sutured to the skin at both the dorsal and ventral aspects of the nasolacrimal duct.

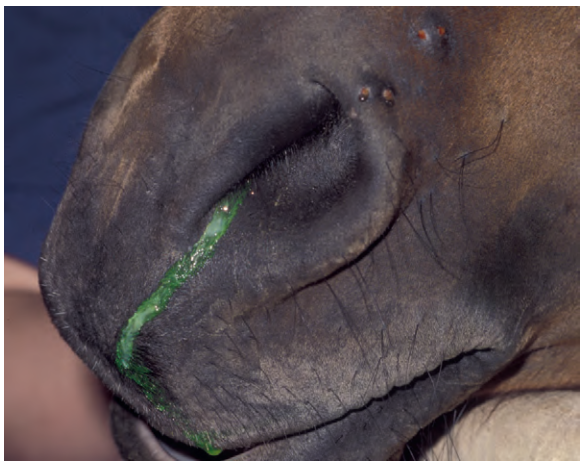


Figure 4-23. Horse in Fig. 4-19 6 weeks after undergoing surgery to correct distal nasolacrimal duct atresia. Positive Jones test confirmed patency of the nasolacrimal outflow tract.

GENERAL THERAPEUTIC CONSIDERATIONS WHEN TREATING HORSES FOR ACQUIRED ADNEXAL OR NASOLACRIMAL DISEASE

OVERVIEW

Whenever appropriate, specific medical or surgical therapies unique to particular equine adnexal or nasolacrimal disease will be addressed in the discussion of those pathologic processes. Medical therapy for equine adnexal and nasolacrimal diseases, regardless of whether or not surgery is part of the treatment regime, is frequently similar for a variety of infectious, inflammatory, and neoplastic diseases. For this reason, a brief review of medical therapy for these two ophthalmic anatomic regions in the horse merits discussion by way of a broad overview to avoid redundancy throughout the remainder of this chapter.

It is worth noting that the majority of ocular pharmacokinetic ophthalmic drug studies have been performed in nonequine species, rendering much of the current clinical medical practice to be based on extrapolation from other species. This approach is problematic in that horses may be more prone to complications when systemic antimicrobial and antiinflammatory agents are used than what is commonly observed using

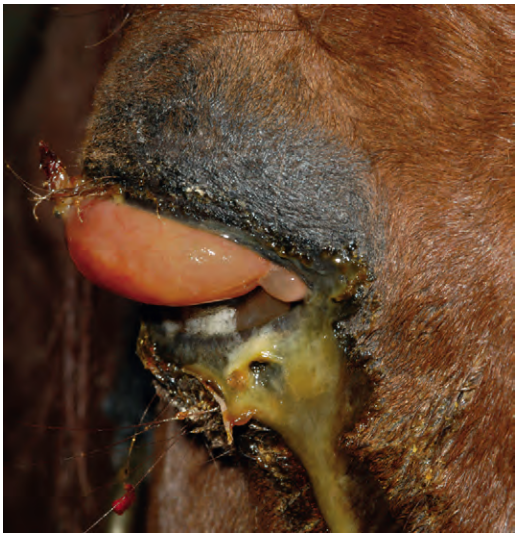


Figure 4-24. Horse with severe conjunctival chemosis and periocular swelling in the right eye (OD) secondary to being struck by lightning.

Table 4-3 | **Common Systemic Antibiotic Agents Currently Used in Horses With Eyelid or Nasolacrimal Disease***

ANTIBIOTIC	DOSE AND ROUTE	FREQUENCY AND DURATION
Ceftiofur	2.2 mg/kg intramuscularly	Twice daily for 5-7 days
Trimethoprim/ sulfamethoxazole	15-20 mg/kg orally	Twice daily for 5-7 days
Penicillin V potassium	22,000 IU/kg intravenously	Four times daily for 5-7 days and used together with gentamicin
Gentamicin	6.6 mg/kg intravenously	Once daily for 5-7 days and used together with penicillin V potassium

*When deemed necessary at the University of Missouri Veterinary Medical Teaching Hospital.

similar therapeutic strategies in other species. Additionally, there are, no doubt, significant differences in the pharmacokinetics of topical drugs resulting from such factors as relative ocular size, tear production and flow dynamics, blink rate, and presence and motility of the third eyelid.[4,40]

The overall medical goal when treating horses with congenital or acquired adnexal or nasolacrimal disease is to achieve therapeutically effective levels of an appropriate drug or combination of drugs at the affected site. Specifically, the clinician's goals are to: (1) decrease/control inflammation of the affected tissue; (2) prevent secondary infection; and (3) treat specific bacterial, fungal, or parasitic disease—diagnosed by cytology, biopsy, and/or culture and sensitivity testing—which may be the primary cause of disease or secondary to some other primary pathologic process (e.g., neoplasia with secondary bacterial infection). As previously discussed, the adnexa of horses are richly vascularized, affording excellent blood supply to an infected (or potentially infected) area and thus greatly facilitating wound healing. However, the adnexa are also capable of a pronounced inflammatory response secondary to infectious, inflammatory, neoplastic, or traumatic processes (Fig. 4-24). Considering the essential role of the adnexa and nasolacrimal system in preserving corneal clarity and ocular comfort, therapeutic agents are frequently administered to address the primary treatment goals. Often, regardless of the primary etiologic process, adnexal and nasolacrimal equine diseases are treated with a combination of systemic and topical medications. Detailed pharmacologic review of a wide variety of therapeutic agents currently used in horses is beyond the scope of this chapter; the reader is encouraged to seek additional information as needed.[41,42]

ANTIMICROBIAL THERAPY

Systemic antimicrobial agents are frequently used in horses with eyelid or nasolacrimal disease, but in many cases, their use is empirical and may not be necessary. Furthermore, the route and type of antimicrobial administered is frequently based on nonmedical directives such as cost, availability, or ease of administration. The gastrointestinal tract of horses is highly susceptible to the adverse effects of antimicrobial drugs, owing to disruption of normal intestinal microbial populations and proliferation of enteropathogens. Diarrhea, especially when accompanied by signs of endotoxemia, is the usual clinical manifestation of this potentially life-threatening complication of systemic antimicrobial use in horses. Consequently, judicious use of any systemic antimicrobial is recommended, and careful consideration must be made as to whether or not a systemic antimicrobial is truly indicated in each individual case. This decision process is often in stark contrast to the more "general therapeutic approach" typical in small-animal surgical ophthalmic patients where preoperative and postoperative antimicrobial medications are routinely used. When deemed necessary to treat obvious infection, antimicrobial selection is most appropriately made based on culture and sensitivity results of the affected area. Examples of systemic antibiotic usage, dose, and duration by the University of Missouri Veterinary Medical Teaching Hospital can be found in Table 4-3.

Topical antimicrobial therapy for adnexal disease is dispensed commonly in ointment form to help "buffer" the cornea from any adnexal contour irregularities while the eyelid(s) is/are healing and may be useful to prevent secondary corneal infection or abrasion. Ointments should not be used in cases where the cornea has already, or is at risk of, rupture(d). If nasolacrimal infection is present, ophthalmic drops are preferred because solutions or suspensions will more easily course down the nasolacrimal outflow pathway than ointments to reach the affected target tissue. Perhaps the most common broad-spectrum topical antibiotic ointment routinely dispensed for eyelid trauma (including after surgical intervention) in North America is triple antibiotic ointment (e.g., neomycin, bacitracin, polymyxin) at a frequency of 3 to 4 times daily. Some clinicians may elect to use broad-spectrum ophthalmic antibiotic ointment preparations containing topical steroids as well; however, in areas where fungal keratitis is prevalent, caution is recommended because of the risk of keratomycosis. Other relatively routine topical ophthalmic ointments dispensed in the face of adnexal disease include topical erythromycin,

tetracycline, chloramphenicol, or nonophthalmic preparations of silver sulfadiazine ointment. Marked differences in normal ocular equine surface flora exist among individual horses, geographic location, and seasonal variation.[2,43,44] The inherent variability of possible or primary infectious microbes that may affect the equine adnexa or nasolacrimal system can render empirical treatment with standard antibiotics unsuccessful, especially if the horse has already been treated with topical or systemic antimicrobials prior to referral to a specialist. Whenever possible, further diagnostic testing is advisable. Even then, however, in vitro sensitivity data may not necessarily reflect in vivo clinical response, particularly if only topical medications are used to treat adnexal disease. Systemic routes of administration are more effective at reaching therapeutic drug levels in the adnexa.

ANTIINFLAMMATORY THERAPY

Veterinarians have long been familiar with the important role antiinflammatory therapy plays in the treatment of periocular and ocular inflammation. Numerous systemic and topical corticosteroid and nonsteroidal antiinflammatory drugs (NSAIDs) are commercially available. Again, the challenge clinicians are continually faced with when electing to treat a horse with periocular inflammation is to balance the potential therapeutic benefits of antiinflammatory therapy against the occasional life-threatening risks of these drugs, especially when administered systemically. Systemic NSAID usage in horses is associated with the risk of both gastrointestinal disturbance and kidney damage.[45-47] For these reasons, the use of systemic NSAIDs should be restricted to the requirements of necessity and not provided beyond the recommended treatment period without further veterinary examination or consultation. If complications occur, horses typically manifest reduced appetite, lethargy, colic, poor performance, diarrhea, weakness, abnormal water consumption, and/or discolored urine. While uncommon, owing to the severity of potential complications, owners should be advised to seek veterinary attention promptly if adverse side effects are observed. Furthermore, risks of systemic NSAID toxicosis are increased if the horse fails to drink a normal quantity of water,[47] so clients should be urged to ensure that their horse's water consumption be carefully scrutinized to ensure adequate intake. Common systemic NSAIDs currently used in horses with adnexal or nasolacrimal disease when deemed necessary to control inflammation and help alleviate periocular discomfort are listed in Table 4-4. Topical ophthalmic ointments, solutions, and suspensions of steroid and NSAIDs (e.g., dexamethasone, prednisolone acetate, flurbiprofen, diclofenac, suprofen) are also readily available or can be obtained through a licensed compounding pharmacy.[48] The same general principles discussed previously regarding topical therapy for adnexal or nasolacrimal disease apply. In most cases, if appropriate drug levels are to be reached in these two ophthalmic anatomic areas, systemic administration of antiinflammatory therapy is more appropriate.

EQUINE OCULAR LAVAGE SYSTEMS

Horses may resent topical ophthalmic drug administration and can become dangerous to themselves and their owners or handlers when being medicated. Although more commonly used in the treatment of ophthalmic diseases affecting the globe, equine ocular lavage systems may be useful in the treatment of adnexal or nasolacrimal disease. Lavage tubes are typically categorized into two groups: indwelling nasolacrimal and subpalpebral (SPL) systems. The latter may be further subcategorized as single- or double-entry systems.[49] Within the last 10 years, an alternative single-entry SPL system for horses that is inserted in the medial aspect of the inferior eyelid has been described (inferomedial SPL system, or ISPL)[50] and is now routinely used by several veterinary ophthalmologists (Fig. 4-25). Data from 86 horses demonstrated that the ISPL can be easily and safely placed in the lower medial eyelid, is well

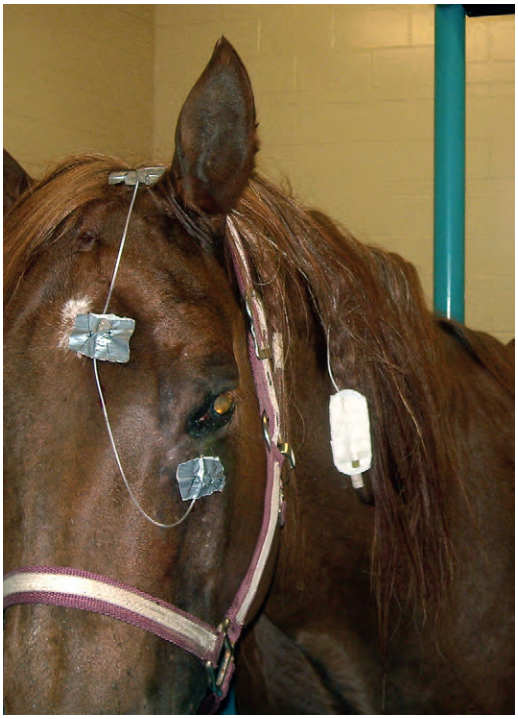


Figure 4-25. Horse with an inferomedial subpalpebral lavage system (ISPL) in place.[49]

Table 4-4 | **Common Systemic NSAIDs Currently Used in Horses With Eyelid or Nasolacrimal Disease***

NSAID	DOSE AND ROUTE	FREQUENCY AND DURATION
Phenylbutazone	4.4 mg/kg *(high dose)* intravenously or orally 2.2 mg/kg *(low dose)* intravenously or orally	High dose twice daily for 24-48 hours, then decrease to low dose twice daily for 5 days
Flunixin meglumine	1.1 mg/kg *(high dose)* intravenously or orally 0.5 mg/kg *(low dose)* intravenously or orally	High dose twice daily for 24-48 hours, then decrease to low dose twice daily for 5 days
Firocoxib	0.1 mg/kg orally	Once daily for 5-7 days

NSAIDS, Nonsteroidal antiinflammatory drugs.
*When deemed necessary at the University of Missouri Veterinary Medical Teaching Hospital.

tolerated for periods of greater than a month, and can be used to successfully treat a wide variety of medical and surgical conditions with a marked reduction in frequency and severity of complications compared with the more traditional superior eyelid SPL systems.[50] Regardless of the type of SPL system the clinician may prefer to use, instructions on the care and use of an indwelling lavage system are helpful to provide to owners/trainers. An example of such discharge instructions is provided in Box 4-1. See Chapter 2 for more information on the placement of SPL catheter systems.

ACQUIRED ADNEXAL DISEASE

EYELID LACERATIONS

CLINICAL APPEARANCE AND DIAGNOSIS

The environment in which many horses are stabled, together with the prominent lateral positioning of their eyes, renders this species particularly susceptible to periocular trauma. Environmental and natural anatomic susceptibilities are compounded by the horse's acute "flight response" which causes most to react to stimuli by exaggerated and sometimes uncontrolled movements of their heads. Eyelid lacerations, as a result, are commonly encountered in horses. Generally, lacerations occur acutely and are easily noted by the horse's caretaker. Occasionally, if the horse is not monitored closely, presentation to a veterinarian may occur several days after the injury occurred and secondary infection/inflammation will result in severe mucopurulent ocular discharge. In most cases, the severity of the appearance of the lesion does not correlate well with overall prognosis. Thanks to the excellent blood supply to the eyelids,[12] most lacerations can be repaired to achieve a relatively well-functioning and cosmetic eyelid, even in the presence of significant secondary blepharitis. Therefore, every attempt should be made to surgically repair all eyelid lacerations, taking care to avoid removing any hanging eyelid pedicles (Figs. 4-26 and 4-27). Despite the severity of the eyelid laceration (whether major or minor), a thorough ocular examination should be

Box 4-1 | **Instructions for Use and Maintenance of a Subpalpebral Lavage Tube***

Use and Maintenance of the Equine Subpalpebral Lavage Tube

Your horse has had a subpalpebral lavage tube placed in his/her eye(s). This should make medication administration much easier and safer for you and your horse. The tubes can be safely left in for several weeks and can be removed by your veterinarian when no longer needed. The following is an outline of how to use and care for these tubes.

1. Administration of medications: Approximately 0.1 mL of the desired medication should be drawn up into a small (1-mL) syringe by inverting the eye drop bottle and entering the dropper with a small (25-gauge) needle. The solution will be drawn up more easily if you squeeze the bottle slightly at the same time as drawing back on the syringe plunger. While the horse is well restrained, insert the needle into the rubber injection port on the end of the tube near the mane. Inject the solution (approximately 0.1 mL) and then inject approximately 1 mL of air into the tube in the same manner. This will expel the medication gently onto the eye surface. If you stand on the same side as the eye to be treated, you should see a small amount of liquid bubble up inside the lower eyelid. It is critical that the air is injected very slowly so as not to cause pain for your horse. Because long-term medication is frequently needed in these cases, we must insure that your horse does not begin to object to this technique.
   - Only solutions thin enough to pass through the tube may be administered with this system. Please do not put any ointments through the tube.
   - Keep the syringes and dropper bottles as clean as possible.
   - Refrigerate the eye medications as directed.
   - When administering more than one medication at the same time of day, leave at least 5 minutes (preferably longer) between eye medications, and begin with the least viscous medication. In your case, the preferred order would be:
     i. _____
     ii. _____
     iii. _____
     iv. _____
2. Care of the tube: There are three common sites where the tube may require some maintenance, particularly if it is left in place for extended periods (i.e., weeks).
   - The first is at the rubber injection port near the mane. You should have been provided with some spare parts for this. The modified (dull) needle is inserted into the end of the silicone lavage tube and pushed into the tubing until it is up against the hub. The rubber injection port is then screwed onto the modified needle hub. The needle should be retained on the silicon tube with some tape. Occasionally, a small leak in the silicone tube will occur at the end of the metal needle; in this case, the tube can be shortened. Using very clean scissors, remove as little as possible of the leaking section, and then refit the same or a new modified needle and injection port.
   - The second point where leaks are sometimes seen is at the point of entry into the skin of the lower eyelid. This may be associated with some lower-eyelid inflammation if the solutions leak into the subcutaneous tissues. This usually requires tube replacement. Please call your local veterinarian if you are concerned about leaks at this position.
   - Finally, the sutures attaching the duct-tape "wings" to the head may break free. If this occurs, they may be resutured by your veterinarian. Alternatively, you can reaffix them using a small drop of superglue *(do not get superglue in the animal's eye)* or with more adhesive tape.
3. Complications: Complications with the inferonasal tube system are fortunately uncommon. Things to watch for are increasing levels of ocular discomfort (squinting, tearing, etc.); swelling, particularly at the point where the tube enters the lower lid; or movement of the tube, especially if the footplate migrates up out of the lower eyelid and could rub on the cornea. If the latter complication is seen, gently pull downward on the tube to reseat the footplate deeper in the eyelid, and *call your veterinarian.*

*Example of instructions that can be provided to equine owners on the use and maintenance of an equine subpalpebral lavage tube. These instructions were specifically written for the ISPL[50] used at the University of Missouri Veterinary Medical Teaching Hospital, but they can be easily adapted for other types of subpalpebral lavage systems.

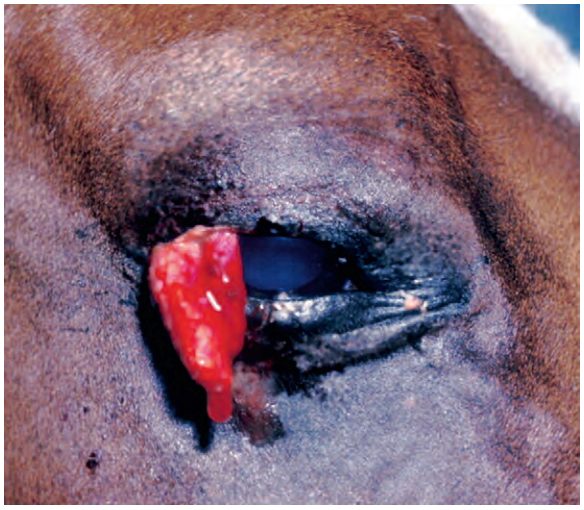


Figure 4-26. Eyelid laceration of a horse, beginning medially and extending laterally. This tissue tag or hanging eyelid fragment should not be excised, but instead, because of the excellent eyelid blood supply, this fragment can be replaced and usually remains viable. (Photograph courtesy Dr. Mike Davidson.)

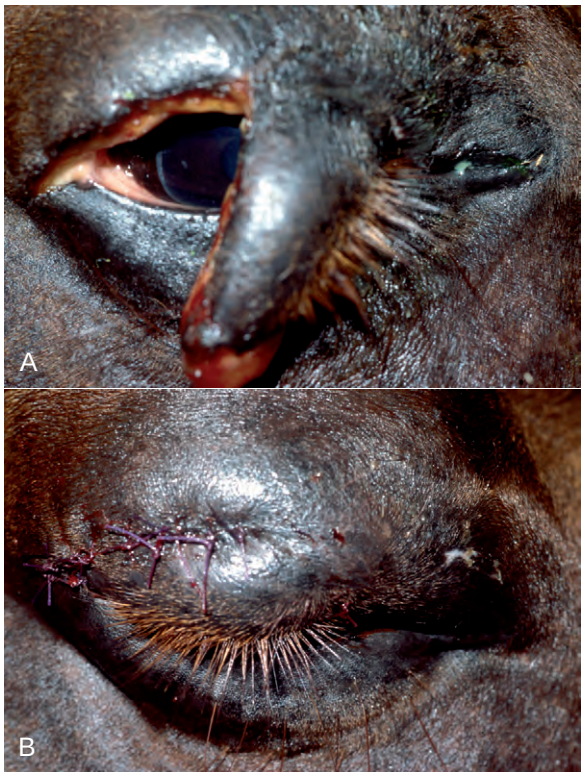


Figure 4-27. Equine upper-eyelid laceration secondary to trauma. **A,** The horse caught the temporal aspect of his upper eyelid on a foreign object, resulting in over half the superior eyelid being torn. **B,** Two-layer eyelid closure immediately following repair. Note that the horse was still under the effects of systemic sedation and regional eyelid akinesia.

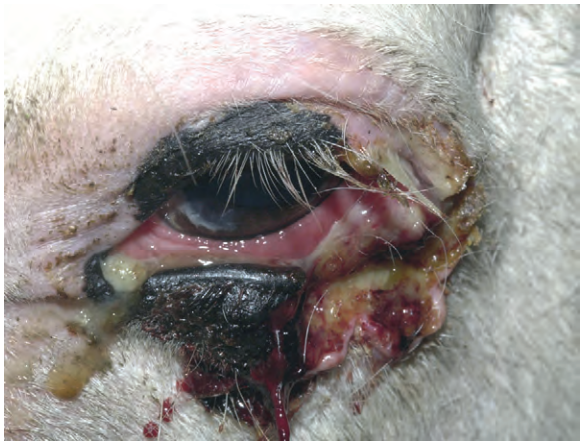


Figure 4-28. This horse was affected with severe ulcerative lower-eyelid squamous cell carcinoma, which can sometimes mask as blepharitis or an eyelid laceration.

performed to identify and appropriately treat any associated ocular lesions (e.g., corneal ulcer or uveitis).[51]

COMMON DIFFERENTIAL DIAGNOSIS

Severe ulcerative eyelid blepharitis or certain neoplasms (e.g., squamous cell carcinoma) may appear as an eyelid laceration or trauma (Fig. 4-28). Careful history will demonstrate that most of the former are chronic and progressive, unlike lacerations that occur acutely. If in doubt of the pathogenesis, biopsy and/or culture with sensitivity testing are warranted.

PATHOGENESIS OF DISEASE PROCESS AND PROGRESSION

Lacerations likely occur in three ways: (1) blunt trauma from a crushing injury against the orbital rim may cause an irregular laceration and substantial eyelid swelling; (2) direct contact with sharp objects, such as a nail or metal edge, can result in focal, relatively straight lacerations; and (3) ripping of the eyelid along its orbitopalpebral sulcus (see Fig. 4-2), usually the result of the eyelid margin being caught on a hook or sharp object, and the horse suddenly moving away in reaction to the pain. Types 1 and 2 are frequently associated with underlying ocular damage, emphasizing the importance of a complete ocular exam. Wounds resulting from the third type of laceration (i.e., "ripping" lacerations) affect the superior eyelid more commonly than the inferior eyelid and extend parallel to the eyelid margin (see Fig. 4-26). Often the clinician can find evidence of a focal "nick" or skin wound at the nasal or temporal canthus, likely representing the area of initial injury before the eyelid was subsequently torn due to the horse's rapid head movement (see Fig. 4-27, *A*). The globe is often spared additional injury in this type of laceration.

TREATMENT

Prompt surgical repair is the recommended treatment of all eyelid lacerations to avoid infection, reduce scarring and secondary corneal damage, and thereby optimize long-term outcome. Failure to repair an eyelid laceration (Fig. 4-29), or amputation of a torn eyelid pedicle instead of primary repair, can result in keratitis. Surgical repair can often be performed with sedation and local akinesia/anesthesia (motor block, ring

Figure 4-29. Horse with a chronic upper-eyelid laceration that was never surgically repaired. The dorsal half of the torn eyelid pedicle has contracted to a small pedunculated remnant. Chronic mucopurulent ocular discharge and white corneal scarring is evident as a result of this traumatic eyelid laceration and secondary trichiasis. (Photograph courtesy Dr. Marie Kerl.)

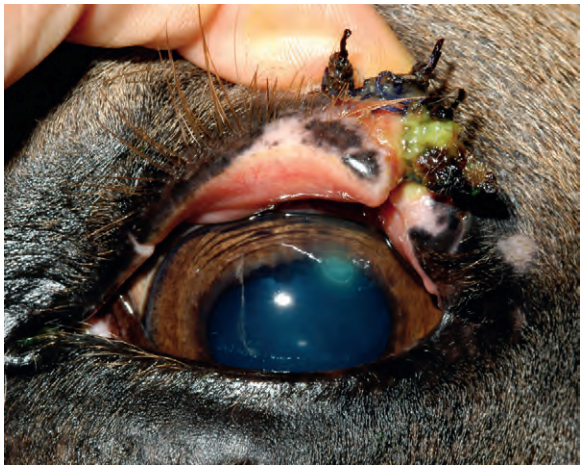


Figure 4-30. A single-layer closure eyelid laceration repair with secondary corneal ulceration. Note that the eyelid margin is not apposed, and there is gapping evident at the conjunctival aspect of the wound bed.

block and topical anesthetic) but may require general anesthesia.[52] Minimal débridement is required, owing to the richly vascular nature of the lids; because the eyelid margin cannot be recreated surgically, every attempt must be made to preserve it.[4] Meticulous repair of an eyelid laceration is crucial to avoid keratitis resulting from scar tissue formation and lid deformity (see Fig. 4-29). Due to the frequency with which eye injury is associated with metal objects, horses should be vaccinated or boostered for tetanus following eyelid laceration. Judicious use of antimicrobial and antiinflammatory therapy may be indicated (see previous discussion in this chapter on general therapeutic considerations).

The wound edges should first be gently cleaned with a dilute (1:50) Betadine solution, and the deep subconjunctival layer should be closed initially. Two-layer closure is required to ensure that the conjunctival aspect of the eyelid does not gape during healing and induce scar formation, which may be irritating to the underlying cornea (Fig. 4-30). Absorbable suture, such as 5-0 to 6-0 polyglactic 910, may be used in a simple interrupted pattern for the deep-layer wound closure. No suture material should contact the cornea. A useful surgical landmark to help avoid placing any sutures too close to the conjunctival surface is the gray line, or the opening of the meibomian glands, which may be used as a reference point denoting the approximate mid-thickness plane of the eyelids. The surgeon should take care that the eyelid margin be meticulously reapposed with the first (i.e., deep) layer of sutures. Following completion of the deep layer closure, the eyelid skin is first closed at the margin with a figure-eight suture pattern or a mattress pattern of nonabsorbable 4-0 to 6-0 suture (see Fig. 4-27, *B*).[4,53,54] Additional simple interrupted skin sutures are placed as needed every 2 to 3 mm until eyelid repair is complete. Incorrect closure of the eyelid margin or failure to use a two-layer closure may lead to chronic corneal irritation (see Figs. 4-29 and 4-30). Skin sutures may be removed in 10 to 14 days, and a protective eye cup may be needed to prevent the horse from rubbing at the repaired laceration site.

LONG-TERM PROGNOSIS

Prognosis after eyelid laceration repair is generally very good, provided the surgery was performed accurately. Prognosis will be adversely affected based on the presence and severity of any concurrent ocular disease. A thorough ocular examination with careful search for possible retained foreign body material is indicated for all eyelid laceration cases. In rare cases, when eyelid trauma is so severe that repair is not possible, the horse may need to be exenterated and allowed to heal by second intention (Fig. 4-31).

BLEPHAROEDEMA

The equine eyelid possesses a minimal amount of adipose tissue.[4,12] This may be a contributing factor in the horse's ability to demonstrate profound chemosis in response to injury or infection (Fig. 4-32). A swollen, drooping eyelid is referred to as *pseudoptosis*.[4] Common differential diagnoses for unilateral and bilateral blepharoedema are listed in Table 4-5. Treatment is directed at the underlying cause and protecting the cornea if eyelid function is compromised.

INFECTIOUS BLEPHARITIS

Inflammation of the eyelids, or blepharitis, is not a common primary cause of eyelid disease in horses. The numerous causes for equine blepharitis typically arise secondary to trauma, bacterial or fungal infection, or parasitic infestation.

The most common cause of blepharitis in the horse is bacterial infection after penetrating trauma.[2] Blepharitis has been reported after blunt trauma associated with an orbital bone sequestrum.[55] Primary infectious causes of equine blepharitis have been reported due to *Moraxella* spp.[56] and *Listeria monocytogenes*.[57] Fungal surface infections or granulomas can also cause blepharitis.[2,4] Fungal organisms reported to cause blepharitis include *Trichophyton* spp., *Microsporum* spp., *Histoplasma farciminosus* (i.e., epizootic lymphangitis), *Cryptococcus mirandi*, *Aspergillus* spp., and *Rhinosporidium seeberi*.[2,4,58,59] Parasites may also cause variable degrees of eyelid inflammation and include habronemiasis, *Thelazia lacrymalis*, and demodecosis.[2,33,60-67] *Thelazia* and *Demodex* infestations are

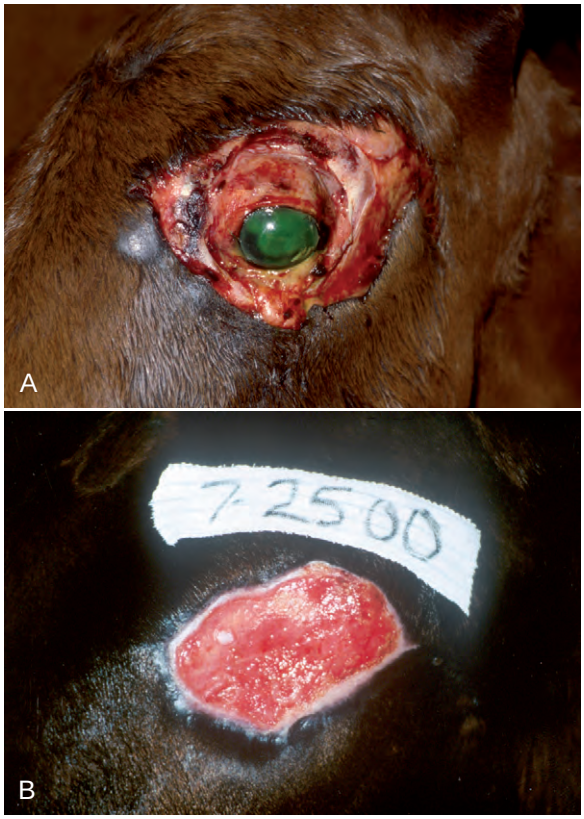


Figure 4-31. A 6-month-old foal that suffered total eyelid removal after being caught in a barbed-wire fence. Note that the entire cornea was fluorescein-stain positive, and there was complete eyelid avulsion precluding any possibility of repair **(A).** Exenteration was performed, and by 3 months postoperatively, a healthy bed of granulation tissue had filled the orbital space and wound closure was nearing completion **(B).**

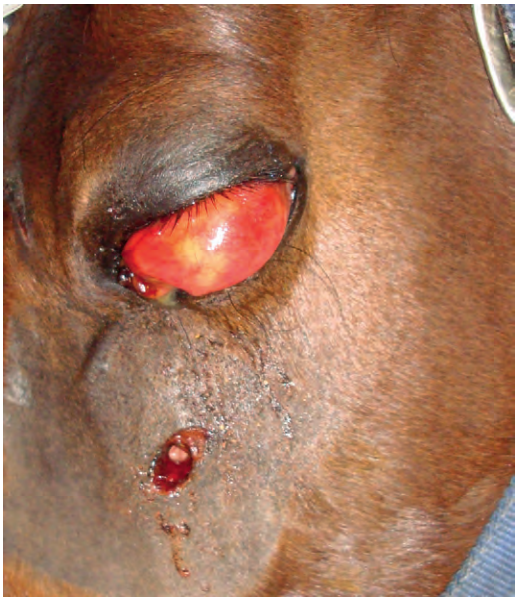


Figure 4-32. Profound blepharoedema with significant superior left-eyelid chemosis and conjunctivitis secondary to an automobile accident. Several periocular skin lacerations are also evident.

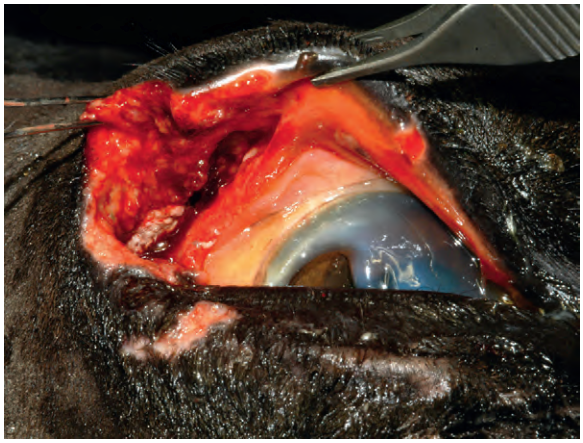


Figure 4-33. Eyelid trauma with secondary bacterial eyelid infection and caseous necrosis. A deep corneal ulcer is also present.

Table 4-5 | **Causes for Blepharoedema of the Equine Eyelid**

UNILATERAL	BILATERAL
Blunt trauma	Self-trauma
Self trauma	Systemic diseases*
Insect bite	Equine viral arteritis
Snake bite	Babesiosis
Foreign body reaction	Lymphosarcoma
Abscess formation	Influenza
Orbital fat prolapse	Allergic/hypersensitivity
	Ocular parasites

From references 2, 4.
*See Chapter 13 on Ocular Manifestations of Systemic Diseases.

usually asymptomatic, but a rare blepharitis characterized by meibomian gland inflammation, hair loss, and papulopustular dermatitis has been reported secondary to *Demodex* infestation.[2] With the widespread use of ivermectin in the 1990s, the prevalence of habronemiasis decreased; however, the development of resistant strains remains a distinct possibility.

CLINICAL APPEARANCE AND DIAGNOSIS

Blepharitis, in general, appears as swelling and inflammation of the eyelid. Because of its prominence, the upper eyelid is more commonly affected than the lower eyelid. Bacterial infections following trauma have swelling surrounding an open wound with or without necrotic draining tracts (Fig. 4-33). Dermal fungal infections may appear as bacterial infections or have an alopecic scaling of the eyelid skin.[2] Habronemiasis (*Habronema muscae*, *H. microstoma*, and *Draschia megastoma* are potential causative organisms)[4] appears as a raised, granulomatous, ulcerative lesion on the conjunctiva or mucocutaneous junction of the eyelid (Fig. 4-34). This disease is also known as *summer sores, swamp cancer,* and *granular dermatitis*,[60,64,67] because the condition appears during the hot, humid summer months when the main vectors, house and stable flies, are most severe. Infection of the ocular tissue is by *Habronema* larvae. Adult *Habronema* organisms live in the equine stomach, larvae are passed in the feces, ingested by fly larvae, become infective in the fly pupae, and are deposited near the eye (or other mucocutaneous junctions or wounds).[4,67] Dermal lesions may also develop on other areas on the body (Fig. 4-35). The

Figure 4-34. Equine habronemiasis often presents as raised, granulomatous, multifocal, white nodular lesions, as seen in the medial canthal region of this horse's left inferior eyelid.

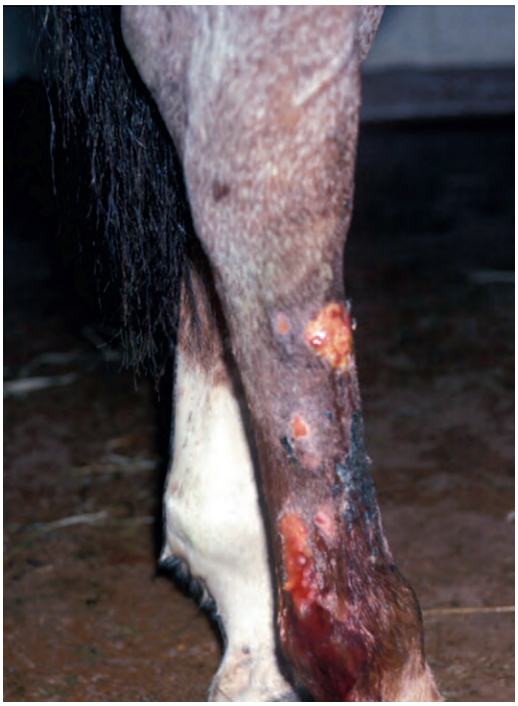


Figure 4-35. Habronemiasis infections can occur at mucocutaneous junctions or at sites of injury. Here is habronemiasis on a front leg. (Photograph courtesy Dr. Mike Davidson.)

medial canthus and the caruncle area are the most common periocular areas affected, and the lesion typically has discrete nodules or multilobulated masses (see Fig. 4-34) with occasional mineral or "sulfur-appearing" nodules. Hypersensitivity to the organisms (especially dead organisms) results in pruritus, periocular alopecia, and occasionally secondary ocular disease such as corneal ulceration and uveitis.

COMMON DIFFERENTIAL DIAGNOSIS AND METHODS FOR DEFINITIVE DIAGNOSIS

Blepharitis is often associated with conjunctivitis, and Table 4-6 lists the main causes of both diseases. In cases of infectious (bacterial or fungal) blepharitis, the definitive diagnosis is based on identifying the organism(s) on cytology and culture. Biopsy and histopathology are recommended if the lesion is chronic and unresponsive to initial therapy. Habronemiasis is presumptively diagnosed based on the clinical appearance of the lesion and response to therapy. Lesions typically occur during fly season and have a raised, white to yellow, ulcerated appearance, sometimes with fistulous tracts, and a yellow caseous exudate with gritty foci of necrotic mineralized tissue. Due to the numerous neutrophils, eosinophils, mast cells, and plasma cells in the cytology from habronemiasis lesions, one must differentiate it from mast cell tumors, *Phycomycetes*, eosinophilic granulomas (nodular necrobiosis), and eosinophilic keratoconjunctivitis.[2,4,60,68-70] Therefore, if the organisms are not found on cytology, biopsy and histopathology are recommended for definitive diagnosis.

MEDICAL TREATMENT OF INFECTIOUS BLEPHARITIS

Penetrating eyelid trauma with secondary infectious bacterial or fungal blepharitis usually heals rapidly with appropriate treatment because of the eyelid's excellent blood supply. The wound should be cultured (for bacterial [+/– fungal] culture and sensitivity) and a cytology sample collected. The wound is then débrided, flushed with copious amounts of dilute (1:50) Betadine solution, and a careful search and removal is performed for any remaining foreign material. Judicious use of systemic and/or topical antimicrobial and antiinflammatory therapy may be considered (see earlier section on general therapeutic principles for acquired adnexal disease). Warm compresses can be applied every 8 to 12 hours for the initial 5 days. Habronemiasis is treated by regular standard deworming recommendations (typically, oral ivermectin at a dose of 200 mcg/kg, repeated in 30 days), debulking the affected lesion, controlling eyelid inflammation associated with larvae dying in situ, and educating owners about environmental strategies to control flies in an effort to decrease recurrence.[72] In one study, ivermectin alone caused marked improvement in habronemiasis lesions within 7 days in 87% of horses.[73] Topical therapies for habronemiasis lesions vary. Recommendations have included preparations of trichlorfon, nitrofurazone, and dimethyl sulfoxide (DMSO)[64]; trichlorfon, nitrofurazone, dexamethasone, and DMSO[61]; and nitrofurantoin, ronnel solution, dexamethasone, and DMSO,[60] each applied every 12 hours to the lesion. Topical 0.03% echothiophate every 12 hours may be helpful as a larvacide,[4] but it is not likely needed in addition to systemic ivermectin. Intralesional injections of triamcinolone or methylprednisolone may decrease inflammation in the affected areas.[2,4]

SURGICAL THERAPY OF INFECTIOUS BLEPHARITIS

For most blepharitis cases, wound management (as described previously) and judicious use of appropriate systemic antibiotics (based on culture and antimicrobial susceptibility testing) will help the lesion resolve. However, in cases of significant abscessation, the fluid and any caseous necrotic tissue should be removed, the wound flushed copiously with sterile saline, and co-management of any ocular disease be instituted (see Fig. 4-33). If necessary, a drain may be placed for 3 to 7 days. In one study examining habronemiasis lesions, debulking or excising granulomatous lesions (to remove a source of chronic immune stimulation[4]), appropriate deworming, and administra-

Table 4-6 | **Conjunctivitis and/or Blepharitis in the Horse**

CLASSIFICATION	ETIOLOGY	PREDOMINANT CLINICAL SIGNS
SECONDARY CONJUNCTIVITIS (+/– BLEPHARITIS)	Corneal disease	Corneal ulcer, stromal abscess, blepharospasm, epiphora, etc.
	Uveitis	Epiphora, aqueous flare, miosis, conjunctival hyperemia, etc.
	Glaucoma	Elevated intraocular pressure, diffuse corneal edema, etc.
	Dacryocystitis	Purulent ocular discharge, negative Jones test
	Keratoconjunctivitis sicca[19-22,83,122]	Lackluster appearance to cornea, mucopurulent discharge, etc.
PRIMARY CONJUNCTIVITIS (+/– BLEPHARITIS)		
Immune-mediated	Follicular	Follicles on bulbar conjunctiva, epiphora
	Eosinophilic[20,68,69]	Thick, cheesy exudates, +/– corneal disease
	Allergic	Hyperemia, chemosis, serous discharge "conjunctival pseudotumor," nodular lymphocytic conjunctivitis
	Nodular[274,286]	
Bacterial	*Moraxella equi*[56,287]	Mucocutaneous erosions, mucopurulent ocular discharge, blepharospasm
	Streptococcus equi[288]	Regional lymphadenitis (strangles), conjunctivitis, mucopurulent nasal discharge
	Listeria monocytogenes[57]	
	Chlamydia Mycoplasma[289]	Possible respiratory disease or polyarthritis
Fungal	Histoplasmosis[59] and blastomycosis[4]	Conjunctivitis and lymph node involvement
	Aspergillus spp.[4]	Granulomatous conjunctivitis
	Rhinosporidium seeberi[4]	Granulomatous conjunctivitis
Viral	Equine herpes type 2[80,290,291]	Recurrent conjunctivitis +/– corneal ulceration
	Equine herpes type 1[292]	
	Equine herpes type 2[87,293]	
	Equine viral arteritis[294-296]	Conjunctivitis and blepharoedema
	Adenovirus[297]	Keratouveitis, mucopurulent discharge
Parasitic	Onchocerchiasis[298]	Lateral limbal depigmentation +/– uveitis
	Thelazia lacrymali[66,299]	Mild conjunctivitis, epiphora
	Ophthalmomyiasis externa[300]	
	Habronemiasis[60,301]	Granuloma formation, mucopurulent exudate
	Trypanosoma evansi[302,303]	Fever, anemia, conjunctivitis, edema of the legs and lower parts of the body, progressive weakness, loss of condition, and loss of appetite
TRAUMA	Blunt trauma	Subconjunctival hemorrhage
	Foreign body	Severe blepharospasm and epiphora
SOLAR/ACTINIC	Ultraviolet radiation	Neoplastic precursor

tion of topical, intralesional, or systemic corticosteroids provided healing within a few weeks.[72]

LONG-TERM PROGNOSIS

With appropriate diagnosis and treatment, most of these lesions heal readily. Eyelid defects and other ocular damage as a result of the blepharitis depend on the extent and chronicity of the blepharitis.

ALLERGIC, IMMUNE-MEDIATED, AND ACTINIC BLEPHARITIS

Blepharitis can also be caused by local or systemic allergic diseases (see more information in systemic disease chapter), immune-mediated diseases, and from exposure to sunlight, with or without photosensitization (see Table 4-6). Local or systemic allergic diseases usually cause acute-onset bilateral blepharoedema, hyperemia, and pruritus. Chronically, allergic conditions can cause hyperpigmentation and scarring. Causes include chronic fly-bite irritation and environmental allergens such as molds, dust, sprays, and certain drugs. The eyelids can also be affected with immune-mediated diseases such as pemphigus foliaceus and bullous pemphigoid.[2] Typically, other mucocutaneous junctions on the body are also affected, and these lesions are chronic, bilateral, and pruritic. Actinic blepharitis can occur in nonpigmented periocular tissues that have chronically been exposed to sunlight. The lesions appear hyperemic and ulcerated, typically at the eyelid margin (Fig. 4-36). Actinic blepharitis may be a precursor lesion to squamous cell carcinoma.[6,71] Use of a high ultraviolet radiation–blocking fly mask is encouraged for all horses that lack periocular pigmentation to prevent actinic blepharitis and squamous cell carcinoma.

EYELASH (CILIARY) DISORDERS

The three types of eyelash or ciliary disorders include trichiasis (normal eyelash hairs turned inward that rub on the conjunctiva/cornea), distichiasis (extra eyelashes, often seen exiting the meibomian gland openings, that may irritate the ocular surface), and ectopic cilia (an eyelash that exits through the conjunctiva, usually at the middle of the upper eyelid, and often results in blepharospasm, epiphora, and corneal ulceration). All three eyelash disorders are uncommon in horses, especially compared to other domestic species.[74-76] Trichiasis is the most common cilia abnormality and most frequently occurs after eyelid scarring following laceration or surgery[75] or secondary to entropion.[31] Distichia or ectopic cilia may be congenital, but the clinical manifestations may not be evident for months to years.[2,77]

Figure 4-36. Actinic blepharitis in the eyelids of an Appaloosa horse. Notice the hyperemic, ulcerated, and scarred eyelid and third eyelid margins. (Photograph courtesy Dr. Mike Davidson.)

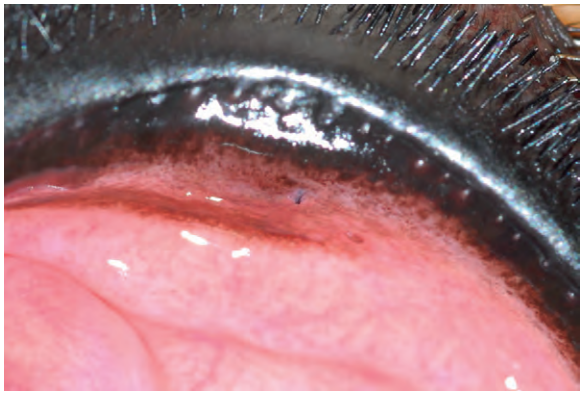


Figure 4-37. Ectopic cilia in the lower eyelid. Note the short dark cilia eroding through the palpebral conjunctiva.

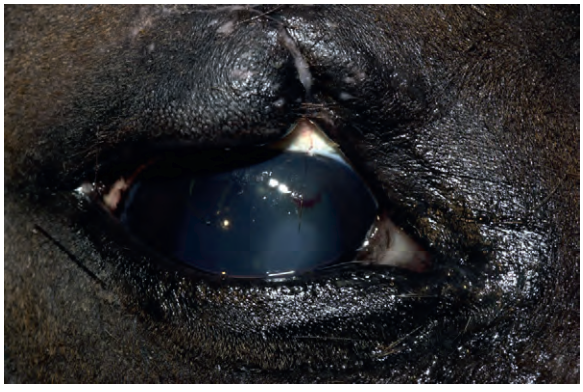


Figure 4-38. Eyelid scarring 2 months following a skin-only closure of a central upper-eyelid laceration. Trichiasis is now present from the upper cilia, resulting in a superficial cornea ulcer.

CLINICAL APPEARANCE AND DIAGNOSIS

Any eyelash disorder has the potential to create chronic ocular irritation. As a result, presenting complaints include blepharospasm, epiphora, corneal ulceration, and/or corneal scarring. Careful evaluation using high magnification (usually via biomicroscopy) of the eyelid margin for any abnormal hairs touching the cornea during normal blink response is essential. Initially, examination without eyelid manipulation should be performed to evaluate for trichiasis. Eyelids should also be everted to search for distichia or ectopic cilia. Most commonly, distichia and ectopic cilia involve the upper eyelid in horses but may involve either eyelid (Fig. 4-37). If secondary corneal scarring or ulceration result from an eyelash abnormality, the scar or ulcer will typically correspond anatomically with the offending eyelash problem (see Fig. 4-29).

COMMON DIFFERENTIAL DIAGNOSIS AND METHODS FOR DEFINITIVE DIAGNOSIS

The causes for chronic irritation to the surface of the eye should be considered in addition to cilia abnormalities. Differentials to be considered include burdock bristle keratitis (see Chapter 2 for more information),[78] other foreign bodies, infectious keratitis,[79-82] keratoconjunctivitis sicca,[19-22,83] and other noninfectious keratopathies.[68,69,82,84]

PATHOGENESIS OF DISEASE PROCESS AND PROGRESSION

Ectopic cilia and distichiasis are considered to be "extra" cilia that develop similarly to normal cilia but exit the eyelid at abnormal locations. For example, developing cilia may enter a meibomian gland and exit through its ductule, a path of least resistance, to then clinically manifest as distichiasis. Multiple distichia may exit a single meibomian gland orifice (districhiasis). Ectopic cilia exit directly through the palpebral conjunctiva instead of the eyelid margin.

TREATMENT FOR EYELASH ABNORMALITIES

The mainstay of therapy for any abnormal eyelash problem is removal of the abnormal or misdirected cilia (or eyelid hair) and correction of any eyelid scarring. Medical therapy alone (e.g., topical ophthalmic ointment) may help protect the cornea until surgery can be performed, but it will not correct the underlying problem or alleviate the chronic irritation. The underlying cause for trichiasis (e.g., eyelid scarring, entropion, dermoid) should be surgically corrected. If eyelid scarring is the primary problem, the abnormal palpebral margin should be surgically excised and the margin reapposed with careful anatomic alignment using the principles discussed in eyelid laceration repair (Figs. 4-38 and 4-39). Temporary tacking sutures or a permanent Hotz-Celsus procedure can be done to correct the entropion (see Figs. 4-12 to 4-15).[4,75] Distichia may be treated with cryotherapy, the treatment of choice if numerous distichia are present or if they emerge from eyelid margin in locations other than from the meibomian gland orifice, or with electroepilation in cases where only a few distichia are present and the cilia emerge from the meibomian gland orifices, allowing easy probe placement and less eyelid scarring secondary to electrocautery. The goal with either modality is to destroy the base of the hair follicle such that the hair does not regrow. When cryotherapy is elected, the affected margin eyelid is held in a chalazion clamp, which will enable the surgeon to both hold the eyelid in place and also slow the blood supply to and from the affected site, ensuring a "slow thaw" secondary to the freezing cycle (see Fig. 4-67, *B*). Once the affected eyelid margin is secured in the chalazion clamp, a 4-mm cryoprobe is placed on the

Figure 4-39. Repair of the cicatricial eyelid lesion in Fig. 4-37. A V-plasty procedure was performed to remove the scarred portion of the eyelid, followed by a standard two-layer closure.

Figure 4-40. A 29-year-old horse with bilateral lateral eyelid entropion. The horse had mild enophthalmos from muscle atrophy, entropion, and mild blepharospasm and epiphora *(arrows)*.

conjunctival surface of the eyelid and centered over the base of the meibomian gland adjacent to the distichia that is to be removed. As the conjunctiva freezes, it will appear white. The probe should be held in a fixed location on the conjunctival surface until the tissue freezing is visualized to extend just beyond the distichia. If nitrous oxide cryo units are used, this cycle may be repeated two to three times in each location. Care must be taken to not cause tissue necrosis of the eyelid by overfreezing the eyelid margin. This risk is much greater when using liquid nitrogen units, because the freezing temperature is substantially colder (approximately –200°C) than that obtained with nitrous oxide (approximately –80°C). Once the eyelid thaws, epilation of the distichia is attempted. Adequate cryotherapy was performed if there is no resistance to the epilation of the distichia. Partial tarsal plate excision or lid splitting has been attempted, but scarring and contracture may occur after surgery.[76] Ectopic cilia usually consist of a single hair or a focal group of hairs that should be removed by en block excision and ancillary cryotherapy of the wound bed.

LONG-TERM PROGNOSIS

If all offending hairs can be located and removed, or the eyelid abnormality or scarring is minor and repairable, the long-term prognosis is excellent. Eyelash disorders are relatively uncommon in horses compared to dogs, so repeat treatment for new distichia or ectopic cilia is not a frequent problem.

ENTROPION IN ADULT HORSES

Entropion, or inward turning of the eyelid, results in the eyelashes rubbing the cornea (as in trichiasis) and can cause significant ocular irritation and corneal damage in the horse. Conformational (or anatomic) entropion is rare in the horse. In this species, entropion typically occurs secondary to eyelid trauma (i.e., cicatricial entropion) or severe blepharospasm (i.e., spastic entropion).[4,75] Spastic entropion resulting from primary ocular inflammation may subside spontaneously once the inciting cause has been removed. Entropion can also occur with decrease in orbital support of the eyelids, such as with phthisis bulbi or enophthalmos from severe dehydration or loss of orbital fat, observed in young foals with neonatal maladjustment syndrome or elderly cachectic horses.[40]

CLINICAL APPEARANCE AND DIAGNOSIS

Whether present in a foal or adult horse, entropion has a similar appearance. The eyelid margin is turned inward toward the cornea, with the cilia and eyelid hairs rubbing the surface of the cornea (Fig. 4-40; also see Fig. 4-11). Associated conditions, such as corneal ulceration, enophthalmos, eyelid scarring, and/or phthisis bulbi may be present.

DIFFERENTIAL DIAGNOSIS AND PATHOGENESIS OF DISEASE

It is important to determine if the entropion is a primary or secondary ophthalmic problem. As previously discussed, the majority of horses affected have secondary entropion to some other primary problem. Primary ocular problems that may result in secondary entropion in horses include blepharitis, enophthalmos, eyelid scarring, phthisis bulbi, or any cause of keratoconjunctivitis (e.g., burdock bristle keratitis,[78] foreign bodies, infectious keratitis,[79-82] keratoconjunctivitis sicca,[19-21,83] or other noninfectious keratopathies[68,69,82,84]). Regardless of the cause, entropion will result in ocular irritation, which in turn will exacerbate the spastic component of any anatomic entropion (see earlier discussion under foal entropion).

TREATMENT

To adequately treat adult-onset entropion in horses and to prevent recurrence, the primary underlying cause must be managed. Cicatricial entropion can be repaired surgically by removing the scarred eyelid.[75] Resolving the cause of ocular irritation, such as corneal ulceration or removal of a foreign body, will help the spastic entropion resolve. However, some conditions cannot be reversed, such as phthisis bulbi or enophthalmos from fat atrophy. Enucleation of a severely phthisical eye is recommended. Entropion repair can be considered for mild phthisis bulbi or enophthalmos. Treatment goals and strategies are the same in all ages of horses. Additional details regarding the medical and surgical management of entropion have been previously discussed (see Entropion in the congenital ocular disease section of this chapter; also see Figs. 4-13 and 4-15).

LONG-TERM PROGNOSIS

Prognosis for entropion depends on the underlying cause. If the primary problem can be corrected while the eyelid margins are temporarily tacked (to address any spastic entropion that may be contributing to the primary ocular disease process), the long-term prognosis is excellent. However, if the entropion is secondary to phthisis bulbi or enophthalmos that cannot be reversed by correcting an underlying systemic disease (e.g., emaciation/dehydration), the prognosis is more guarded. In some cases, definitive surgical repair of the entropion may offer the horse improved ocular comfort even if the globe is non-visual and blind (e.g., mild phthisis bulbi). In severe cases of entropion secondary to a blind, shrunken (phthisical) or sunken (enophthalmic) globe, enucleation may offer the horse the most comfortable long-term outcome. Finally, if the horse has primary entropion, properly performed definitive surgical repair carries a favorable prognosis.

CONJUNCTIVITIS

By definition, conjunctivitis implies inflammation of the palpebral and bulbar conjunctival tissues of the eye. The conjunctiva is richly vascularized and contains organized lymphoid tissue (CALT[14,15] [see Fig. 4-7]) which results in its innate ability to become easily inflamed in either primary or secondary conjunctivitis. When inflamed, the conjunctiva may demonstrate profound clinical changes such as hyperemia (redness) and chemosis (edema). Common causes of conjunctivitis are listed in Table 4-6.

CLINICAL APPEARANCE AND DIAGNOSIS

One of the most common presenting complaints associated with the majority of ocular problems in most domestic animals is that of a "red eye." It is essential that the clinician determine if the conjunctivitis is a primary or secondary problem. Secondary conjunctivitides are frequently associated with vision-robbing diseases (see Table 4-6) such as uveitis, glaucoma, or significant corneal disease (Fig. 4-41). This differentiation is made based on careful external and internal ophthalmic examination as well as performing a minimum ophthalmic database: Schirmer tear testing, fluorescein stain, intraocular pressure measurement, and when indicated, cytology, culture and sensitivity, or biopsy. Depending on the cause, the appearance of conjunctivitis will vary and may include significant chemosis and hyperemia (see Figs. 4-24 and 4-32) to more mild conjunctival changes but significant mucopurulent discharge (see Fig. 4-19). A combination of both significant hyperemia and severe ocular discharge can be found in diseases such as eosinophilic keratoconjunctivitis (Fig. 4-42).

COMMON DIFFERENTIAL DIAGNOSIS AND METHODS FOR DEFINITIVE DIAGNOSIS

A complete and thorough ophthalmic examination should be done to rule out all ocular causes of secondary conjunctivitis. With rare exceptions (e.g., tonometry is not performed on globes at risk of corneal perforation), the minimum ophthalmic database (Schirmer tear testing, fluorescein stain, intraocular pressure measurement) should be obtained prior to slit-lamp biomicroscopy and funduscopy being performed. Bacterial and/or fungal culture and antimicrobial susceptibility testing followed by cytologic examination of conjunctival scrapings should be performed on all eyes with a history of chronic conjunctivitis and eyes with mucopurulent ocular discharge. A thorough understanding of the normal bacterial and fungal flora of the conjunctiva is essential when interpreting the results of diagnostic testing.[13,44,85-89] See Chapter 5 for a review of various studies of the normal equine corneal and conjunctival bacterial and fungal flora. If an infectious etiology (see Table 4-6) is suspected, appropriate diagnostic testing is recommended and may necessitate that samples be sent to specialized laboratory facilities equipped to appropriately isolate and diagnose certain fungal or viral agents. Systemic disease must also be considered when evaluating a horse with conjunctivitis (see Chapter 13).

TREATMENT

Conjunctivitis is merely a clinical sign and not an etiologic diagnosis, therefore treatment should be directed at the primary or secondary cause for this ocular finding. Medical therapy for conjunctivitis is typically delivered via topical ophthalmic ointments administered 3 to 4 times daily. If more frequent application of medication is deemed necessary, then placement of a subpalpebral lavage tube administration of ophthalmic solutions/suspensions may be a more convenient method of treatment (see earlier discussion in this chapter on general therapeutic

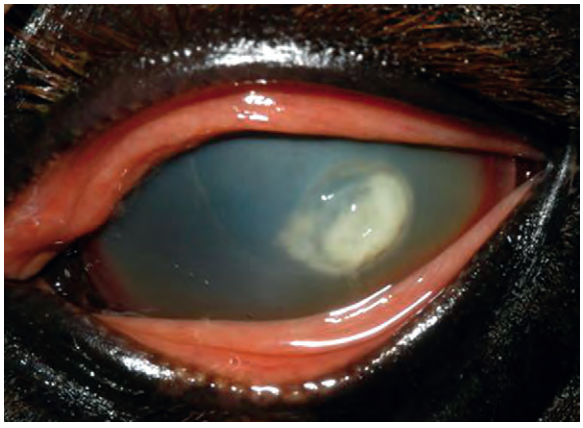


Figure 4-41. Significant conjunctival hyperemia and moderate chemosis are present in this horse with fungal keratitis.

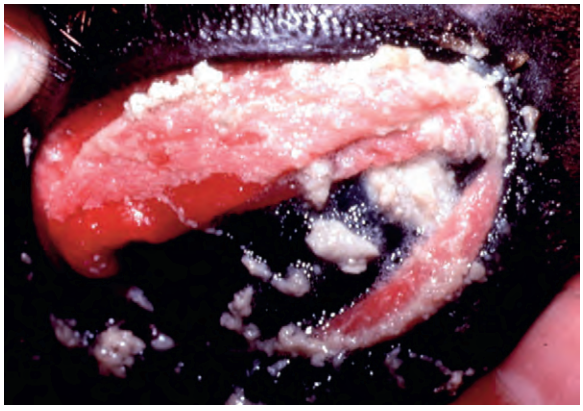


Figure 4-42. Severe caseous discharge and conjunctivitis in a horse with eosinophilic keratoconjunctivitis. (Photograph courtesy Dr. Mike Davidson.)

considerations). Topical antibiotic therapy based on culture and antimicrobial susceptibility testing and cytology results is the mainstay of therapy. Topical broad-spectrum antibiotics, such as oxytetracycline or triple antibiotic ointment 3 to 4 times daily are good initial therapeutic choices. If antiviral or antifungal agents are required for treatment, formulations via a compounding pharmacy may be necessary. (See Chapter 5 for more information on equine corneal disease.) Clinicians should exercise caution in the use of topical antiinflammatory therapy, particularly topical steroids, if treating equine patients in regions where fungal pathogens are endemic. No definitive surgical therapies exist for the treatment of conjunctivitis, with the possible exception of debulking a mass in the diagnosis and/or treatment of certain infectious (e.g., parasitic), inflammatory (e.g., pseudotumor), or neoplastic lesions (e.g., squamous cell carcinoma, melanoma).

LONG-TERM PROGNOSIS

The prognosis for conjunctivitis is usually good with primary infections; most conjunctival infections respond well to topical therapy, generally within 5 to 7 days (see Table 4-6). However, primary viral infections can be recurrent, and many systemic diseases that manifest with conjunctivitis as part of the horse's overall clinical findings can have serious and life-threatening complications (see Chapter 13 on systemic disease).

NEUROLOGIC DISORDERS OF THE EYELIDS

Several neurologic conditions may affect the eyelids and periocular structures. Neurologic conditions affecting the orbit and extraocular muscles are reviewed in Chapter 3. The two most common neurologic diseases of the ocular adnexa in the horse are Horner's syndrome and facial nerve paralysis.

HORNER'S SYNDROME

The autonomic nervous system (ANS) is an involuntary motor system composed of the parasympathetic and sympathetic divisions. It is known as the *involuntary, visceral,* or *vegetative nervous system*. Horner's syndrome results from loss of sympathetic innervation to the head, either unilaterally or bilaterally.[9] Knowledge of the sympathetic nerve pathway is essential to understanding the pathogenesis, diagnostic testing, treatment, and prognosis of a horse with Horner's syndrome. The sympathetic nervous system pathway begins in the hypothalamus, extends down the intermediolateral cell columns of the spinal cord to synapse at C8 to T3. The axons from these cells exit the anterior nerve root of the spinal cord through the white ramus. The fibers (preganglionic fibers) course through the brachial plexus, the thoracic inlet, and ascend in the sympathetic trunk (with the jugular vein) to synapse at the cranial cervical ganglion. Postganglionic fibers then pass near the middle ear, through the orbital fissure, and form the sympathetic root of the ciliary ganglion. Short ciliary nerves (along with contributory fibers to the long ciliary nerves) extend to the dilator muscle of the iris (Fig. 4-43), so damage of the pathway from the hypothalamus to the short ciliary nerves may cause denervation, resulting in Horner's syndrome. Lesions that occur proximal to the ciliary ganglion are termed *preganglionic,* and those distal to the ciliary ganglion are referred to as *postganglionic*.

CLINICAL APPEARANCE AND DIAGNOSIS

The predominant clinical signs of Horner's syndrome in horses are ptosis, sweating on the head and neck, and increased cutaneous temperature in the denervated area (Fig. 4-44).[7-9,90-94] Enophthalmos, miosis, elevated third eyelid, and increased lacrimation (which are common clinical signs in other animals) are variable, inconsistent, or mild in horses.[7,8,90-94] There are no vision deficits with sympathetic denervation; the diagnosis is based on recognition of clinical signs.

COMMON DIFFERENTIAL DIAGNOSIS AND METHODS FOR DEFINITIVE DIAGNOSIS

Damage to the sympathetic trunk anywhere along its pathway may result in signs of Horner's syndrome (Box 4-2). Trauma to the neck and spinal cord or vagosympathetic trunk (i.e., during jugular venipuncture) can also cause Horner's syndrome.[4,93] Horner's syndrome associated with jugular venipuncture was mild and resolved within 14 hours.[93] Other possible causes of Horner's syndrome in horses include idiopathic, guttural pouch infections, obstructive esophageal disorders,[95] melanoma,[7,90,91] anterior thoracic disorders,[91] metastatic squamous cell carcinoma,[92] and surgical procedures such as carotid artery catheterization[7] and cervicothoracic (stellate) ganglion blocks.[96,97] Horner's syndrome may also be associated with concurrent laryngeal hemiplegia.[8] Horner's syndrome has been experimentally induced by transection of the cervical sympathetic and vagosympathetic trunk[8,94] and carotid artery catheterization.[7] The experimentally induced disease appeared nearly identical to naturally occurring clinical cases.[8,94]

Diagnostic workup for horses with unilateral or bilateral Horner's syndrome should consist of a complete ophthalmic and physical examination. Endoscopic examination of the ipsilateral guttural pouch, laryngeal function, and upper esophagus should be considered. Thoracic ultrasound or radiography may be useful to evaluate for anterior thoracic masses or infection.

Pharmacologic testing for Horner's syndrome in horses entails application of certain topical medications to the eye and observing the response to treatment in an effort to localize the site of sympathetic nervous system damage.[98,99] This method does not always reliably localize the lesion.[8] The law of denervation hypersensitivity provides the pharmacologic basis for differentiating preganglionic from postganglionic lesions in autonomic nervous system disorders. Interruption of innerva-

Box 4-2 | Causes of Horner's Syndrome in the Horse

- Idiopathic
- Trauma to neck or spinal cord
- Jugular venipuncture or other trauma to vagosympathetic trunk
- Guttural pouch infections
- Obstructive esophageal disorders
- Anterior thoracic disorders
- Metastatic neoplasia (melanoma, squamous cell carcinoma)
- Surgical procedures (carotid artery catheterization, cervicothoracic [stellate] ganglion blocks)

From references 7-9 and 90-98.

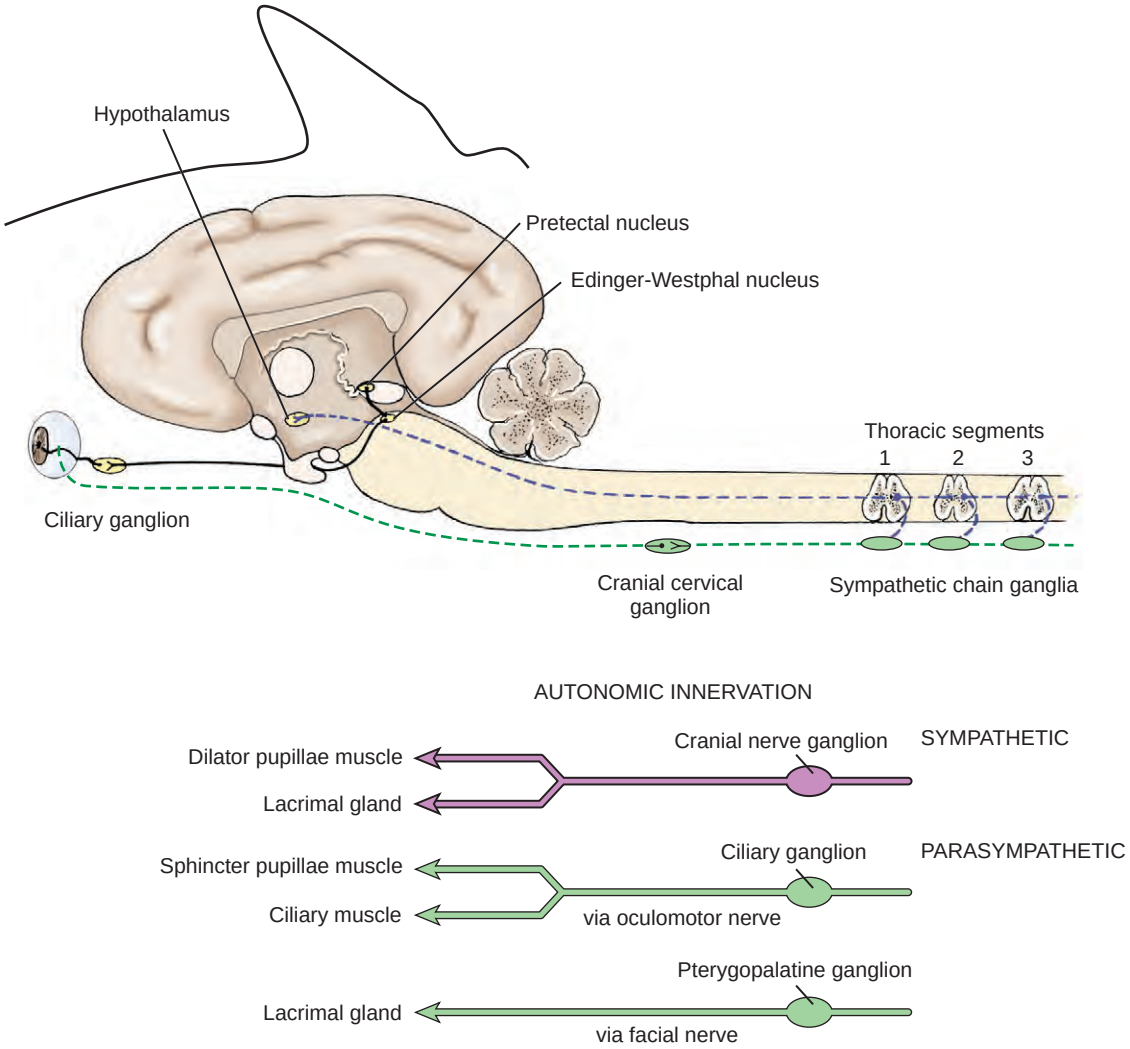


Figure 4-43. Sympathetic pathway to the equine eye and orbit.

tion to an organ results in loss of the degradative enzyme of the neurotransmitter, and as a result, the synaptic receptor becomes extremely sensitive ("supersensitive") to the neurohumoral agent. In other words, the receptors in the adjacent neuron (in the ganglion) or in the neuromuscular junction (effector organ) will be supersensitive to their agonists when the preceding nerve or nerve ending is destroyed. Note that when pharmacologic testing for Horner's is performed, both eyes should receive identical amounts/concentrations of the pharmacologic agent used so that the denervated/affected side can be compared to the normal side for accurate test interpretation.

Topical drugs that have been used for pharmacologic testing for Horner's syndrome include cocaine (not commercially available), hydroxyamphetamine, and phenylephrine. Cocaine and hydroxyamphetamine are indirect-acting sympathomimetic drugs that do not bind adrenergic receptors directly but act to increase norepinephrine in the synaptic cleft. Cocaine (6%) blocks the reuptake of norepinephrine at the receptor sites of the iris dilator cells, which results in an accumulation of this neurotransmitter at the receptor site. There is no direct action on the receptor. Therefore, a dilated pupil in response to topical cocaine would suggest a preganglionic lesion. Hydroxyamphetamine (1%) stimulates endogenous release of norepinephrine from intact adrenergic nerve endings. It does not directly stimulate the receptors. In central or preganglionic neuron lesions, the postganglionic sympathetic neuron remains intact, and hydroxyamphetamine stimulates release of stored norepinephrine, causing pupillary dilation. Lesions of the postganglionic neuron do not respond to hydroxyamphetamine because there are no stores of norepinephrine to be released, and therefore no mydriasis results. Note that because the effects are unrelated to the phenomenon of denervation hypersensitivity (thus are not dose-dependent), multiple drops of a 1% solution or use of a 5% solution may be necessary. Application of a sufficient amount of drug to both eyes to induce mydriasis in the control eye is necessary for accurate test interpretation.

Phenylephrine HCl (commercially available as a 2.5% or 10% solution) is a direct-acting sympathomimetic drug. Specifically, phenylephrine is an α_1-adrenergic agonist with little effect on β-adrenergic receptors. Upregulation of adrenergic receptors on the denervated iris dilator muscle and hypersensitivity to phenylephrine occurs in lesions of the postganglionic sympathetic neuron. Dilation after topical application would suggest a postganglionic lesion. Pharmacologic testing with an

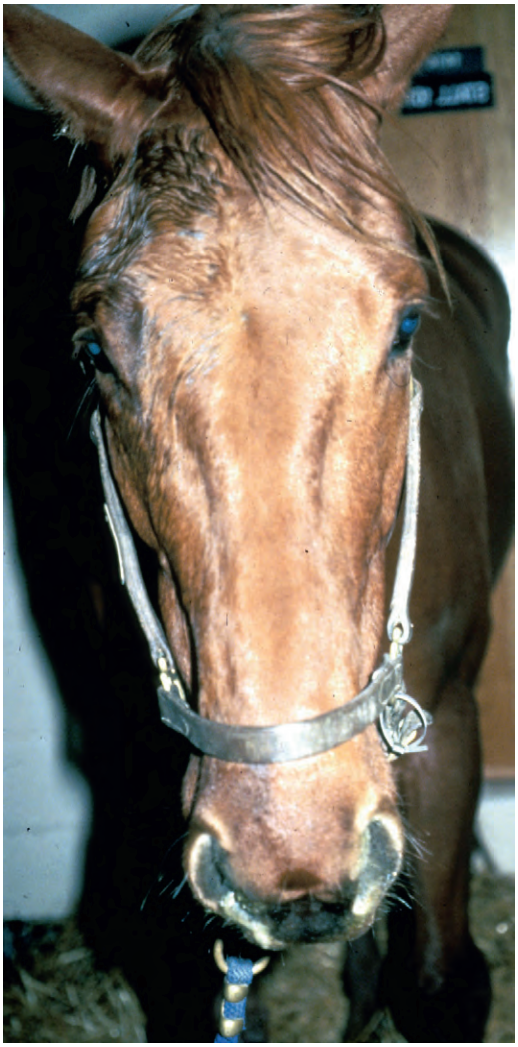


Figure 4-44. Right-sided Horner's syndrome. Note the predominant clinical signs of ipsilateral sweating above the eye and mild ptosis. Enophthalmos, miosis, and elevated third eyelid (which are common clinical signs in other animals) are not prominent in this horse. (Photograph courtesy Dr. David A. Wilkie.)

indirect-acting sympathomimetic (hydroxyamphetamine) and a direct-acting sympathomimetic (phenylephrine) should be performed 24 hours apart.

TREATMENT

Treatment for Horner's syndrome in horses is based on eliminating the underlying cause if possible. Horner's syndrome from minor trauma to the sympathetic trunk will resolve spontaneously in hours to days. Idiopathic Horner's syndrome typically resolves spontaneously in weeks to months. Topical phenylephrine will temporarily resolve some of the clinical signs of Horner's syndrome in horses, but this is used as a long-term therapy. Surgical treatment is indicated if needed to manage the underlying cause, such as guttural pouch infection or esophageal disorders.

LONG-TERM PROGNOSIS

Prognosis depends on the underlying cause and varies tremendously. Prognosis for resolution of clinical signs is excellent for Horner's syndrome associated with mild trauma.[93] Prognosis for resolution of the syndrome and overall life of the horse is poor if Horner's syndrome is the result of metastatic neoplasia.[90-92]

FACIAL NERVE PARESIS/PARALYSIS

Facial nerve paralysis is the most common cranial nerve abnormality in horses.[100] In one study, facial nerve paralysis represented the greatest number of all neurologic diseases in horses in Australia.[100] The facial nerve in the horse originates posterior to the pons, enters the internal acoustic meatus, travels through the facial canal of the petrous temporal bone, passes through the stylomastoid foramen, extends around the guttural pouch and under the parotid salivary gland, crosses the ramus of the mandible (externally) approximately 4 cm ventral to the temporomandibular joint, then divides into dorsal and ventral buccal branches.[4]

CLINICAL APPEARANCE AND DIAGNOSIS

Clinical features of facial nerve paralysis include ptosis, lagophthalmos, ventral displacement and decreased motility of the ear pinna, decreased nostril function, flaccid lips, and deviation of the nose either away from the lesion with acute facial nerve paralysis or toward the lesion with chronic paralysis (Fig. 4-45).[2,4,100-103] Diagnosis is based on clinical signs and lack of facial nerve function (i.e., lagophthalmos and decreased or absent facial muscle function).

COMMON DIFFERENTIAL DIAGNOSIS AND METHODS FOR DEFINITIVE DIAGNOSIS

Facial nerve paralysis should be differentiated from other causes of ptosis, such as Horner's syndrome. The normal anatomic pathway of the facial nerve requires that the clinician consider a variety of possible causes for facial nerve paralysis, including inflammation of the inner ear, guttural pouch, or salivary glands. Additionally, fractures to the stylohyoid bone, petrous temporal bone, or ramus of the mandible can damage the facial nerve.[102] Owing to its external course over the ramus of the mandible, trauma frequently affects this nerve, including prolonged recumbency during disease or anesthesia.[103] A clinical sign of equine protozoal myeloencephalitis (EPM), a disease caused by *Sarcocystis neurona*, is facial nerve paralysis (see Chapter 13 for more information).[104-106] There is a report of facial nerve paralysis associated with temporohyoid osteoarthropathy, diagnosed based on proliferation of the temporohyoid joints and stylohyoid bones on radiographs and guttural pouch endoscopy.[101]

TREATMENT

Treatment for facial nerve paralysis is to provide protection for the cornea while addressing the underlying cause whenever possible. Topically applied artificial tear ointment should be given 4 to 6 times a day to keep the cornea moist and to prevent ulceration. If a corneal ulcer is present, it should be treated with topical antibiotics to help prevent infection and manage any concurrent reflex uveitis. Surgical therapy is indicated if the primary problem necessitates surgical intervention (e.g., fractures or guttural pouch abnormalities). A partial temporary tarsorrhaphy is recommended using a single horizontal mattress suture of 4-0 nylon at the temporal aspect of the palpebral

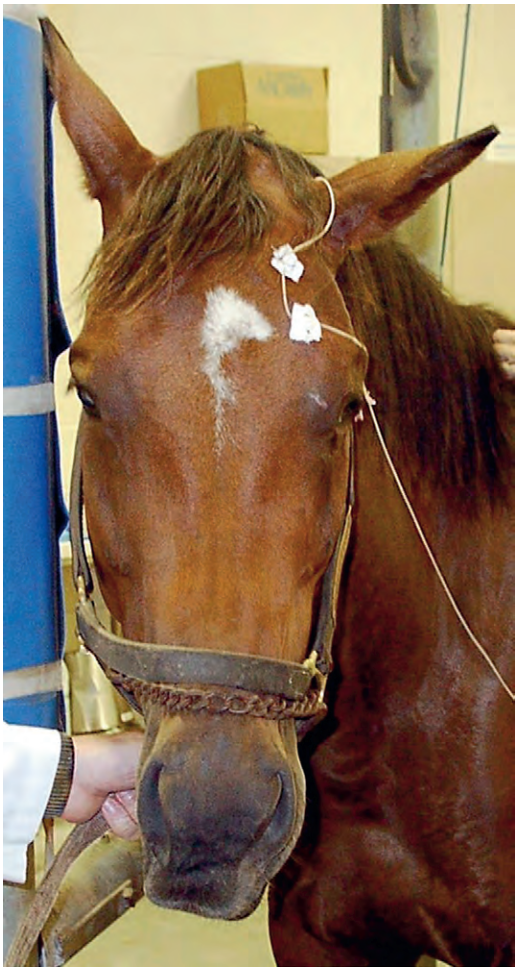


Figure 4-45. Acute left-sided facial nerve paralysis. A subpalpebral lavage catheter has been placed to assist in the medical management of corneal disease. (Photograph courtesy Dr. Stacy Andrew.)

fissure. This will help protect the globe until facial nerve function returns.

LONG-TERM PROGNOSIS

Prognosis depends on the underlying cause. If improvement of the facial nerve paralysis does not occur in 3 or 4 weeks, the prognosis is poor and the nerve damage is likely permanent. In cases of permanent facial nerve deficits, a permanent partial temporal tarsorrhaphy should be considered for increased corneal protection. This involves closing the lateral one-fourth of the eyelid margins by removing the eyelid margins and closing the wound bed in a two-layer manner as described previously in eyelid lacerations. Most horses with facial nerve paralysis maintain retractor bulbi function. The horse can retract the eye, elevate the third eyelid as a form of "blinking," and thus help distribute the tear film over the corneal surface. This action generally protects the medial two-thirds to three-fourths of the cornea, leaving the lateral cornea exposed. A permanent temporal tarsorrhaphy helps to protect the dorsolateral cornea.

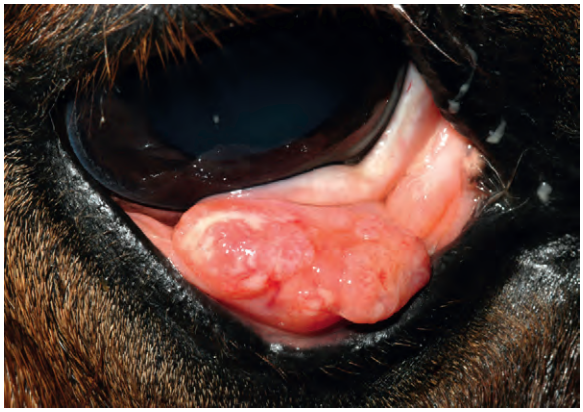


Figure 4-46. Horse affected with squamous cell carcinoma originating from the anterior ventrolateral aspect of the third eyelid.

THIRD EYELID DISORDERS

The equine third eyelid, or nictitating membrane, originates in the ventromedial aspect of the rostral orbit and moves passively in the dorsolateral direction. The bulbar and palpebral surfaces of the third eyelid are covered with conjunctiva, therefore virtually all diseases reviewed previously in the conjunctivitis section may also involve the third eyelid. The base of the third eyelid contains a lacrimal gland (tubuloacinar) that produces portions of the aqueous component of the tear film. Many of the conditions of the third eyelid are secondary to other abnormalities of the globe and orbit. The most common clinical disease affecting the equine nictitating membrane is squamous cell carcinoma (Fig. 4-46).[4]

CLINICAL APPEARANCE AND DIAGNOSIS

The leading edge of the third eyelid is visible in the normal horse and may or may not be pigmented (see Fig. 4-1). Occasionally, a nonpigmented third eyelid may be more obvious and thus erroneously interpreted as being abnormally elevated.[4] An elevated third eyelid can be secondary to enophthalmos (i.e., from fat atrophy), retraction of the globe (e.g., with ocular discomfort such as corneal ulceration, uveitis, or other ocular disease), phthisis bulbi (Fig. 4-47), an orbital space-occupying mass (e.g., neoplasm, granuloma, abscess),[107-110] or as a result of sympathetic denervation and Horner's syndrome.[7,8,90-93] Bilateral third eyelid elevation has been associated with tetanus,[111] ear tick *(Otobius megninii)* infestations,[112] and possible other systemic disease in horses (see Chapter 13 on systemic diseases). Conjunctivitis, ulceration, swelling, and even erosion of the leading edge of the third eyelid is not uncommon in horses (see Fig. 4-36), especially those that have pigmented eyelids but nonpigmented third eyelids.[4] Solar or actinic radiation and environmental irritants are usually the cause. These lesions may be precursors to squamous cell carcinoma. Inflammation of the third eyelid has been associated with granuloma formation with habronemiasis.[72] Prolapsed gland of the nictitans has not been reported in horses, but prolapsed orbital fat (specifically the anteromedial corpus adiposum) around the third eyelid can cause protrusion with a clinical appearance similar to a nictitating gland prolapse, as is typically seen in some canine breeds (Fig. 4-48).[113,114] Trauma to the third eyelid can result in lacerations of the conjunctiva and/or cartilage,

Figure 4-47. An elevated third eyelid secondary to phthisis bulbi. The small size of the eye has allowed the third eyelid to passively extend anteriorly.

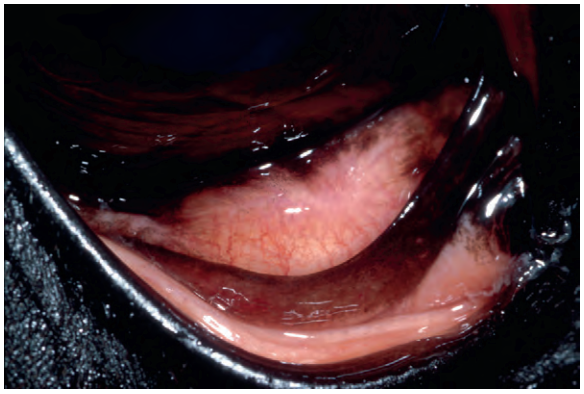


Figure 4-48. Horse with prolapsed orbital fat near the base of the third eyelid. This condition in horses should not be mistaken for a prolapse of the gland of the third eyelid, as is commonly observed in some breeds of dogs but has never been reported in horses.

hemorrhage, and swelling. In general, if the only abnormality is a conjunctival laceration, hemorrhage, or chemosis, the injury will rapidly heal without surgery. Topical antibiotics may be helpful to prevent further ocular irritation and protect the surface of swollen tissue from desiccation. If substantial third eyelid chemosis results in lagophthalmos, a partial temporary tarsorrhaphy is recommended by way of a single horizontal mattress suture placed in the medial one-fourth of the eyelid.[4] The lateral palpebral fissure is allowed to remain open so that the horse can still maintain some vision and topical medications can be instilled on the ocular surface. If the cartilage is lacerated, surgical repair of the third eyelid should be attempted; in severely damaged third eyelids, complete resection may be necessary.

COMMON DIFFERENTIAL DIAGNOSIS AND METHODS FOR DEFINITIVE DIAGNOSIS

Third eyelid position abnormalities must be differentiated from primary ocular and orbital diseases such as mass lesions in the orbit, enophthalmos, ocular discomfort, and phthisis bulbi (see Fig. 4-47). Third eyelid inflammation should be differentiated from medial canthal habronemiasis (see Fig. 4-34) and primary conjunctivitis. Lesions can be differentiated by culture, cytology, and biopsy. These tests are especially recommended in any chronic or unresponsive inflammation or swelling. Evidence of primary orbital (e.g., exophthalmos or inability to retropulse the globe) or ocular disease (e.g., phthisis bulbi) would suggest the need for further diagnostic procedures to determine the cause of the clinical signs. (See Chapter 3, Diseases and Surgery of the Globe and Orbit, for in-depth descriptions.)

TREATMENT

Treatment should be directed at the underlying cause of the inflammation or swelling. Initially, topical antibiotics are generally used; however, if the disease is unresponsive, treatment should be guided by culture and antimicrobial susceptibility testing, cytology, and histopathology. Lacerations involving the cartilage of the third eyelid should be surgically repaired or the third eyelid removed entirely. Partial removal of the third eyelid is not recommended because exposed cartilage of the third eyelid can irritate the cornea. The overall goal of surgical therapy on the third eyelid is to remove the cause of ocular irritation (e.g., squamous cell carcinoma [see Fig. 4-46]) without causing additional injury to the globe. To that end, all sutures and suture knots must be either buried under the conjunctiva or placed on the palpebral (i.e., "external") surface of the third eyelid. General anesthesia is recommended because the third eyelid and retractor bulbi muscles remain functional even when the animal is tranquilized. Retrobulbar nerve block (RNB) may be a useful adjunct when performing surgery on the third eyelid,[115] but RNB and standing sedation may not provide sufficient immobility of the head when microsurgical techniques are required. Removal of the third eyelid is a relatively common procedure that is performed when the third eyelid is affected by squamous cell carcinoma (see Fig. 4-46). Ideally, surgical removal occurs with the horse under general anesthesia; however, if only a portion of the third eyelid need be removed, standing sedation with or without RNB may be sufficient. If complete third eyelid resection is indicated, it is important that all the cartilage, the gland of the third eyelid, and the dense fibrous tissue anchoring the third eyelid to the ventronasal aspect of the orbit be removed. Palpation of the third eyelid before and after excision is recommended. Commonly, if the third eyelid is removed due to a cancerous lesion, ancillary cryotherapy is then performed, taking care not to freeze the cornea. Many ophthalmic surgeons advocate suturing the conjunctival wound bed after third eyelid removal with a continuous pattern of 6-0 polyglactin 910 or similar suture to prevent subsequent orbital fat prolapse.

LONG-TERM PROGNOSIS

Assuming that further damage to the eye does not occur from chronic third eyelid abnormalities, poor placement of sutures during surgery of the third eyelid, or neoplastic processes that have extended beyond the surgical margins of resection, the prognosis for most third eyelid injuries is good.

PROCEDURE FOR RETROBULBAR NERVE BLOCK

Standing sedation protocols and RNB are appropriate for performing certain minor ocular surgical procedures such as biop-

sies and third eyelid removal.[115] When performed correctly, the RNB will paralyze the retractor bulbi muscle and help keep the eye immobile. See Chapters 1 and 2 for more information on RNB.

ACQUIRED NASOLACRIMAL DISORDERS

NASOLACRIMAL DUCT OBSTRUCTION

As noted earlier, congenital nasolacrimal atresia is one of the most common congenital ocular diseases in horses and usually causes clinical signs of copious ocular discharge in foals between 2 and 6 months of age. Acquired nasolacrimal disorders include obstructions from inflammation (dacryocystitis), strictures, foreign bodies, dental disease,[116] and trauma.[2,23,24,117-120]

CLINICAL APPEARANCE AND DIAGNOSIS

Obstruction of the nasolacrimal duct (NLD) occurs most commonly secondary to intraluminal foreign material. Clinical signs include epiphora, conjunctivitis, and often significant mucopurulent discharge (Fig. 4-49). Foreign material can sometimes be successfully removed by retrograde saline flush (see earlier under Nasolacrimal Duct Atresia and Chapter 1 for further details).[4,119] Initial diagnosis is made by inability of topical fluorescein dye to exit the ventral nasolacrimal puncta (a negative Jones test). Inflammation or trauma to the NLD may cause hemorrhage to emanate from the ventral nasolacrimal meatus, a condition called *dacryohemorrhea*.[121]

COMMON DIFFERENTIAL DIAGNOSIS AND METHODS FOR DEFINITIVE DIAGNOSIS

In all cases of epiphora, the clinician needs to differentiate between causes of increased lacrimation versus obstruction of tear outflow (Fig. 4-50). The most common cause of increased lacrimation is ocular pain, indicative of either surface (e.g., conjunctivitis, keratitis, etc.) or intraocular (e.g., uveitis, glaucoma, etc.) disease. Some horses have seasonal epiphora or dacryocystitis and present typically with bilateral disease. This may be caused by environmental changes (e.g., increase in dry, dusty environment), allergies, or insects. The diagnostic approach to any horse with epiphora is to begin with a complete ophthalmic examination and acquisition of the minimum ophthalmic data base, including specific evaluation for a positive Jones test (i.e., presence of fluorescein stain at the nasal punctum indicative of normal tear flow down the nasolacrimal system [see Fig. 4-23]). If mucopurulent discharge is present, antimicrobial susceptibility testing should be performed, as well as cytology of the discharge. Following these tests, retrograde and normograde nasolacrimal irrigation should be attempted with the horse tranquilized (see Chapter 1). If irrigation is successful at clearing an obstruction, copious irrigation of the NLD should then be performed to ensure all debris has been cleared. Excessive force when irrigating the NLD should be avoided so as to prevent rupture or other damage. Unsuccessful irrigation attempts at NLD irrigation with the horse under standing sedation warrant additional diagnostic testing such as dacryocystorhinography (DCR) (see Fig. 4-20 and Chapter 1) to better delineate the site of obstruction and determine if there are any surrounding bony abnormalities.[25,39,118,119] Computed tomography[120] or video endoscopy[24] have also been used to image defects in the NLD.

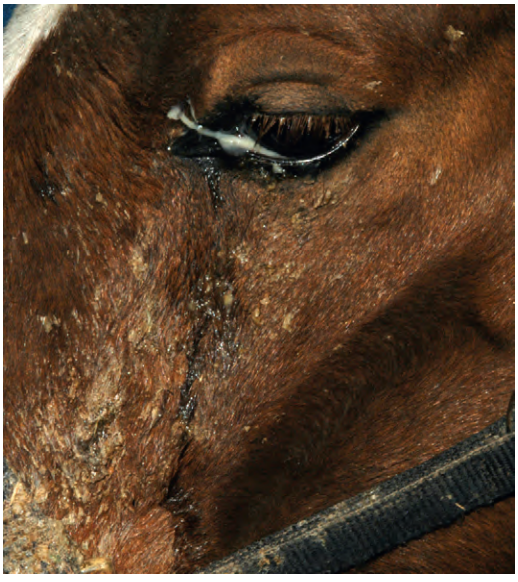


Figure 4-49. Three-month-old foal with significant mucopurulent ocular discharge secondary to nasolacrimal duct obstruction.

PATHOGENESIS OF DISEASE PROCESS AND PROGRESSION

Dacryocystitis, or inflammation of the NLD, is generally the result of a complete or partial obstruction, secondary retention of tears in the duct, and bacterial proliferation in the stagnant tear fluid. Obstructions can occur from environmental debris accumulating in the NLD, especially at areas of normal narrowing of the duct such as immediately prior to its exit from the lacrimal canal of the maxilla bone.[39] Damage to the lacrimal canal of the maxillary bone from external trauma, sinus infections, or upper arcade dental disease may cause strictures of the NLD.[2,23,117,118]

TREATMENT

NLD obstructions should be treated medically; however, surgical intervention may also be required. Topical broad-spectrum antibiotic solution (type based on antimicrobial susceptibility results) should be used every 6 hours once the NLD obstruction has been relieved. Solutions are preferred over ointments because they will pass through the NLD more readily. Antibiotic solutions containing a topical corticosteroid may be beneficial to decrease swelling in the NLD, providing there are no ocular surface contraindications (e.g., a corneal ulcer). Treatment should be continued for at least 2 weeks. If there has been repeated obstruction or episodes of dacryocystitis, if the obstruction was difficult to resolve, or if there was stricture of the duct visualized by DCR or other imaging modalities, then a surgical stent or catheter should be placed for 4 to 6 weeks. A 5 Fr male Silastic or plastic canine urinary catheter (with or without wire stent) is threaded normograde (from proximal to distal) or retrograde. The catheter is advanced until resistance is encountered. The catheter should not be forced if resistance is encountered, because severe hemorrhage may develop.[39] Once passed, the Silastic tubing is sutured in place for 4 to 6 weeks (see Fig. 4-22). Judicious use of oral antiinflammatory

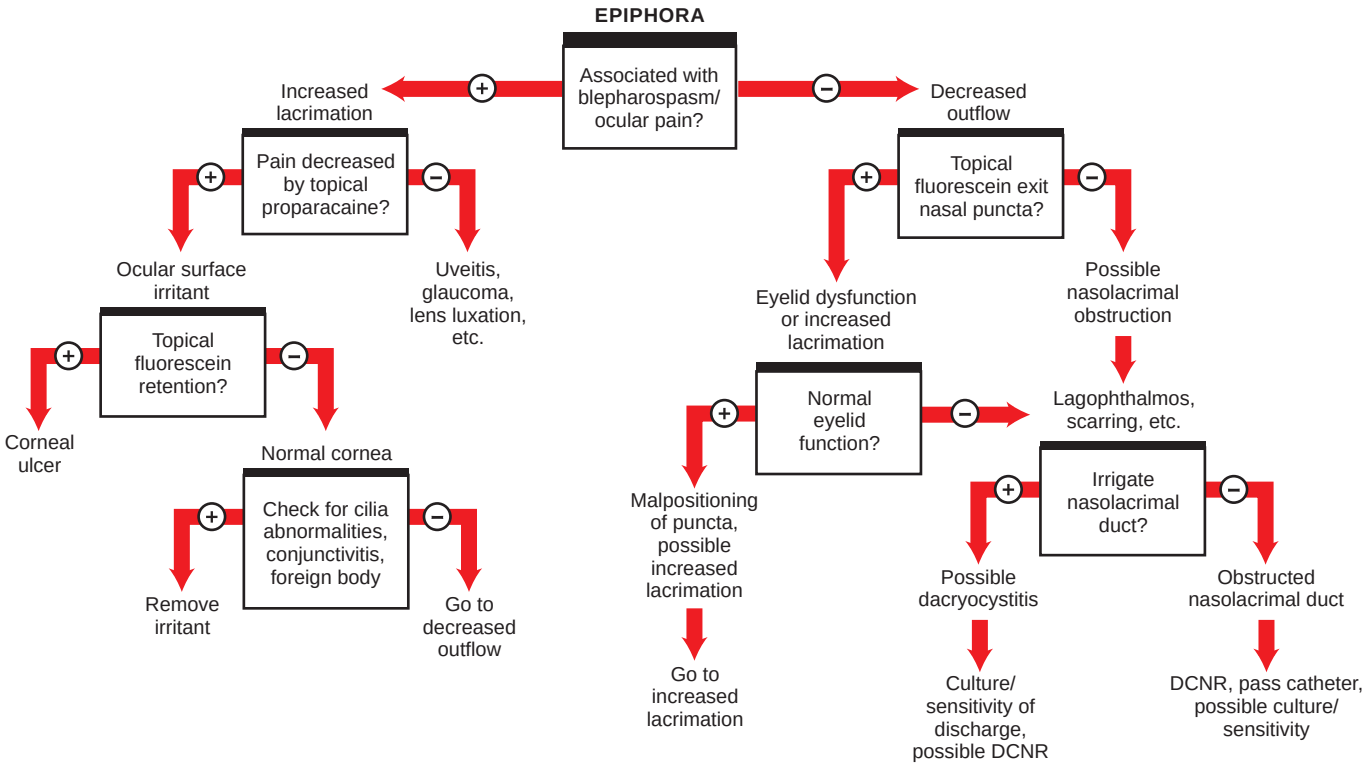


Figure 4-50. Flow chart for diagnosis and treatment of epiphora.

and oral antibiotic medication may be considered in these cases (refer to discussion on general therapeutic principles in this chapter).

Surgery to correct NLD obstruction is sometimes required. If there is any abnormality compressing the NLD, it should be alleviated. This would include surgery to relieve swelling from sinusitis or dental disease or to repair facial fractures or canaliculi lacerations.[2,23,116,117] If, by contrast, the nasolacrimal duct cannot be opened or is permanently destroyed, creating a new tear outflow pathway is needed. Creating a pathway from the canaliculi to the nasal cavity (canaliculorhinostomy)[119] or from the ventral medial conjunctival surface to the maxillary sinus (conjunctivosinostomy)[38] can successful establish this goal. These procedures involve drilling a hole using a Steinman pin or drill through the lacrimal bone into the maxillary sinus or nasal cavity, then placing a stent for 4 to 6 weeks to allow the incisions to heal and epithelialize the new outflow pathway. Although successful, these procedures present their own challenges: extensive hemorrhage, the density of equine facial bones, and the propensity of the newly created outflow pathway to stricture and close over time.

LONG-TERM PROGNOSIS

In general, the prognosis is good for NLD obstructions (typically with secondary dacryocystitis) that can be relatively easily unblocked and are not susceptible to repeat occurrence. It is essential to determine the location, extent, and cause of the obstruction to adequately treat it. Some horses can tolerate mild epiphora if the owners can keep the periocular area ventral to the eye clean and prevent fly infestation. Environmental control efforts aimed at decreasing particulate debris, allergens, and insect infestation all can help to decrease the clinical severity and/or recurrence of nasolacrimal disease in horses. Horses with severe and recurrent NLD obstructions requiring more aggressive surgical intervention (e.g., canaliculorhinostomy or conjunctivosinostomy) have a more guarded successful long-term prognosis, but there are few published reports of these more advanced surgical techniques.[38,119]

KERATOCONJUNCTIVITIS SICCA

Keratoconjunctivitis sicca, or "dry eye," is very uncommon in horses.[19-21,83,122,123] Nearly all cases of KCS in horses have been associated with trauma.[19,21] To date, there has not been a definitive case of immune-mediated lacrimal gland adenitis, which is the most common cause of KCS in dogs.[124-126] More recently, a case report of equine KCS attributable to hypothyroidism has been reported.[22] Some authors have subdivided KCS into tear-deficient dry eye and evaporative dry eye, which is desiccation of the ocular surface secondary to facial nerve paralysis (or other eyelid dysfunction), loss of corneal sensation, and other primary ocular-surface diseases.[123]

CLINICAL APPEARANCE AND DIAGNOSIS

Dry eye in horses may present with a variety of possible clinical signs, including blepharospasm; mucopurulent ocular discharge, a dry, lusterless appearance to the cornea; and keratitis. Definitive diagnosis should be confirmed by assessment of clinical signs together with Schirmer tear test (STT) values. The STT should be performed before manipulation of the periocular or ocular structures and at the onset of complete ophthalmic examination to minimize reflex tearing (see more information about the ocular exam in Chapter 1). Normal horses have been reported to have STT I (measurement of tears

without the use of a topical anesthetic) values between 11 to greater than 30 mm of wetting/min and 15 to 20 mm/30 seconds.[18,127,128] One study evaluating tear testing in horses found no differences in values obtained between STT I and STT II (i.e., with topical anesthetic) and no significant differences based on age, season, environment, gender, time of day or location of placement of strips.[128] Tranquilization does not affect STT values; however, general inhalant anesthesia with halothane does affect the STT for up to 3 hours.[127] STT measurements of 10 to 15 mm/min or less with clinical signs of dry eye would be suggestive of the clinical diagnosis of KCS in horses.

COMMON DIFFERENTIAL DIAGNOSIS AND METHODS FOR DEFINITIVE DIAGNOSIS

Although it is most appropriate to perform the minimum ophthalmic testing (STT, fluorescein stain, and intraocular pressure measurement) on any animal presenting with ocular disease, frequently even veterinary ophthalmologists do not routinely perform tear testing on horses. This is likely because KCS is a rare disease in this species, and many horses present with an ocular disease that results in an overabundance of tears (i.e., epiphora). An STT is indicated if evidence of CN VII dysfunction (i.e., following trauma, facial paralysis, etc.) is observed, if the cornea and/or conjunctiva appear dry, if tenacious mucoid ocular discharge is present, whenever corneal vascularization and/or ulceration is present that is persisting beyond the anticipated time for wound healing to have occurred, or if the ocular problem remains of undetermined etiology. KCS is most commonly the result of CN V or VII trauma but has also been reported in cases of fractures of the mandible and stylohyoid bone, locoweed poisoning, eosinophilic dacryadenitis, hypothyroidism, and in association with corneal stromal sequestration.[2,4,19-22,122] The clinician must differentiate KCS from other much more common diseases, especially primary keratitis and NLD obstruction.

TREATMENT

Medical therapy is the mainstay of treatment of equine KCS. Initial therapy should consist of topical broad-spectrum antibiotic ointment to help reduce the secondary bacterial infections that commonly develop. Topical artificial tear ointments administered 3 or 4 times daily will help keep the cornea of most horses healthy. However, the importance of continued use of the medication must be stressed to its caretakers. Topical 0.25% pilocarpine, vitamin A, and acetylcysteine used once a day have been recommended for treatment of horses with KCS,[4] but their efficacy has not been reported. Topical cyclosporine has also been recommended in equine KCS, with reports of improvement of clinical signs.[122] However, because horses have never been documented to have primary lacrimal adenitis as an etiology for their KCS, the pathophysiology by which topical cyclosporine may improve clinical signs is not completely understood. Topical corticosteroids may also initially improve clinical signs of KCS, but they should be used with extreme caution because of the risk of development of corneal ulceration in KCS eyes. Occlusion of the nasolacrimal puncta by cauterization has been recommended for mild cases of equine KCS,[4] but the efficacy of this technique is unknown. In horses with facial nerve deficits, loss of corneal sensation, or chronic unrelenting KCS, a temporary or permanent lateral tarsorrhaphy may help protect the cornea. A parotid duct transposition (to provide salivary secretion to the corneal surface) has been attempted in a horse, but long-term results were not reported.[129] In severe cases of dry eye that do not respond to therapy and are persistently painful, enucleation of the eye should be considered.

LONG-TERM PROGNOSIS

Acute KCS associated with trauma, anesthesia, or systemic disease generally will resolve as the horse recovers from its primary disease. KCS associated with increased evaporation of tears due to lagophthalmos or loss of corneal sensation will resolve if and when the neurologic disease resolves. Generally, neurologic causes of KCS resolve in 3 or 4 weeks. Regardless of the cause or duration, it is imperative that the cornea be kept moist and well protected, or chronic keratitis/conjunctivitis will result. In chronic cases of equine KCS, most horses will develop progressive corneal edema, vascularization, corneal ulceration, and/or fibrosis, with resultant decreased vision. Enucleation may be indicated to restore comfort to chronically painful, blind horses affected by KCS.

ADNEXAL NEOPLASIA

Approximately 10% of equine neoplasms affect the eye or periocular structures.[130,131] Neoplastic adnexal disease represents the most common and often the most frustrating of all equine eyelid diseases. The most common periocular masses include sarcoid, squamous cell carcinoma, papilloma, lymphosarcoma, and melanoma.[2,4,23,107,130-132] Identical treatments administered to similar-appearing tumor types can have different clinical outcomes. Reasons for which one horse responds well to therapy and another does not warrants further study. Variability in clinical response is likely one important reason why a myriad of different treatment options exists for any given equine neoplasm. It is difficult to draw definitive conclusions regarding biological behavior or response to treatment from reviewing the veterinary literature. Study design varies widely and may be limited to isolated case reports.[133,134] Very few reports exist with greater than 100 horses included and containing at least a year (or longer) follow-up time after specific therapy for a particular tumor type has been used.[135] This is in stark contrast to the studies that are routinely published in physician ophthalmology.[136,137] Treatment efficacy is challenging to critically assess because some studies are not designed with a control population for adequate comparison purposes and are often based on a subset of cases referred to specialty/teaching hospitals. Referral cases are frequently those that are refractory to "conventional" treatment modalities and may have already undergone treatment prior to being included in the study; therefore, the population of horses examined is skewed. Methods of data reporting (i.e., recurrence rate versus disease-free interval) also vary among publications. The reader should be aware of these limitations when reviewing the literature.

SARCOIDS

Sarcoids, cutaneous tumors of fibroblastic origin, are the most common neoplasm of horses.[132,138,139] They often have proliferative and hyperplastic epithelial components, and while metastasis is rare, recurrence is common, especially with the more invasive lesions. Size and location dictates their clinical signifi-

cance. Periocular/eyelid sarcoids are common and may result in significant pathology to the eye, either by disrupting normal eyelid function or by directly rubbing on the eye (i.e., "mass" effect).[140-142] In one series, periocular sarcoids represented 14% of total sarcoids.[143] Owing to the close proximity of periocular structures to the globe, some treatments reported for use on sarcoids elsewhere on the body cannot be used on eyelids without risking significant damage to the globe.[135]

CLINICAL APPEARANCE AND DIAGNOSIS

The clinical appearance of sarcoids varies. They are most commonly classified into five broad categories: occult, verrucose, nodular (A and B), fibroblastic (A and B), and mixed equine sarcoids.[135,144] Occult sarcoid appears as an alopecic area with fine epidermal nodules. Verrucose sarcoids are thickened and hyperkeratotic with extensive flaking of the skin. Nodular type A sarcoids (Fig. 4-51) are well defined, ovoid, and entirely subcutaneous. Nodular type B sarcoids are similar but involve the epidermis (Fig. 4-52). Fibroblastic sarcoids appear fleshy and ulcerated and can be pedunculated (type A) or have a broad base (type B) (Fig. 4-53). Mixed sarcoids have one or more of the features of the other types of sarcoids (Fig. 4-54). Periocular sarcoids are most commonly nodular, fibroblastic, or mixed. Sarcoids usually develop in young horses between 3 and 6 years of age, but horses as young as yearlings have developed them.[143] Nearly all breeds have been reported to develop sarcoids. Quarter Horses, Appaloosas, and Arabians may be at increased risk, while Standardbreds may be at decreased risk.[145,146]

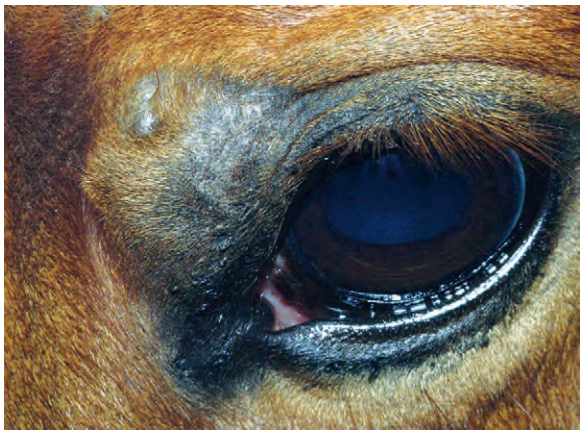


Figure 4-51. A nodular type A sarcoid in the upper medial eyelid of a horse. Nodular type A sarcoids are well defined, ovoid, and entirely subcutaneous.

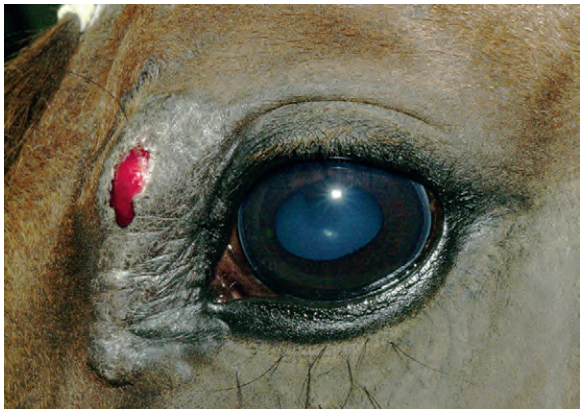


Figure 4-52. A nodular type B sarcoid in the upper medial eyelid and medial canthus of a horse. Nodular type B sarcoids are well defined, ovoid, and involve the epidermis.

COMMON DIFFERENTIAL DIAGNOSIS AND METHODS FOR DEFINITIVE DIAGNOSIS

A surgical biopsy is always required for definitive diagnosis. Exuberant granulation tissue may be present and difficult to distinguish clinically from sarcoid.[143] Histopathology should be used to rule out other eyelid mass lesions such as habronemiasis, melanoma, squamous cell carcinoma, papilloma, or orbital fat prolapse. Histologically, all clinical types of sarcoids have increased density of dermal fibroblasts (i.e., fibroblastic prolif-

Figure 4-53. Fibroblastic sarcoids appear fleshy and ulcerated and can have a pedunculated (type A) or a broad base (type B). Here is a type A fibroblastic sarcoid.

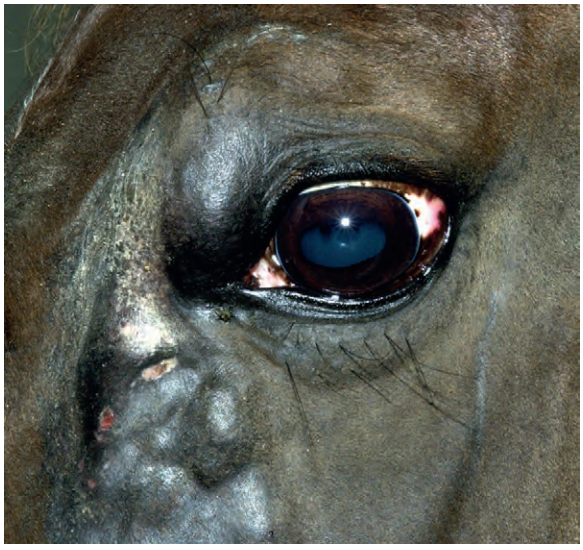


Figure 4-54. An extensive mixed type (i.e., features of one or more types of sarcoids) of the medial upper eyelid and medial canthus of a horse.

eration). Epidermal hyperplasia, hyperkeratosis, and rete peg formation were only found consistently in the verrucous and mixed types but not consistently in occult and nodular sarcoids in one study.[144] Sarcoids commonly invade into the subcutis and the deeper muscular structures around the eye.[135,147]

PATHOGENESIS OF DISEASE PROCESS AND PROGRESSION

The pathologic features of equine sarcoid are generally considered to be well established; debate remains over possible etiologies. Sarcoids have long been thought to have a viral origin. This infectious origin was supported by the fact that epizootics have occurred in individual herds.[143,148] Numerous studies have associated bovine papilloma virus (BPV) and equine sarcoids.[143,144,149-158] Intradermal inoculation of horses with cell-free extracts from bovine skin tumors caused by BPV resulted in lesions that clinically and histologically resembled equine sarcoids.[149,151,159] BPV has not been found in natural cases of equine sarcoid by electron microscopy,[143] but DNA sequences of BVP (BVP-1 and BVP-2) have been found in equine sarcoid by southern blotting and PCR techniques.[153-158,160-162] Equine sarcoids appear to contain detectable viral DNA and RNA. They are also known to express the BPV types 1 and 2 major transforming protein E5, but they appear not to produce infectious virions.[143,154-158,161] In one study, no mutations of the tumor-suppressor gene, p53, were identified in equine sarcoids, suggesting that p53 mutations do not have a primary role in the pathogenesis of this tumor.[163] However, the authors speculated that the high BPV infection in equine sarcoid may indicate the functional inactivation of p53 by BPV-encoded E6 protein.[163] Another study found that no telomerase activity could be detected in equine sarcoids, suggesting that telomerase does not play a major role in pathogenesis.[164]

Genetic predisposition of equine sarcoid has been reported. Sarcoid occurrence was associated with the major histocompatibility complex (MHC) encoded class I equine leukocyte antigen (ELA) W3,B1 haplotype in Irish, Swiss, and French-bred Warmbloods.[165] An association between sarcoid susceptibility and the MHC-encoded class II allele, ELA W13, has also been found in several breeds.[143,166] An association between early-onset sarcoids and A5 ELA, increased recurrence rates after surgery and W13 ELA, and increased prevalence of sarcoid and A3W13 ELA has been reported.[167] Another study demonstrated correlation between the development of sarcoids and heterozygosity for the equine severe combined immunodeficiency (SCID) allele.[168]

TREATMENT

Various treatments have been reported for the treatment of equine periocular sarcoids (Table 4-7) and are summarized in the following paragraphs.

Topical Medical Therapy for Sarcoids

Several topical substances (e.g., oil of rosemary, arsenic powder, engine grease, tea tree oil, etc.)—mostly irritants—have been used for treatment of sarcoids.[4,135] A popular topical product, XXTERRA (Larson Laboratories, Fort Collins, CO) has bloodroot *(Sanguinaria canadensis)* as the active ingredient. The topical herbal substance irritates the sarcoid, which stimulates the immune system to mount a response to the tumor. Anecdotally, there has been a 95% response rate. Because these substances are irritating, they induce severe keratitis and should not be used on or near the eye. AW4 ointment, which consists of 10% 5-fluorouracil and oil of rosemary (once daily for 5 days) was used in 146 periocular sarcoids in one study that resulted in a nonrecurrence rate of 35%.[135]

Immunotherapy

Immunotherapy (i.e., *Mycobacterium* cell wall extracts, live whole-cell Bacille Calmette-Guérin [BCG], *Propionibacterium* cell wall extracts) has been successfully used to treat equine sarcoids.[135,140,141,143,169-174] These products are believed to stimulate the immune system to recognize tumor cell–specific antigens, thereby enhancing tumor cell destruction. The most common immunotherapy for periocular sarcoids has been the injection of BCG.[135,141,170-172,174] The administration technique is to saturate the tumor with BCG, typically at a dose of 1 mL per cm^2 of tumor surface (see Fig. 4-54).[141] The injection is repeated at variable intervals (most commonly every 2 to 4 weeks) until complete regression of the tumor occurs. In one study, complete regression was observed in 100% of periocular tumors in 31 horses, with an average of 11.7 mL per treatment, 3.2 treatments per tumor, and a range of 14 to 252 days to achieve remission.[141] Local and systemic anaphylaxis has been noted, especially after the second injection.[171] Pretreatment with flunixin meglumine, antihistamines, and/or corticosteroids may be required. Other substances have been used for immunotherapy in the treatment of sarcoids and include autogenous tumor vaccines, other mycobacterial cell wall fragments, recombinant human tumor necrosis factor α (TNF-α), and xanthate compounds.[140,171,175] In a large review of periocular sarcoids,[135] immunotherapy with intralesional BCG had poor results with verrucose, occult, or mixed sarcoids, while BCG immunomodulation therapy for fibroblastic and nodular lesions had a good overall response of 69% (see Table 4-7). Side effects observed included sinus tracts in 15% and transient swelling after injections.[135]

Chemotherapy

Intralesional cisplatin has been the most common type of chemotherapy[142,176-178] used for sarcoids. Use of topical 5-fluorouracil (5-FU) has also been reported, with 6 of 9 verrucose or occult sarcoids demonstrating good response.[179] However, only those sarcoids away from the eye and eyelid margins should be treated with 5-FU because of the irritating qualities of the drug. Injection with an oily emulsion of cisplatin consisted of 4 treatments at 2-week intervals at a dose of 1 mg of cisplatin/cm^3 of tumor tissue.[177] Cisplatin injections are performed in a manner similar to the technique described for BCG injection (Figs. 4-55 and 4-56). Complete regression was observed in 95% of the sarcoids, with a 1-year relapse-free rate of 87%.[177] Side effects or toxicity associated with the chemotherapy were deemed minimal.[177] Electrochemical stimulation may enhance the effectiveness of cisplatin chemotherapy of sarcoids.[176] Following cisplatin injection, an electropulsator was used to deliver pulses of 0.1 ms at a 1-Hz frequency with a 1.3-kV voltage to the sarcoid. Although an excellent regression of the tumors was noted, the effect on the eye and the tolerance of a horse to the electrostimulation of the sensitive periocular tissues was not reported. In a review of 18 periocular sarcoids, use of intralesional chemotherapy resulted in nonrecurrence in 33%.[135] Cisplatin beads have also been reported for use in equine cutaneous

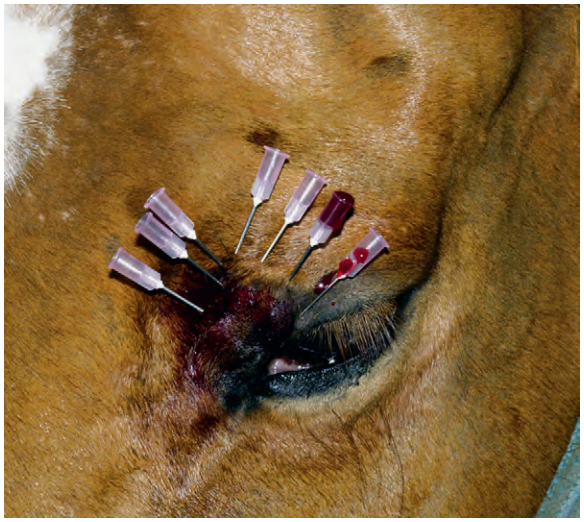


Figure 4-55. Preplaced needles for infiltration with Bacille Calmette-Guérin (BCG) or cisplatin of a nodular sarcoid.

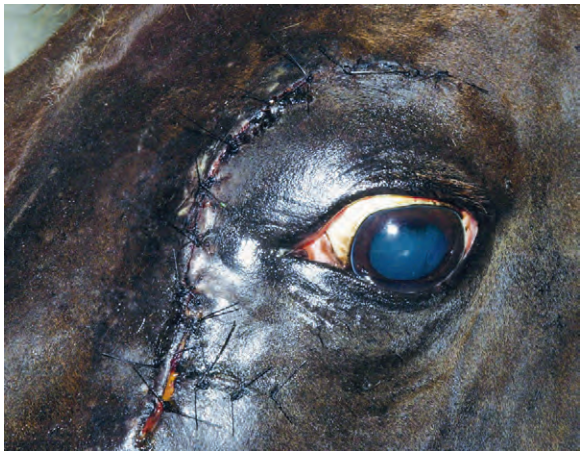


Figure 4-56. Surgical excision of large medial periocular sarcoid.

Table 4-7 | **Literature Review of Treatment for Periocular Sarcoids in Horses**

MEDICAL THERAPY

TYPE OF THERAPY	DRUG	DOSE	NUMBER OF CASES	PERCENT OF NONRECURRENCE
Topical therapy	AW4-LUDES ointment[135]	Once daily for 5 days	146	35%
	5% 5-fluorouracil[135]	Bid × 5 days, then qd for 5 days, then QOD for 5 applications	9	67%
Immunotherapy	BCG[141]	1 mL per cm^2 of tumor surface every 2-4 weeks	26	100%
	BCG[135]	1 mL per cm^2 every 2-4 weeks	52	0%
	Occult, verrucose, mixed nodular, or fibroblastic	1 mL per cm^2 every 2-4 weeks	300	69%
	Cisplatin[135]	1 mL per cm^2 every 2-4 weeks	18	33%

SURGICAL THERAPY FOR PERIOCULAR SARCOIDS

TYPE OF THERAPY	DESCRIPTION	NUMBER OF CASES	PERCENT OF NONRECURRENCE
Surgical excision[138]	Excision	—	50%
Surgical excision[135]	Excision	28	18%
Cryotherapy[186]	Double or triple freeze/thaw to –25°C		
Cryotherapy[135]	Double or triple freeze/thaw to –25°C	23	9%
Hyperthermia[135]	Tissue temperatures between 41°C and 45°C	2	0%

BRACHYTHERAPY FOR PERIOCULAR SARCOIDS

RADIOISOTOPE	DOSE RANGE	NUMBER OF CASES	PERCENT OF NONRECURRENCE
^{222}Radon seeds[195]	6000 cGy	19	92%
^{198}Gold seeds[197]	7000 cGy	19	90%
^{192}Iridium seeds[142,194]	60 Gy	115	87%, 100%
^{192}Iridium pins[135]	7000-9000 cGy	53	98%

tumors, including sarcoids and squamous cell carcinoma,[180] but they are not commercially available at this time.

Surgical Excision

In general, surgical excision of sarcoids (Fig. 4-57; also see Fig. 4-56) without adjunctive therapies (e.g., cryotherapy, interstitial irradiation, immunotherapy, cryotherapy, etc.) is not recommended and has approximately a 50% recurrence rate by 1 year.[138] In a review of 28 periocular sarcoids treated by surgical excision alone, a recurrence rate of 92% was found.[135] Split-thickness autogenous skin grafts improved cosmetic results after excision of sarcoids, and there were no recurrences in the three horses in one study.[181] Carbon dioxide (CO_2) laser ablation of sarcoids has a lower recurrence rate than surgical excision alone, but unless the skin is closed primarily, exuberant granulation may develop.[143,182] Early onset, long duration, and large size all appeared to increase risk of recurrence.[167] There may be a greater likelihood for local recurrence

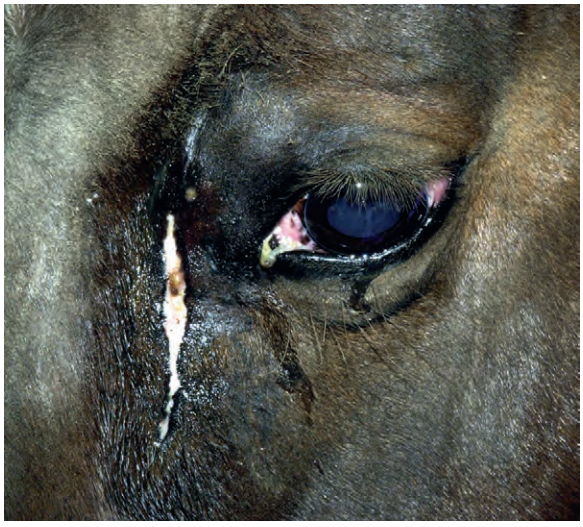


Figure 4-57. Same horse as shown in Fig. 4-55 after excision of a large mixed sarcoid and three intralesional cisplatin treatments.

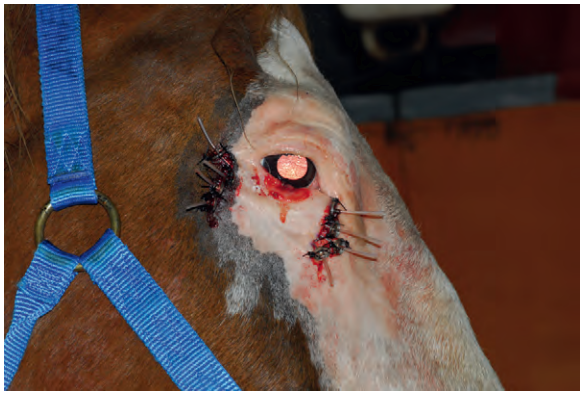


Figure 4-58. Iridium implants for treatment of an upper-eyelid sarcoid. The plastic tubes are preplaced and then the iridium inserted. Total treatment time is typically 7 days, then the tubes are removed.

when sarcoids have a surgical margin that is positive for BPV DNA.[161]

Cryotherapy

Cryotherapy is a commonly used surgical treatment for sarcoids,[4,135,183-185] either alone or following surgical debulking of the tumor. The sarcoid is destroyed, and the ensuing eschar separates from the underlying granulation bed. Healing following cryotherapy always occurs by second intention. Principles of cryotherapy to ensure proper freezing include a double or triple freeze/thaw cycle with a rapid freeze and slow thaw. Tissues must be frozen to at least –25°C, and the frozen area should encompass a margin of 0.5 cm around the tumor periphery.[186] Use of thermocouple temperature needles are recommended to ensure that the desired tissue temperature is achieved. Two commonly used types of cryotherapy include nitrous oxide or liquid nitrogen. Delivery of cryotherapy for equine sarcoids is recommended via a probe. If nitrous oxide is used, increased time and overlapping of the sites must be done to compensate for the slow freezing and lack of penetration.[186] Liquid nitrogen provides a faster freeze and can achieve tissue temperatures that are substantially lower (approximately –200°C) than those obtained with nitrous oxide (approximately –80°C). Care must be taken to not cause tissue necrosis of the eyelid by over-freezing the eyelid margin. Sloughing of tissue will occur 2 to 4 weeks after cryotherapy, and tissue depigmentation may remain for 6 months or more. Repeated treatments may be required for large or recurrent lesions.[187]

Hyperthermia

Neoplastic tissues are more sensitive to elevated temperatures than normal cells, and temperatures between 41°C and 45°C will preferentially destroy neoplastic tissue but not normal cells.[186] Minimal changes were seen on the normal equine eye from hyperthermia.[188] There have been several studies evaluating hyperthermia in the treatment of equine squamous cell carcinoma,[2,4,189,190] but only a few with treatment of sarcoids. In a review of periocular sarcoids, two were treated by hyperthermia, and both of them recurred.[135] In another case series, 10 of 11 sarcoids demonstrated no evidence of tumor regrowth after final hyperthermia treatment, and the authors recommended initial surgical debulking with a minimum of five hyperthermia treatments at 2- to 4-week intervals, with the first treatment to be performed prior to wound-bed closure.[191]

Brachytherapy

Brachytherapy[142,192-194] uses small gamma radioactive sources that are placed on or within neoplasms, allowing a high dose of radiation to be delivered to the tissue and minimal radiation exposure to surrounding tissues.[186] The radioactive sources are usually removed once the desired dose is delivered to the tissue. The length of time required depends on the isotope used. Isotopes that have been used include gold-198, iridium-192, radon-222, cesium-137, and tantalum-186.[195] Iridium-192 is most commonly used, and the isotope is contained within stainless steel rods at 1-cm intervals in a plastic coating or within needles placed in the tumor in parallel rows approximately 1 cm apart (Fig. 4-58).[142,193,196] Iridium-192 has a half-life of 74.2 days, and typical doses of 5000 to 9000 cGy take approximately 7 to 14 days of implantation prior to removal.[196] A 94% tumor-free incidence at 1 year in 16 sarcoids was found in one study.[196] In a study of periocular sarcoids treated by iridium-192 brachytherapy at a dose of 60 Gy (minimum dose), the 1-year and 5-year progression-free survival rates for sarcoids were 86.6% and 74.0%, respectively.[142] In another study of periocular sarcoids that received iridium-192 brachytherapy, (n = 53) a nonrecurrence rate of 98% was found.[135] In a more recent study, eight horses with periocular sarcoids were successfully treated with iridium-192 interstitial brachytherapy.[194] Use of other brachytherapy modalities in sarcoids have had similar results (see Table 4-7).[142,192,193,195-198] Side effects of radiation therapy are uncommon, but some chronic ocular effects such palpebral fibrosis, cataract, keratitis, corneal edema, bone sequestrum, and corneal ulceration have been reported.[135,142,199] Special licensure, isolation requirements, possibility of human radiation exposure, overall cost, and availability make this treatment option more challenging in some cases.

LONG-TERM PROGNOSIS

Failure to induce complete regression of periocular sarcoids will frequently result in regrowth of the tumor, and recurrence may be more aggressive (i.e., extensive local infiltration and faster growth). Therefore, if treatment is pursued, potent

and aggressive therapy is recommended from the outset of treatment to more quickly destroy the tissue and prevent recurrences.[135] Patients should be closely monitored with regular follow-up examinations and retreatment promptly initiated if recurrence is noted. However, the clinician must be aware that extensive debulking around the eye is not possible because of the horse's facial anatomy and lack of skin-flap surgical options. Certain treatment methods such as surface irritants should be used with great caution in the vicinity of the eye, least the globe be secondarily damaged and vision compromised.[135]

SQUAMOUS CELL CARCINOMA

Squamous cell carcinoma (SCC) is the most common neoplasm of the equine eye and ocular adnexa[107,200] and the second most common tumor of the horse overall.[130] At one institution, ocular SCC represented approximately 10% of all equine ocular disease.[6]

SCC may involve the corneoconjunctiva, bulbar conjunctiva, third eyelid, and eyelids.[107,201] Biological behavior of ocular SCC is reported to differ depending on location,[202] with the prognosis for eyelid SCC worse compared to the other sites of the eye.[203] Typically, SCC is locally invasive and slow to metastasize.[132] Metastasis to local lymph nodes, salivary glands, olfactory regions, and lungs can occur.[204,205]

CLINICAL APPEARANCE AND DIAGNOSIS

Increased prevalence of SCC is associated with various environmental factors: geographic influences of increased longitude, decreased latitude, increased altitude, and increased mean annual solar radiation exposure.[71] An increased prevalence of ocular SCC may occur with age, and a breed predilection for draft breeds and Appaloosas has been reported.[6,71] Horses with light hair and minimal skin pigmentation have higher prevalence of ocular SCC.[6,71] Mean equine age at diagnosis with ocular/periocular SCC has been reported to be 9.8 years,[204] 11 years,[206] 11.8 years,[6] and 11.1 years,[71] with a range of 3 to 26 years.[207] Gender predisposition of ocular SCC is unknown. One study noted a high prevalence of SCC in geldings, double the rate of mares and five times that of stallions affected, suggesting the possibility that endogenous sex-hormone levels may be associated with ocular SCC development in horses.[71] However, this finding may simply reflect gender distribution of the general client-owned equine population. Another study found no gender predisposition differences.[190] Unilateral involvement is most common, but in one study bilateral ocular SCC was observed in 16% of horses.[203] The most common ocular locations for SCC are the nictitating membrane or medial canthus (approximately 28%) (Fig. 4-59), limbus (approximately 28%) (Fig. 4-60), lower eyelid (approximately 23%) (Fig. 4-61), and other locations (21%) (i.e., cornea, conjunctiva, orbit, etc.).[6,107,203,208] Actinic solar keratitis may transform to carcinoma in situ SCC (see Fig. 4-36) that often appears as hyperemic eyelid erosive plaques with dark-staining crusts. These lesions frequently undergo further cellular change to become papillomatous SCC (Fig. 4-62) or alternatively, SCC may appear as a raised mass with a pink, cobblestone appearance (see Fig. 4-59) and may progress to large, fleshy masses with variable degrees of ulceration, necrosis, and inflammation that can infiltrate the orbit (Fig. 4-63).[4,202,209-211]

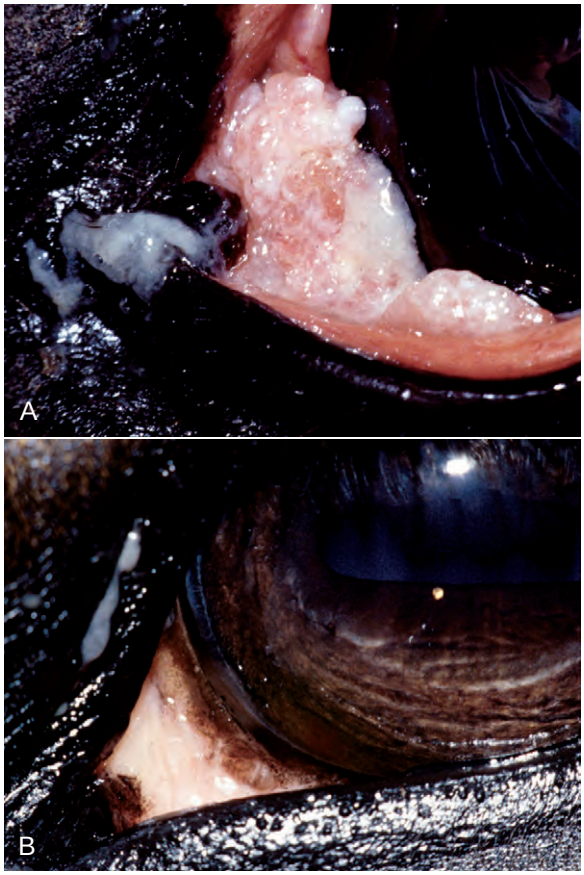


Figure 4-59. **A,** An infiltrating third-eyelid squamous cell carcinoma. **B,** Two weeks after total excision of the third eyelid and continuous suturing of limbal conjunctiva. (Photographs courtesy Dr. Riccardo Stoppini.)

COMMON DIFFERENTIAL DIAGNOSIS AND METHODS FOR DEFINITIVE DIAGNOSIS

SCC should be suspected with any erosive, erythematous, or raised ocular mass.[209] Atypical, pigmented SCC has been reported,[212] emphasizing the need for histologic confirmation of all abnormal periocular and ocular lesions. Differential diagnosis for SCC includes other tumors (papilloma, melanoma, mastocytoma, basal cell carcinoma, schwannoma, adenoma and adenocarcinoma, hemangioma and hemangiosarcoma, lymphoma and lymphosarcoma), conjunctivitis (lymphoid hyperplasia and follicular conjunctivitis), inflammatory lesions (abscesses, granulation tissue, foreign body reaction, solar-induced inflammation), and parasites *(Habronema, Onchocerca, Thelazia).**

Histologically, SCC has been subdivided into four basic types: plaque (i.e., carcinoma in situ), papillomatous, noninvasive SCC, and invasive SCC.[218] Plaque formation involves primarily the proliferation of the stratum spinosum, but all layers of the epithelium can be proliferative. Papilloma formation will occur when underlying connective tissue invades hyperkeratotic epithelium. Noninvasive SCC exhibits malignant transformation of the basilar layer of the epithelium, with development

*References 4, 60, 107, 108, 113, 114, 135, 209, and 213-217.

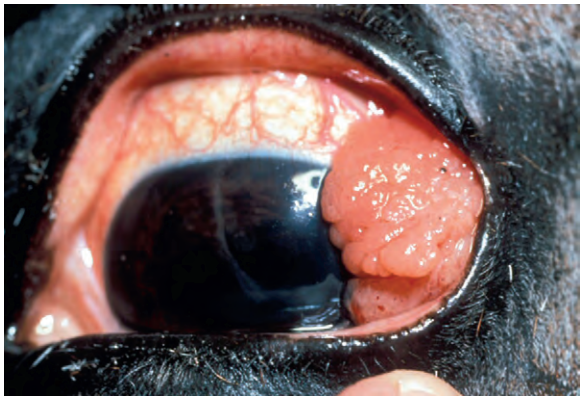


Figure 4-60. Large proliferative lateral limbal squamous cell carcinoma.

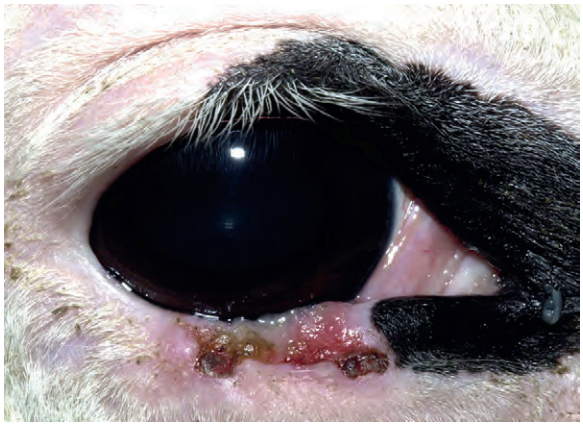


Figure 4-61. Lower-eyelid squamous cell carcinoma in a paint horse. Notice how the neoplastic tissue involves only the nonpigmented eyelid margin and stops where the pigmentation begins.

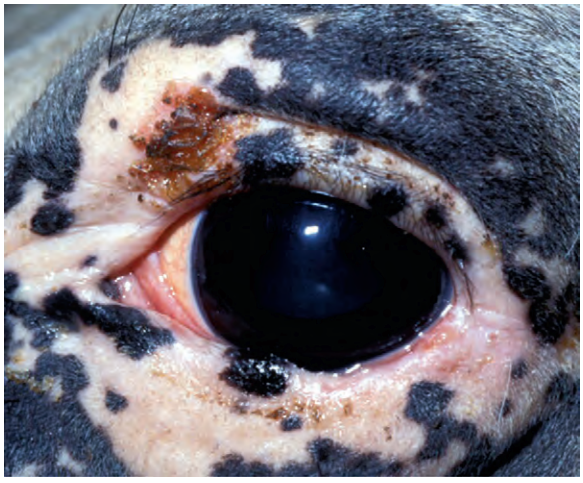


Figure 4-62. Proliferative papillomatous inferior-eyelid squamous cell carcinoma.

of hyperchromatic nuclei, increased mitotic figures, pleomorphism, and loss of polarity. Invasive SCC extends past the basal epithelium into the subepithelial tissue and can have variable degrees of differentiation. Well-differentiated neoplasms are characterized by whorl formation, keratinized foci (i.e., "keratin pearls"), and intercellular bridges (Fig. 4-64). In poorly differentiated SCC, neoplastic cells are frequently arranged in cords or nests but have minimal cellular keratinization.[218] An inflammatory infiltrate composed mostly of $CD3^+$ T lymphocytes, $CD79^+$ B cells, macrophages, and numerous IgG plasma cells is commonly associated with SCCs.[219] In one study, no significant correlation was found between the nature of the inflammatory infiltrate and the SCC histologic grade or degree of invasion.[219] However, expression of MHC class II by neoplastic epithelial cells may induce an improved local antitumor immune response.[219]

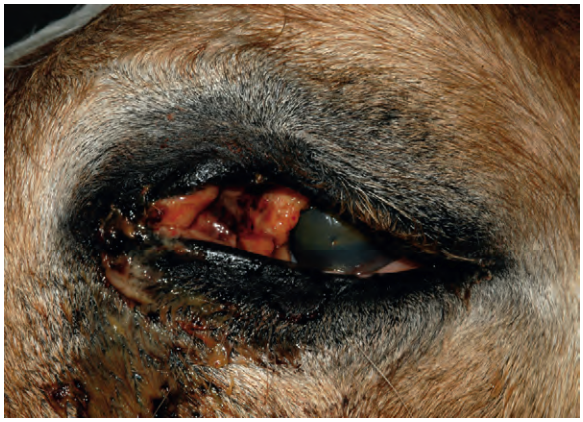


Figure 4-63. Belgian horse affected by an extensive third eyelid squamous cell carcinoma with orbital invasion.

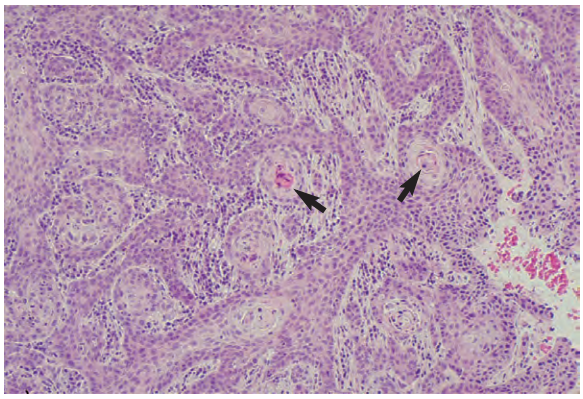


Figure 4-64. Histologic section of an eyelid squamous cell carcinoma (H&E stain ×400). This well-differentiated neoplasm is characterized by whorl formation, keratinized foci (i.e., "keratin pearls" *[arrows]*), and intercellular bridges.

PATHOGENESIS OF DISEASE PROCESS AND PROGRESSION OF SCC

Any chronic irritation may promote neoplastic transformation of epithelium into SCC, especially at mucocutaneous junctions. Unlike sarcoids, equine SCC has not been shown to exhibit viral antigens,[220] although recent preliminary evidence suggests that a viral etiology may play a role in SCC pathogenesis.[221] Irritation from actinic and/or ultraviolet (UV) radiation has been thought to promote the development of SCC. Clinically, horses living at higher elevations with increased sunlight exposure have a higher incidence of SCC.[71] Overexpression of the tumor-suppressor protein, p53, possibly mutated due to UV radiation, plays an important role in SCC development in many animals.[30,163,222,223] The p53 antigen has been detected immuno-

histochemically in formalin-fixed tissues of SCCs of domestic animals.[163,222,223] In two separate studies, 100% of equine ocular SCCs overexpressed p53.[30,223]

The role of cyclooxygenase (COX) in the pathogenesis of equine SCC is still undetermined. Cyclooxygenases are a family of enzymes responsible for conversion of arachidonic acid to prostaglandins. Multiple isoforms of COX exist, with COX-1 and COX-2 being the most biologically active.[224] High levels of COX-2 expression have been detected in many human and veterinary neoplasms, including SCC of the head and neck.[225] Correlations have been made in humans with head and neck SCC between overexpression of COX-2 in neoplastic tissues and poor prognostic factors.[225] A limited number of investigations specifically examining the role of COX in naturally occurring equine ocular and periocular SCC have been conducted to date,[224,226,227] and interest in this area appears to have arisen largely from a single case report.[133] One report examined three equine conjunctival SCCs, as well as specimens from other affected regions and from normal horses.[227] In that study, all tissues, both nonneoplastic and SCC tissues, expressed both COX-1 and COX-2 proteins.[227] A second study found weak positive immunostaining of COX-2 expression in 6 of 22 ocular SCCs, and all positive samples were from corneal specimens.[224] A third immunohistochemical study examined 15 SCC-affected tissues (5 corneal, 5 eyelid, and 5 third eyelid) against site-matched controls and found immunoreactivity for both COX-1 and COX-2 to be significantly greater in affected equine corneas compared to control corneas, but no significant differences were detected in COX-1 or COX-2 reactivity in the eyelid or third eyelid SCC compared with site-matched controls.[226]

TREATMENT

Treatment for SCC is variable; commonly reported therapies are summarized in (Table 4-8) and described in more detail in the following paragraphs.

Immunotherapy

Historically, immunotherapy[203,208,228] for ocular SCC has not been employed as commonly as for equine sarcoids. Immunotherapy, when used, should be limited to SCC affecting the eyelid only to avoid globe injury. The most common immunotherapy for ocular SCC has been the injection of BCG, although other "vaccines" have been used.[203,208,228] The goal and treatment for eyelid SCC using BCG is identical to that described earlier for equine sarcoids.[141]

Chemotherapy

Intralesional cisplatin has been the most common type of chemotherapy used for treatment of ocular SCC.[178,229] Treatment

Table 4-8 | **Literature Review of Treatment for Ocular Squamous Cell Carcinoma in Horses**

MEDICAL THERAPY

TYPE OF THERAPY	DRUG	DOSE	NUMBER OF CASES	PERCENT OF NONRECURRENCE
Immunotherapy	BCG[228]	2 mL per cm^2 of tumor surface every 2-4 weeks	1	100%
	Noncommercial vaccine[203]	—	2	—
Chemotherapy	Cisplatin[177]	1 mg/cm^3 every 2 weeks for 4 treatments	7	71%

SURGICAL THERAPY FOR OCULAR SQUAMOUS CELL CARCINOMA

TYPE OF THERAPY	DESCRIPTION	NUMBER OF CASES	PERCENT OF NONRECURRENCE
Surgical excision[190]	Excision	18	56%
Cryotherapy[190]	Double or triple freeze/thaw to –25°C	6	33%
Cryotherapy[238]	Double or triple freeze/thaw to –25°C	5	100%
Cryotherapy[236]	Double or triple freeze/thaw to –25°C	3	67%
Hyperthermia[190]	Tissue temperatures between 41°C and 45°C	1	100%
Hyperthermia[189]	Tissue temperatures between 41°C and 45°C	8	75%
CO_2 laser ablation[233]	Ablate tissue	4	00%

BRACHYTHERAPY FOR OCULAR SQUAMOUS CELL CARCINOMA

RADIOISOTOPE	DOSE RANGE (cGY)	NUMBER OF CASES	PERCENT OF NONRECURRENCE
^{60}Cobalt or ^{137}Cesium[240]	5000	19	73.6%
^{198}Gold seeds[197]	7000	3	100%
^{192}Iridium pins[304]	7000	21	100%
^{222}Radon, ^{125}Iodine, ^{192}Iridium[207]	5000-10,000	10	80%
^{192}Iridium[190]	—	10	75%
^{192}Iridium[142]	6000	52	81.8%
^{90}Strontium[305]	25,000	27	89%
^{90}Strontium[207]	10,000	8	88%
^{90}Strontium[306]		24	76%
^{90}Strontium[190]	—	7	100%

with an oily emulsion of cisplatin for SCC is identical to that described earlier for equine sarcoids. Complete regression was observed in 5 of 7 (71%) SCCs, with a 1-year relapse-free rate of 65% (see Table 4-8).[177] Side effects or toxicity associated with the chemotherapy were deemed minimal.[177] Another study found no difference in outcome between tumors that were injected immediately after cytoreductive surgery versus those treated after the skin had healed, except in aggressive tumors that had cellular regrowth within the postoperative period.[178] Therefore, it was recommended that cisplatin treatment immediately follow surgery when tumor proliferation index is not known.[178]

Other chemotherapeutic agents for equine SCC include 5-FU, mitomycin C, and piroxicam. Use of topical 5-FU has also been successfully used on SCC of the external genitalia,[179] but there are no published reports of the use of 5-FU on ocular tissues with SCC. Recently, a study examining the effectiveness of mitomycin C as an adjunctive therapy to CO_2 laser ablation treatment of ocular SCC in eight horses reported a success rate of 70%, with follow-up times ranging from 11 to 24 months.[230] To the author's knowledge, mitomycin C use in the treatment of adnexal SCC has not been reported to date. A single case of successful treatment (i.e., no recurrence 5 years following therapy) of metastatic SCC (i.e., from the primary site at the lip to the submandibular lymph nodes) with oral piroxicam (80 mg orally every 24 hours) has been reported.[133] After 90 days of treatment, the primary and metastatic SCC had resolved. Several bouts of colic occurred, and the piroxicam was reduced to a maintenance dose of 80 mg orally every 48 hours indefinitely, without further gastrointestinal difficulties.[133] The usefulness of NSAIDs as inhibitors of cyclooxygenase in the treatment of periocular and ocular equine SCC is not known (see earlier discussion of cyclooxygenase and equine SCC).

Surgical Therapy

Surgical excision is almost always indicated to obtain definitive histologic diagnosis of any periocular/eyelid mass and to debulk total tumor size prior to administration of ancillary therapy. Surgical excision can be curative if the surgeon removes a 2-cm tumor-free margin on all sides of the mass. This degree of surgical margin is nearly impossible to achieve on any ocular or periocular SCC. Preservation of eyelid function is essential to ocular comfort and vision. Extensive blepharoplastic procedures, commonly used in canine patients affected by eyelid masses that involve greater than a third of the total eyelid margin, are fraught with complications in horses because of their facial anatomy. Equine facial skin is firmly attached to the underlying connective tissue and has poor superficial blood supply, so blepharoplastic procedures (i.e., advancement flaps, rhomboidal flaps) are rarely successful, and some portion of the flap will often necrose (Fig. 4-65).[4,231] Depending on the primary ophthalmic site of SCC, tumor-free margins can be obtained with enucleation/exenteration or complete excision of a third eyelid (for focal SCC affecting the leading edge of the nictitans). In most cases of equine eyelid, limbal, or corneal SCC, surgical excision using sharp dissection (i.e., debulking all grossly affected neoplastic tissue) and adjunctive therapy (e.g. chemotherapy, cryotherapy, hyperthermia, or radiation therapy) is recommended for optimal long-term prognosis.[209] CO_2 laser ablation has been reported for use on corneal/conjunctival SCC, but not with adnexal SCC (Fig. 4-66).[230,232,233] If used, the surgeon must be cautious to ensure that deep corneal penetration from laser does not occur by taking care to use the laser on a defocused setting. Corneal scarring or corneal perforation can occur with CO_2 laser ablation if the surgeon is not experienced with this modality. With extensive invasive SCC, partial orbital rim resection, mesh skin expansion, and second-intention healing can be used to close the large skin wounds.[234] In one study, surgical excision alone (without ancillary therapy) of the third eyelid had an SCC recurrence rate of 33% (6 of 14 cases), whereas 66% (2 of 3) of limbal SCCs recurred with surgical excision alone (see Table 4-8).[190]

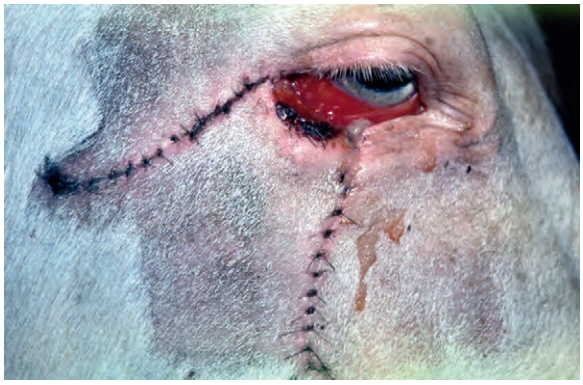


Figure 4-65. An "H-plasty" or advancement eyelid flap for reconstruction after excision of a lower-eyelid squamous cell carcinoma. The leading edge of the flap has become necrotic, which is common after blepharospastic procedures in the horse. (Photograph courtesy Dr. Mike Davidson.)

Cryotherapy

Cryotherapy is a commonly used surgical treatment for ocular SCC, usually following surgical debulking of the tumor.[183,187,190,203,235-237] The technique for use of cryotherapy for adnexal SCC is identical to what was described previously for sarcoids, using a double or triple freeze/thaw cycle (–25°C) with a rapid freeze and slow thaw (Fig. 4-67).[186] When treating eyelid SCC with cryotherapy (or sarcoids), care must be taken to protect the underlying cornea. Often, corneal protective devices are crudely fashioned using sections of a styrofoam cup and a liberal amount of sterile lubrication. Repeated treatments may be required for large or recurrent lesions.[187] In three small studies of ocular SCC treated with cryotherapy, 1 of 3 (33%),[236] 1 of 6 (17%),[190] and 0 of 5[238] cases had recurrence (see Table 4-8).

Hyperthermia

Hyperthermia has been used as an adjunctive therapy for equine sarcoids and bovine and equine SCC. It is recommended for eyelid, conjunctival, and limbal SCC, but not for SCC with deep penetration.[189] Temperatures between 41°C and 45°C will preferentially destroy neoplastic tissue but not normal cells.[186] Typically a radiofrequency hyperthermia device is placed against the tissue and heated to 50°C for 30 seconds. Minimal changes were seen on the normal equine eye from hyperthermia.[188] Several studies evaluating hyperthermia in the treatment of equine SCC have been published.[4,189,190,203] In one, ocular SCC in eight horses was treated by radiofrequency hyperthermia, resulting in 75% complete regression and 25% partial

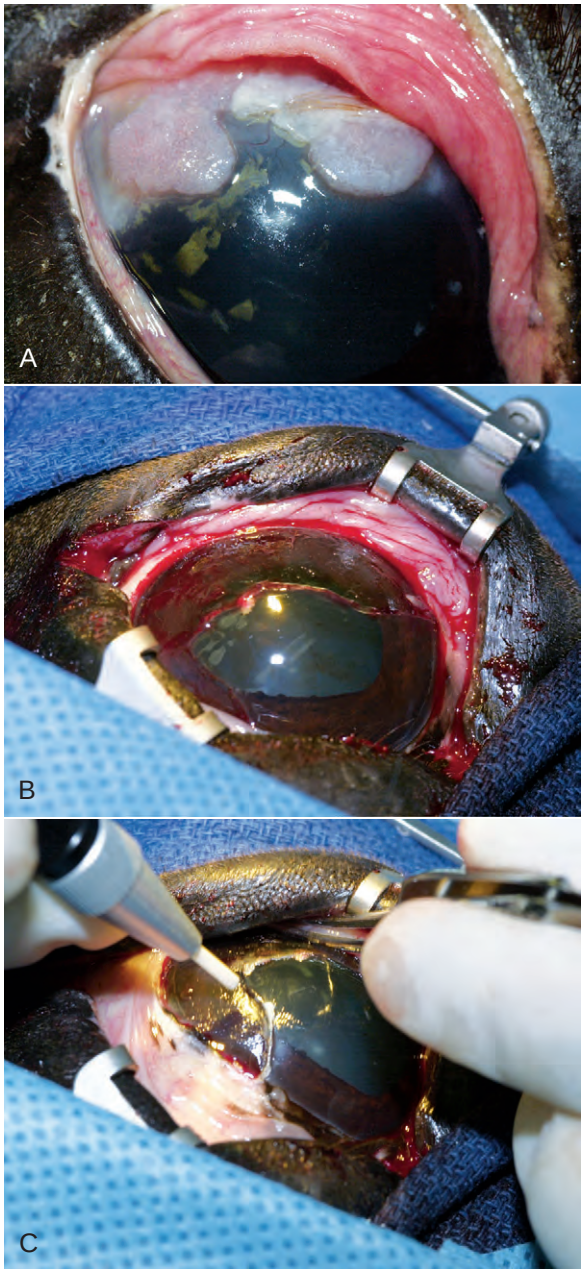


Figure 4-66. **A,** Extensive lateral corneal squamous cell carcinoma (SCC) that had extended from the lateral limbus. **B,** Superficial keratectomy has been performed to remove the corneal and limbal SCC. **C,** CO_2 laser ablation is being performed on the surgical bed to destroy remaining SCC cells.

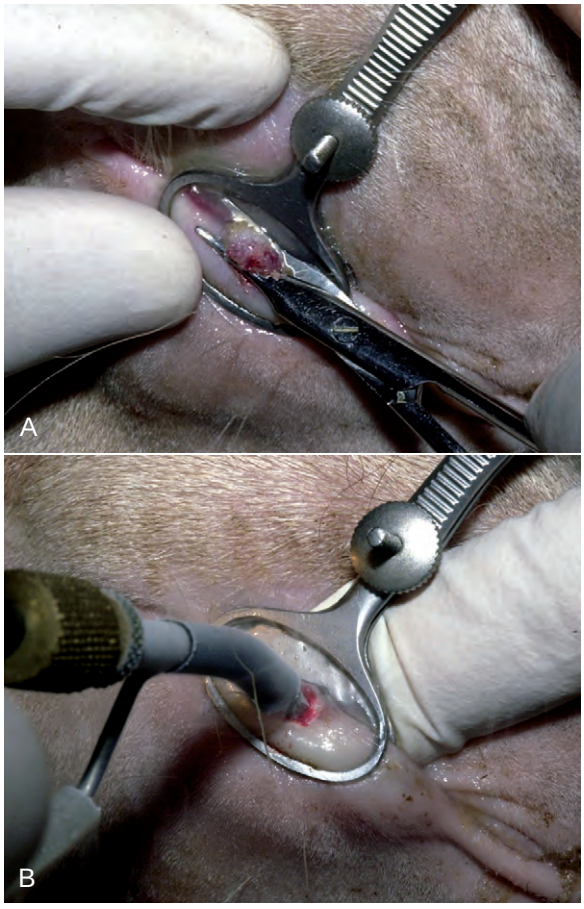


Figure 4-67. **A,** Surgical debulking of a papillomatous lower-eyelid squamous cell carcinoma using a chalazion clamp and Stevens tenotomy scissors. **B,** Following surgical debulking, the tumor bed is treated with cryotherapy (double freeze/thaw cycle).

regression. Complete regression occurred in 66% of tumors given a second hyperthermia treatment (see Table 4-8).[189]

Brachytherapy

Brachytherapy uses small gamma radioactive sources that are placed on or within neoplasms, allowing a high dose of radiation to be delivered to the tissue and minimal radiation to surrounding tissues (see Fig. 4-58).[186,239] Brachytherapy is recommended for eyelid and conjunctival SCC, but not for limbal or orbital SCC. The type of radioactive sources, surgical technique, and complications of brachytherapy for use with ocular SCC are identical to that described earlier for sarcoids.[142,192,197,207,240-242] Brachytherapy has been successful and often has some of the highest nonrecurrence rates of any ancillary therapy for equine ocular SCC (see Table 4-8). However, the high cost, limited availability, licensure issues, and human radiation exposure risks make this mode of therapy less desirable or not a viable option in many cases.

Photodynamic Therapy

Photodynamic therapy (PDT) is an evolving modality for the treatment of a variety of ailments, including solid tumors, age-related macular degeneration, and atherosclerotic plaques.[243-245] PDT involves the use of photochemical reactions mediated through the interaction of photosensitizing agents, light, and oxygen.[246] Selective uptake and retention of a photosensitizer by the target cells and microvascular endothelial cells, followed by irradiation with light of a specific wavelength, initiates necrosis and apoptosis of the target cells, vascular shutdown, and inflammation through formation of toxic singlet oxygen and free radicals.[246] Tumor selectivity in treatment occurs through a combination of selective retention of the photoactive chemical by neoplastic cells and delivery of light to a highly specific area.[246]

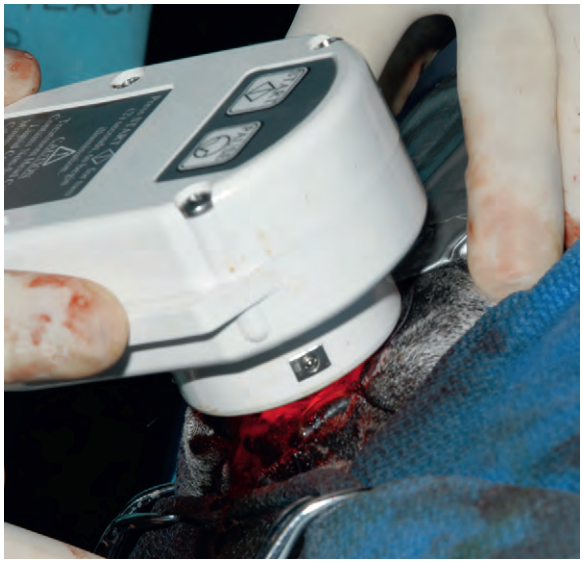


Figure 4-68. Horse with medial lower-eyelid squamous cell carcinoma treated with surgical debulking and local photodynamic therapy. The photosensitizing agent has been injected and is now being activated by a light-emitting diode (LED) delivering red light at a wavelength of approximately 690 nm.

Photosensitizers are typically administered to the patient by intravenous injection. However, intravenous injection of a photoactive drug to a horse is not deemed feasible at this time. Recent studies have investigated the use of local PDT in the treatment of equine periocular tumors in both clinical patients and a murine model.[206,247-250] In these ongoing clinical investigations, a photoactive agent is injected locally into the wound bed immediately after surgical resection of the tumor and followed by light irradiation. Preliminary results have been favorable, and a total of 28 spontaneously occurring equine eyelid neoplasms have been treated (20 SCC,[206,251] 7 sarcoids, and 1 melanoma[252]) with surgical resection and local PDT (Giuliano et al., unpublished data) (Fig. 4-68). However, more research is needed before PDT can be adequately compared to other more established treatment modalities for equine periocular tumors.

LONG-TERM PROGNOSIS

Recurrence rates within a year of treatment have been reported between 50% and 66.7% with surgery alone, and range from 25% to 67% with surgery and ancillary irradiation or cryotherapy.[190,239] A 42.4% recurrence rate for ocular SCC with surgical excision, radiofrequency hyperthermia, or both has also been reported.[6] In another study, treatments included surgical excision, surgical excision with strontium-90 beta irradiation, surgical excision with cryotherapy, surgical excision with radiofrequency, surgical excision with cesium-137 interstitial radiotherapy, and/or immunotherapy. The overall recurrence rate was 30.4%.[203] Poorer prognosis is associated with SCC originating at the eyelid compared to the third eyelid, nasal canthus, or limbus in one study.[203] Larger-sized masses, orbital extension, and recurrent SCC were associated with lower survival times.[203] Metastasis of ocular SCC to local lymph nodes, salivary glands, and lungs can occur. Metastasis of ocular SCC is uncommon and was observed in a case report,[205] 6% of cases in one study,[6] and 15.4% in another.[204] Metastasis occurs most commonly to the regional (submandibular) lymph nodes, salivary glands, thorax, or extension into the orbit, sinus, and calvarium. Local invasion of the tumor often accompanies ulcerative necrosis and inflammation, resulting in significant ocular discomfort. No single treatment modality has proven to be effective, and either the SCC itself or treatment complications may threaten both visual outcome and long-term survival.

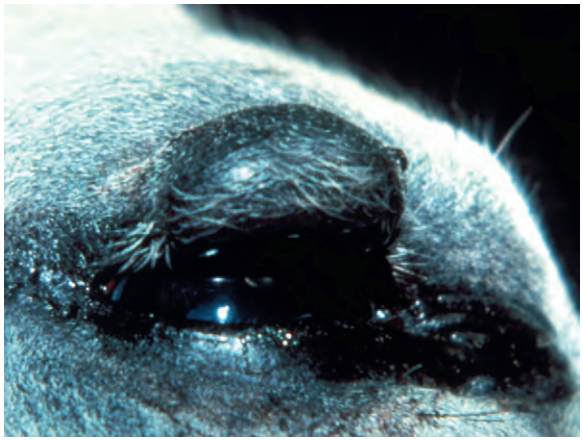


Figure 4-69. Large upper-eyelid melanoma. (Photograph courtesy Dr. Mike Davidson.)

MELANOMA

Melanoma is a relatively uncommon tumor of the horse, involving between 3.8% and 4.8% of total neoplasms.[130-132] In one study reviewing 84 melanomas in horses, the most common sites of occurrence were under the tail (93.9%), the perianal region (43.0%), the lips (33.0%), and the eyelids (24.0%).[253] Melanoma is most common in horses with grey or white hair.[4,208] A slowly progressive, cutaneous, partially alopecic, pigmented mass of the eyelids is the typical clinical appearance of most equine adnexal melanoma (Fig. 4-69). The size and location of the mass will dictate the clinical signs, varying from no ocular irritation to blepharospasm and corneal irritation. Older horses are predisposed to the development of melanoma, possibly because proliferation of melanocytes is a manifestation of aging.[208,254] Fleury et al.[255] found that melanoma development, size of mass, and number of masses were significantly correlated with older Camargue-type gray-skinned horses (a prevalence of 67% at ages >15 years). Development of melanoma was not associated with gender or sun exposure.[255] In a study of 296 grey Lipizzaner horses, dermal melanomas were present in 148 horses (50%), with higher incidence in older horses.[256] A genetic predisposition for dermal melanoma was also suggested.[256] A malignant conjunctival melanoma of a horse has been described.[257]

COMMON DIFFERENTIAL DIAGNOSIS AND METHODS FOR DEFINITIVE DIAGNOSIS

Differential diagnosis for adnexal melanoma includes all other causes of eyelid tumors or swelling such as sarcoid, habronemiasis, SCC, papilloma, lymphosarcoma, and orbital fat prolapse. Biopsy and histopathology are recommended for definitive diagnosis.

Equine melanomas have highly variable histologic and cytologic patterns that can make definitive diagnosis difficult. Four distinct clinical syndromes of dermal melanomas have been

described in horses: melanocytic nevus, dermal melanoma, dermal melanomatosis, and anaplastic malignant melanoma.[258] Epithelioid, round, and spindle cellular morphology occur in equine melanomas with variable and inconsistent tumor pigmentation. The site of the tumor, the depth of invasion, and the number of mitotic figures per high-power field are used histologically to predict biological behavior. However, in one study, histologic characteristics of dermal melanomas were not predictive of malignancy in most horses.[259] Special stains may help confirm the diagnosis. Melanoma cells are usually positive for vimentin, S100, neuron-specific enolase, and melan-A, and negative for cytokeratin.[260] Currently, there is no single definitive diagnostic test capable of differentiating between benign and malignant melanocytic neoplasms or that would serve as a predictor for survival time. In one study, most metastatic melanomas showed overexpression of p53 and demonstrated apoptosis, but no differences were observed between malignant and benign dermal melanomas in growth fraction, S-phase index, or in DNA configuration.[261] It was concluded that equine melanomas had substantially different phenotypic characteristics in comparison with melanocytic tumors in dogs, cats, and humans.[261]

TREATMENT

There are few reports of the treatment of equine adnexal melanomas, so success rates of various treatments are not known. Prior to initiating therapy, careful evaluation of the entire horse is recommended to rule out metastatic disease. Examination of affected horses should include a thorough skin evaluation, with particular attention to the area under the tail and perianal area, oral inspection, chest radiography and/or ultrasonography, and rectal palpation. There are no known studies on the effectiveness of intralesional chemotherapy or immunotherapy on melanomas. Oral cimetidine (dose 2.5 mg/kg of body weight orally every 8 hours) has been used to shrink non-ocular melanomas in horses,[262] but no studies have been published on this treatment modality for adnexal melanomas. Surgical excision, CO_2 laser ablation, and cryotherapy have been recommended. Success rates have not been published, but one study described the successful removal of a non-ocular dermal melanoma in a horse by CO_2 laser ablation.[263] Surgical resection and local photodynamic therapy for a lower-eyelid melanoma has also been performed,[252] resulting in a disease-free interval of 5 years. Excision of an eyelid melanoma is usually curative, because most of the masses are benign. However, a case report of a conjunctival melanoma described recurrence and metastasis.[257]

LONG-TERM PROGNOSIS

Malignant melanoma occurs in horses,* but the overall rate of malignancy is unknown. In one study, the most common sites for metastases were the lymph nodes, liver, spleen, skeletal muscle, lungs, and vascular beds.[259] Horses may have dermal melanomas for years (range 1 to 6 years) before developing metastatic disease.[259]

LYMPHOSARCOMA

Lymphosarcoma (LSA) is a relatively uncommon neoplasm in the horse, especially when compared to other domestic animals such as cows, dogs, and cats. Isolated case reports of equine adnexal LSA have been published,[267-269] and LSA represented 1.3% and 4.8% of all tumors in the horse in two separate studies.[130,131] Unilateral and bilateral ocular lesions have been reported with equine LSA.[215,216,270,271]

COMMON DIFFERENTIAL DIAGNOSIS AND METHODS FOR DEFINITIVE DIAGNOSIS

Ocular lesions occurred in 27% of horses with systemic LSA in one study.[215] Infiltration of the eyelids and conjunctiva is the most common ocular manifestation of LSA (Fig. 4-70).[215,270,271] Orbital and/or third eyelid involvement can also occur (Fig. 4-71).[215,269,271] Adnexal LSA must be differentiated from other causes of eyelid tumors or swelling such as sarcoid, habronemiasis, SCC, papilloma, melanoma, and orbital fat prolapse. Biopsy and histopathology are required for definitive diagnosis.

PATHOGENESIS OF DISEASE PROCESS AND PROGRESSION

Immunohistochemical classification of equine malignant LSA has been reported in one study and revealed that equine LSA was composed of a heterogeneous cell population, with most tumors containing B and T lymphocytes.[272] In this study, 42% of tumors contained primarily neoplastic B lymphocytes, 35% had diffuse large B-cell lymphoma with 40% to

Figure 4-70. Inferotemporal eyelid and conjunctival lymphosarcoma (LSA).

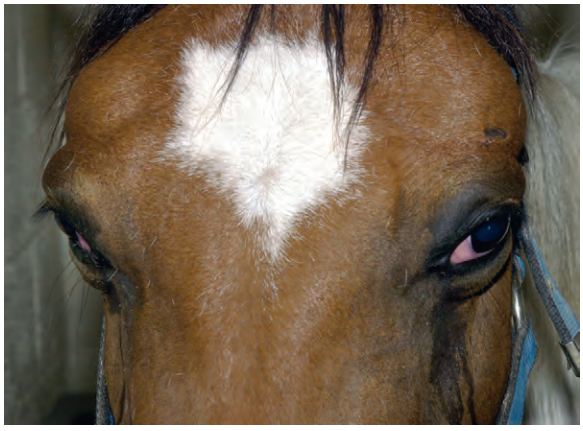


Figure 4-71. Yearling paint horse with systemic lymphosarcoma with ocular and orbital invasion.

*References 90, 91, 253, 256, 257, 259-261, and 264-266.

80% non-neoplastic T lymphocytes (called *T-cell-rich, large B-cell lymphomas*), and 19% had primarily neoplastic T lymphocytes.[272]

TREATMENT

Treatment for horses affected with adnexal manifestations of LSA are limited. In one report with bilateral eyelid involvement, treatment with oral prednisolone (400 mg orally once daily) had no effect, but intramuscular injection of dexamethasone (30 mg every other day) resulted in marked reduction of eyelid swelling attributed to LSA during the limited time the horse received follow-up examinations.[270] In a second case report of primary bilateral third eyelid LSA, the horse underwent complete third eyelid removal and remained disease free for 3 years.[269] Localized eyelid lesions treated with surgical debulking and intralesional corticosteroids may be successful in some cases (Dr. D. Wilkie, personal communication). Further study is needed.

LONG-TERM PROGNOSIS

In general, the long-term prognosis for survival is poor for horses with LSA due to multicentric or disseminated disease.[4]

CONJUNCTIVAL PSEUDOTUMORS OR BILATERAL NODULAR LYMPHOCYTIC CONJUNCTIVITIS

Conjunctival pseudotumors or nodular lymphocytic conjunctivitis (NLC) appears as unilateral or bilateral, nodular or smooth, pink, nonulcerated conjunctival mass (Fig. 4-72).[273,274] In one study of five horses, the masses were nodular in two cases and relatively flat and more diffuse in three cases.[274] The third eyelid was involved in three cases and bulbar conjunctival and cornea in two cases.[274]

COMMON DIFFERENTIAL DIAGNOSIS AND METHODS FOR DEFINITIVE DIAGNOSIS

Conjunctival pseudotumors must be differentiated from other causes of eyelid masses or swelling such as sarcoid, habronemiasis, neoplasia (e.g., squamous cell carcinoma, papilloma, or melanoma), and orbital fat prolapse. Biopsy and histopathology are required for definitive diagnosis. Histopathologically, these lesions are characterized by nodular lymphoid components and presence of lymphocytes, plasma cells, and histiocytes.[273] The bulbar conjunctiva may be infiltrated by small nodular masses composed of dense aggregates of primarily small, mature lymphocytes admixed with less mature, usually intermediate-sized, lymphoblasts, histiocytes, and rare neutrophils. The cellular infiltrate can form follicles of lymphocytic hyperplasia. Etiologic agents should be ruled out using special stains.[273,274] Immunohistochemical characterization of lesions in one report detected B and T lymphocytes, macrophages, and other histiocytes.[273]

PATHOGENESIS OF DISEASE PROCESS AND PROGRESSION

Equine conjunctival inflammatory pseudotumor is suspected to have an immune-mediated pathogenesis based on the characterization of inflammatory cell infiltrate and the absence of infectious agents (bacterial, fungal, or parasitic) or foreign bodies.[273,274]

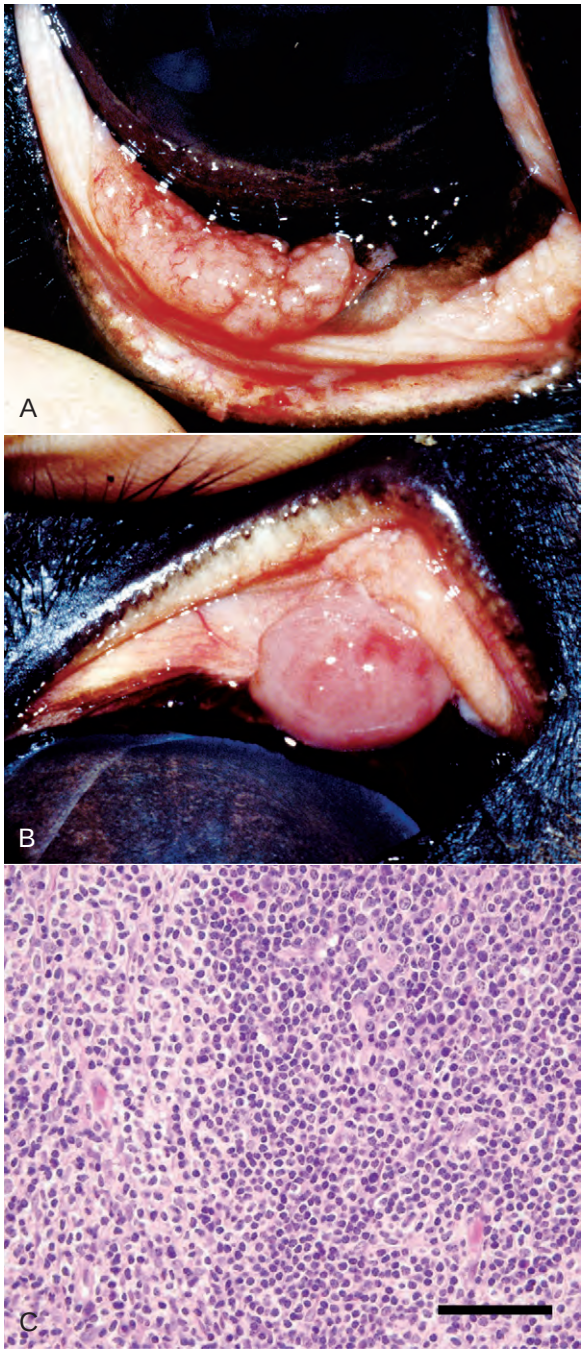


Figure 4-72. **A,** Conjunctival proliferative lobulated mass at the basal portion of the third eyelid diagnosed after histopathology as a nodular lymphocytic conjunctivitis or conjunctival pseudotumor. **B,** Another proliferative conjunctival mass located at the dorsal limbus, also confirmed on histopathology as nodular lymphocytic conjunctivitis or conjunctival pseudotumor. **C,** Histologically, both masses had similar findings of a heterogeneous population of mononuclear cells with predominantly small mature lymphocytes on the right half of the field and larger histiocytes on the left half (bar = 50 mm). (Photographs courtesy Dr. Riccardo Stoppini.)

TREATMENT

Surgical debulking and local administration of antiinflammatory agents (i.e., intralesional corticosteroids +/– topical corticosteroids) are the mainstays of therapy.[273,274]

LONG-TERM PROGNOSIS

The prognosis for equine conjunctival pseudotumors appears to be good when lesions are treated as described earlier.[274] Rapid recurrence is possible, requiring repeated treatment.[273]

OTHER ADNEXAL NEOPLASMS

Various other equine adnexal and/or conjunctival tumors have been reported, including angiomas, angiosarcomas, hemangiosarcoma,[275-280] fibroma, fibrosarcoma,[198,281] adenoma, adenocarcinoma,[282] lacrimal gland carcinoma,[130] basal cell carcinoma,[283] and mast cell tumors.[202] Similar to other mass lesions of the eyelid or conjunctiva, histopathology is required for definitive diagnosis and to rule out all previously discussed mass lesions affecting this region of the equine eye. Immunohistochemical staining can be helpful to further characterize a tumor, such as staining with factor VIII–related antigen to confirm whether or not the mass has a vascular endothelial origin (e.g., angiomas, angiosarcomas, hemangiosarcoma).[278,284] Vascular neoplasms must be differentiated from intravascular papillary endothelial hyperplasia, a benign proliferative lesion.[285] Treatment varies depending on the neoplasm, but excision with an adjunctive therapy such as cryotherapy is generally recommended.

FUTURE RESEARCH FOR EYELID, CONJUNCTIVAL, AND NASOLACRIMAL DISEASES IN HORSES

Additional research is warranted for a wide variety of diseases affecting the equine eyelid, conjunctiva, and nasolacrimal system. For example, very little is known regarding the specific genetic defect and mode of inheritance for many equine adnexal diseases, especially entropion and nasolacrimal duct atresia. Pharmacokinetic and ocular distribution of most systemically administered antibiotics have yet to be determined for horses. Enhanced imaging techniques represent an exciting new area of potential development in the diagnosis and treatment of many equine ocular diseases. Finally, well-designed, prospective clinical trials with adequate case numbers and appropriate case follow-up are lacking for equine adnexal neoplastic disease. The further study of equine ocular adnexal and nasolacrimal disease will only improve our ability to better restore and preserve ocular comfort and vision.

Acknowledgment

The author acknowledges and appreciates the work of Drs. Brian C. Gilger and Riccardo Stoppini, who co-authored this chapter in the previous edition. The author wishes to thank past ophthalmology residents of the University of Missouri College of Veterinary Medicine (Drs. Marnie Ford, Gia Klauss, Jacqueline Pearce, and Juri Ota) for assisting with photographic documentation of our clinical cases presented to the teaching hospital, and Mr. Howard Wilson for technical assistance.

References

1. Duke-Elder S, Wybar K: The eyelids. Systems of ophthalmology Vol 2, the anatomy of the visual system, London, 1961, Henry Kimpton, pp 499–540.
2. Moore CP: Eyelid and nasolacrimal disease, Vet Clin North Am Equine Pract 8:499–519, 1992.
3. Samuelson D: Ophthalmic anatomy. In Gelatt KN, editor: Veterinary ophthalmology, ed 4, Ames, Iowa, 2007, Blackwell, pp 37–148.
4. Lavach JD: Large animal ophthalmology, St. Louis, 1990, The CV Mosby Company.
5. Rajesh R, Bhardwaj RL, Virender P: Structure of the eyelids of the hill horse, Centaur 24:50–52, 2008.
6. Schwink K: Factors influencing morbidity and outcome of equine ocular squamous cell carcinoma, Equine Vet J 19:198–200, 1987.
7. Firth EC: Horner's Syndrome in the horse: experimental induction and a case report, Equine Vet J 10:9–13, 1978.
8. Simoens P, Lauwers H, De Muelenare C, et al: Horner's syndrome in the horse: a clinical, experimental and morphological study, Equine Vet J Suppl 1990:62–65.
9. Hahn CN: Miscellaneous disorders of the equine nervous system: Horner's syndrome and polyneuritis equi, Clin Tech Equine Pract 5:43–48, 2006.
10. Wyman M, Anderson BG: Anatomy of the equine eye and orbit: gross anatomy of the lids, J Small Anim Pract 2:307–311, 1978.
11. Bhardwaj RL, Rajesh R, Virender P: Histological studies on the third eyelid of horse, Centaur 24:53–55, 2008.
12. Anderson B, Wyman M: Anatomy of the equine eye and orbit: histological structure and blood supply of the eyelids, J Equine Med Surg 3:4–14, 1979.
13. Bourges-Abella N, Raymond-Letron I, Diquelou A, et al: Comparison of cytologic and histologic evaluations of the conjunctiva in the normal equine eye, Vet Ophthalmol 10:12–18, 2007.
14. Giuliano EA, Moore CP, Phillips TE: Morphological evidence of M cells in healthy canine conjunctiva-associated lymphoid tissue, Graefes Arch Clin Exp Ophthalmol 240:220–226, 2002.
15. Knop N, Knop E: Ultrastructural anatomy of CALT follicles in the rabbit reveals characteristics of M-cells, germinal centres and high endothelial venules, J Anat 207:409–426, 2005.
16. Fix AS, Arp LH: Quantification of particle uptake by conjunctiva-associated lymphoid tissue (CALT) in chickens, Avian Dis 35:174–179, 1991.
17. Fix AS, Arp LH: Conjunctiva-associated lymphoid tissue (CALT) in normal and Bordetella avium-infected turkeys, Vet Pathol 26:222–230, 1989.
18. Williams RD, Manning JP, Peiffer RL, Jr: The Schirmer tear test in the equine: normal values and the contribution of the gland of the nictitating membrane, J Equine Med Surg 3:117–119, 1979.
19. Joyce J, Bratton G: Keratoconjunctivitis sicca secondary to fracture of the mandible, Vet Med 68:619–620, 1973.
20. Speiss B, Wilcock B, Phyick-Sheard P: Eosinophilic granulomatous dacryadenitis causing bilateral keratoconjunctivitis sicca in a horse, Equine Vet J 21:226–228, 1989.
21. Spurlock SL, Spurlock GH, Wise M: Keratoconjunctivitis sicca associated with fracture of the stylohyoid bone in a horse, J Am Vet Med Assoc 194:258–259, 1989.
22. Schwarz BC, Sallmutter T, Nell B: Keratoconjunctivitis sicca attributable to parasympathetic facial nerve dysfunction associated with hypothyroidism in a horse, J Am Vet Med Assoc 233:1761–1766, 2008.
23. Freestone JF, Seahorn TL: Miscellaneous conditions of the equine head, Vet Clin North Am Equine Pract 9:235–242, 1993.
24. Cassotis NJ, Schiffman P: Calcification associated with the nasolacrimal system of a horse: case report and mineralogic composition, Vet Ophthalmol 9:187–190, 2006.

25. Latimer CA, Wyman M, Diesem CD, et al: Radiographic and gross anatomy of the nasolacrimal duct of the horse, Am J Vet Res 45:451–458, 1984.
26. USDA: Equine morbidity and mortality: national health monitoring system, USDA:APHIS 1–2, 1998.
27. Latimer CA, Wyman M: Neonatal ophthalmology, Vet Clin North Am Equine Pract 1:235–259, 1985.
28. Turner AG: Ocular conditions of neonatal foals, Vet Clin North Am Equine Pract 20:429–440, vii–viii, 2004.
29. Barnett K: The eye of the newborn foal, J Reprod Fertil Suppl 23:701–703, 1975.
30. Sironi G, Riccaboni P, Mertel L, et al: p53 protein expression in conjunctival squamous cell carcinomas of domestic animals, Vet Ophthalmol 2:227–231, 1999.
31. Plummer CE: Equine eyelid disease, Clin Tech Equine Pract 4:95–105, 2005.
32. Fox L, Thurmon J: Bilateral ankyloblepharon in a newborn foal, Vet Med Sm Anim Clin 63:237–238, 1969.
33. Grant B, Slatter DH, Dunlap JS: *Thelazia* sp. (Nematoda) and dermoid cysts in a horse with torticollis, Vet Med Small Anim Clin 68:62–64, 1973.
34. Priester WA: Congenital ocular defects in cattle, horses, cats, and dogs, J Am Vet Med Assoc 160:1504–1511, 1972.
35. Baumgartner WA, Storey ES, Paulsen DB: Bilateral intraocular glandular choristomas in a Thoroughbred foal, Vet Ophthalmol 12:106–114, 2009.
36. Mason TA: Atresia of the nasolacrimal orifice in two thoroughbreds, Equine Vet J 11:19–20, 1979.
37. Lundvall R, Carter J: Atresia of the nasolacrimal meatus in the horse, J Am Vet Med Assoc 159:289–291, 1971.
38. Theoret CL, Grahn BH, Fretz PB: Incomplete nasomaxillary dysplasia in a foal, Can Vet J 38:445–447, 1997.
39. Latimer CA, Wyman M: Atresia of the nasolacrimal duct in three horses, J Am Vet Med Assoc 184:989–992, 1984.
40. Brooks DE, Matthews AG: Equine ophthalmology. In Gelatt KN, editor: veterinary ophthalmology, ed 4, Ames, Iowa, 2007, Blackwell, pp 1165–1274.
41. Bertone JJ, Horspool LJI: Equine clinical pharmacology, Philadelphia, 2004, Elsevier.
42. Moore CP: Ocular therapeutics, Vet Clin North Am Small Anim Pract 34:XI–XII, 2004.
43. McLaughlin SA, Brightman AH, Helper LC, et al: Pathogenic bacteria and fungi associated with extraocular disease in the horse, J Am Vet Med Assoc 182:241–242, 1983.
44. Moore C, Heller N, Majors L, et al: Prevalence of ocular microorganisms in hospitalized and stabled horses, Am J Vet Res 49:773–777, 1988.
45. Collins LG, Tyler DE: Experimentally induced phenylbutazone toxicosis in ponies: description of the syndrome and its prevention with synthetic prostaglandin E2, Am J Vet Res 46:1605–1615, 1985.
46. Gunson DE: Renal papillary necrosis in horses, J Am Vet Med Assoc 182:263–266, 1983.
47. Gunson DE, Soma LR: Renal papillary necrosis in horses after phenylbutazone and water deprivation, Vet Pathol 20:603–610, 1983.
48. Giuliano EA: Nonsteroidal anti-inflammatory drugs in veterinary ophthalmology, Vet Clin North Am Small Anim Pract 34:707–723, 2004.
49. Schoster JV: The assembly and placement of ocular lavage systems in horses, Veterinary Medicine 87:460–471, 1992.
50. Giuliano EA, Maggs DJ, Moore CP, et al: Inferomedial placement of a single-entry subpalpebral lavage tube for treatment of equine eye disease, Vet Ophthalmol 3:153–156, 2000.
51. Schaer BD: Ophthalmic emergencies in horses, Vet Clin North Am Equine Pract 23:49–65, 2007.
52. Robertson SA: Standing sedation and pain management for ophthalmic patients, Vet Clin North Am Equine Pract 20:485–497, 2004.
53. Schoster J: Surgical repair of equine eyelid lacerations, Vet Med 83:1042–1049, 1988.
54. Rebhun WC: Repair of eyelid lacerations in horses, Vet Med Small Anim Clin 75:1281–1284, 1980.
55. Boulton CB, Campbell K: Equine recurrent blepharitis and ulcerative keratitis, Vet Med Sm Anim Clin 1057–1058, 1982.
56. Hughes DE, Pugh GW, Jr: Isolation and description of a *Moraxella* from horses with conjunctivitis, Am J Vet Res 31:457–462, 1970.
57. Evans K, Smith M, McDonough P, et al: Eye infections due to *Listeria monocytogenes* in three cows and one horse, J Vet Diagn Invest 16:464–469, 2004.
58. Connole M: Equine phycomycosis, Aust Vet J 49:1973.
59. Singh T: Studies on epizootic lymphangitis, Indian J Vet Sci 36:1966.
60. Rebhun WC, Mirro EJ, Georgi ME, et al: Habronemic blepharoconjunctivitis in horses, J Am Vet Med Assoc 179:469–472, 1981.
61. Moore CP, Sarazan R, Whitley RD: Equine ocular parasites: a review, Eq Vet J (Suppl) 2:76–85, 1983.
62. Lyons ET, Swerczek TW, Tolliver SC, et al: Prevalence of selected species of internal parasites in equids at necropsy in central Kentucky (1995–1999), Vet Parasitol 92:51–62, 2000.
63. Desch CE, Jr, Nutting WB: Redescription of *Demodex caballi* (= *D. folliculorum* var. equi Railliet, 1895) from the horse, *Equus caballus*, Acarologia 20:235–240, 1979.
64. Glaze MB: Equine adnexal habronemiasis, Equine Vet J Suppl 2:71–76, 1983.
65. Joyce JR, Hanselka DW, Boyd CL: Treatment of habronemiasis of the adnexa of the equine eye, Vet Med Sm Anim Clin 1008–1009, 1972.
66. Patton S, McCracken MD: The occurrence and effect of *Thelazia* in horses, Equine Pract 3:53, 1981.
67. Vasey JR: Equine cutaneous habronemiasis, Comp Cont Ed 3:290–298, 1981.
68. Ramsey DT, Whiteley HE, Gerding PA, Jr, et al: Eosinophilic keratoconjunctivitis in a horse, J Am Vet Med Assoc 205:1308–1311, 1994.
69. Yamagata M, Wilkie DA, Gilger BC: Eosinophilic keratoconjunctivitis in seven horses, J Am Vet Med Assoc 209:1283–1286, 1996.
70. Hum S, Bowers JR: Ocular mastocytosis in a horse, Aust Vet J 66:32, 1989.
71. Dugan SJ, Curtis CR, Roberts SM, et al: Epidemiologic study of ocular/adnexal squamous cell carcinoma in horses, J Am Vet Med Assoc 198:251–256, 1991.
72. Pusterla N, Watson JL, Wilson WD, et al: Cutaneous and ocular habronemiasis in horses: 63 cases (1988–2002), J Am Vet Med Assoc 222:978–982, 2003.
73. Herd RP, Donham JC: Efficacy of ivermectin against cutaneous *Draschia* and *Habronema* infection (summer sores) in horses, Am J Vet Res 42:1953–1955, 1981.
74. Miller W: Aberrant cilia as an aetiology for recurrent corneal ulcers: a case report, Equine Vet J 20:145–146, 1988.
75. Vestre WA, Brightman AH: Correction of cicatricial entropion and trichiasis in the horse, Equine Pract 2:13–16, 1980.
76. Wilkinson JD: Distichiasis in the horse treated by partial tarsal plate excision, Vet Rec 94:128–129, 1974.
77. Hurn S, Turner A, Mc Cowan C: Ectopic cilium in seven horses, Vet Ophthalmol 8:199–202, 2005.
78. Rebhun W, Georgi M, Georgi J: Persistent corneal ulcers in horses caused by embedded burdock pappus bristles, Vet Med 86:930–935, 1991.
79. Hamor RE, Whelan NC: Equine infectious keratitis, Vet Clin North Am Equine Pract 15:623–646, 1999.
80. Kershaw O, von Oppen T, Glitz F, et al: Detection of equine herpesvirus type 2 (EHV-2) in horses with keratoconjunctivitis, Virus Res 80:93–99, 2001.
81. Andrew SE, Brooks DE, Smith PJ, et al: Equine ulcerative keratomycosis: visual outcome and ocular survival in 39 cases (1987–1996), Equine Vet J 30:109–116, 1998.
82. Gratzek AT, Kaswan RL, Martin CL, et al: Ophthalmic cyclosporine in equine keratitis and keratouveitis: 11 cases, Equine Vet J 27:327–333, 1995.
83. McLellan GL, Archer FJ: Corneal stromal sequestration and keratoconjunctivitis sicca in a horse, Vet Ophthalmol 3:207–212, 2000.
84. Moore CP, Halenda RM, Grevan VL, et al: Post traumatic keratouveitis in horses, Equine Vet J 30:366–372, 1998.
85. Giuliano EA, Moore CP: Eyes and ocular adnexa. In Cowell RL,Tyler RD, editors: Diagnostic cytology and hematology of the horse, ed 2, St. Louis, Missouri, 2002, Mosby, Inc., pp 43–64.
86. Barsotti G, Sgorbini M, Nardoni S, et al: Occurrence of fungi from conjunctiva of healthy horses in Tuscany, Italy, Vet Res Commun 30:903–906, 2006.
87. Borchers K, Ebert M, Fetsch A, et al: Prevalence of equine herpesvirus type 2 (EHV-2) DNA in ocular swabs and its cell tropism in equine conjunctiva, Vet Microbiol 118:260–266, 2006.
88. Nardoni S, Sgorbini M, Barsotti G, et al: Conjunctival fungal flora in healthy donkeys, Vet Ophthalmol 10:207–210, 2007.
89. Sgorbini M, Barsotti G, Nardoni S, et al: Fungal flora of normal eyes in healthy newborn foals living in the same stud farm in Italy, J Equine Vet Sci 28:540–543, 2008.

90. Milne JC: Malignant melanomas causing Horner's syndrome in a horse, Equine Vet J 18:74–75, 1986.
91. Murray MJ, Cavey DM, Feldman BF, et al: Signs of sympathetic denervation associated with a thoracic melanoma in a horse, J Vet Intern Med 11:199–203, 1997.
92. Bacon CL, Davidson HJ, Yvorchuk K, et al: Bilateral Horner's syndrome secondary to metastatic squamous cell carcinoma in a horse, Equine Vet J 28:500–503, 1996.
93. Sweeney RW, Sweeney CR: Transient Horner's syndrome following routine intravenous injections in two horses, J Am Vet Med Assoc 185:802–803, 1984.
94. Purohit RC, McCoy MD, Bergfeld WA, 3rd: Thermographic diagnosis of Horner's syndrome in the horse, Am J Vet Res 41:1180–1182, 1980.
95. Craig DR, Shivy DR, Pankowski RL, et al: Esophageal disorders in 61 horses. Results of nonsurgical and surgical management, Vet Surg 18:432–438, 1989.
96. Skarda RT, Muir WW, Couri D: Plasma lidocaine concentrations in conscious horses after cervicothoracic (stellate) ganglion block with 1% lidocaine HCl solution, Am J Vet Res 48:1092–1097, 1987.
97. Skarda RT, Muir WW, Swanson CR, et al: Cervicothoracic (stellate) ganglion block in conscious horses, Am J Vet Res 47:21–26, 1986.
98. Morgan RV, Zanotti SW: Horner's syndrome in dogs and cats: 49 cases (1980–1986), J Am Vet Med Assoc 194:1096–1099, 1989.
99. Bistner S, Rubin L, Cox TA, et al: Pharmacologic diagnosis of Horner's syndrome in the dog, J Am Vet Med Assoc 157:1220–1224, 1970.
100. Tyler CM, Davis RE, Begg AP, et al: A survey of neurological diseases in horses, Aust Vet J 70:445–449, 1993.
101. Yadernuk LM: Temporohyoid osteoarthropathy and unilateral facial nerve paralysis in a horse, Can Vet J 44:990–992, 2003.
102. Waldridge BM, Holland M, Taintor J: What is your neurologic diagnosis? Stylohyoid bone fracture and possible petrous temporal bone fracture, J Am Vet Med Assoc 222:587–589, 2003.
103. Grandy JL, Steffey EP, Hodgson DS, et al: Arterial hypotension and the development of postanesthetic myopathy in halothane-anesthetized horses, Am J Vet Res 48:192–197, 1987.
104. MacKay RJ, Granstrom DE, Saville WJ, et al: Equine protozoal myeloencephalitis, Vet Clin North Am Equine Pract 16:405–425, 2000.
105. Gray LC, Magdesian KG, Sturges BK, et al: Suspected protozoal myeloencephalitis in a two-month-old colt, Vet Rec 149:269–273, 2001.
106. Furr M, MacKay R, Granstrom D, et al: Clinical diagnosis of equine protozoal myeloencephalitis (EPM), J Vet Intern Med 16:618–621, 2002.
107. Lavach JD, Severin GA: Neoplasia of the equine eye, adnexa, and orbit: a review of 68 cases, J Am Vet Med Assoc 170:202–203, 1977.
108. Rebhun WC: Tumors of the eye and ocular adnexal tissues, Vet Clin North Am Equine Pract 14:579–606, vii, 1998.
109. Barnett KC, Cottrell BC, Rest JR: Retrobulbar hydatid cyst in the horse, Equine Vet J 20:136–138, 1988.
110. Freestone JF, Glaze MB, Pechman R, et al: Ultrasonic identification of an orbital tumor in a horse, Eq Vet J 21:135–136, 1989.
111. Green SL, Little CB, Baird JD, et al: Tetanus in the horse: a review of 20 cases (1970 to 1990), J Vet Intern Med 8:128–132, 1994.
112. Madigan JE, Valberg SJ, Ragle C, et al: Muscle spasms associated with ear tick (*Otobius megninii*) infestations in five horses, J Am Vet Med Assoc 207:74–76, 1995.
113. Vestre WA, Steckel RR: Episcleral prolapse of orbital fat in the horse, Equine Pract 5:135–137, 1983.
114. Bedford PGC, Barnett KC, Boydell P, et al: Partial prolapse of the anteromedial corpus adiposum in the horse, Equine Vet J 10:2–4, 1990.
115. Gilger BC, Davidson MG: How to prepare for ocular surgery in the standing horse, American Association of Equine Practitioners 48:266–271, 2002.
116. Ramzan PH, Payne RJ: Periapical dental infection with nasolacrimal involvement in a horse, Vet Rec 156:184–185, 2005.
117. Wilson D, Levine SA: Surgical reconstruction of the nasolacrimal system in the horse, J Equine Vet Sci 11:232–234, 1991.
118. Cruz AM, Barber SM, Grahn BH: Nasolacrimal duct injury following periorbital trauma with concurrent retinal choroidal detachment in a horse, Equine Pract 19:20–23, 1997.
119. McIlnay TR, Miller SM, Dugan SJ: Use of canaliculorhinostomy for repair of nasolacrimal duct obstruction in a horse, J Am Vet Med Assoc 218:1323–1324, 1271, 2001.
120. Nykamp SG, Scrivani PV, Pease AP: Computed tomography dacryocystography evaluation of the nasolacrimal apparatus, Vet Radiol Ultrasound 45:23–28, 2004.
121. Schumacher J, Dean P, Welch B: Epistaxis in two horses with dacryohemorrhea, J Am Vet Med Assoc 200:366–367, 1992.
122. Reilly L, Beech J: Bilateral keratoconjunctivitis sicca in a horse, Equine Vet J 26:171–172, 1994.
123. Crispin SM: Tear-deficient and evaporative dry eye syndromes of the horse, Vet Ophthalmol 3:87–92, 2000.
124. Kaswan R, Salisbury M, Ward D: Spontaneous canine keratoconjunctivitis sicca. A useful model for human keratoconjunctivitis sicca: treatment with cyclosporine eye drops, Arch Ophthalmol 107:1210–1216, 1989.
125. Kaswan RL, Martin CL, Dawe DL: Keratoconjunctivitis sicca: immunological evaluation of 62 canine cases, Am J Vet Res 46:376–383, 1985.
126. Kaswan RL, Martin CL, Chapman WL, Jr: Keratoconjunctivitis sicca: histopathologic study of nictitating membrane and lacrimal glands from 28 days, Am J Vet Res 45:112–118, 1984.
127. Brightman AH, Manning JP, Benson GJ, et al: Decreased tear production associated with general anesthesia in the horse, J Am Vet Med Assoc 182:243–244, 1983.
128. Beech J, Zappala R, Smith G, et al: Schirmer tear test results in normal horses and ponies: effect of age, season, environment, sex, time of day and placement of strips, Vet Ophthalmol 6:251–254, 2003.
129. Wolf ED, Merideth R: Parotic duct transposition in the horse, J Equine Vet Sci 1:143–145, 1981.
130. Sundberg JP, Burnstein T, Page EH, et al: Neoplasms of equidae, J Am Vet Med Assoc 170:150–152, 1977.
131. Baker JR, Leyland A: Histological survey of tumours of the horse, with particular reference to those of the skin, Vet Rec 96:419–422, 1975.
132. Cotchin E: A general survey of tumours in the horse, Equine Vet J 9:16–21, 1977.
133. Moore AS, Beam SL, Rassnick KM, et al: Long-term control of mucocutaneous squamous cell carcinoma and metastases in a horse using piroxicam, Equine Vet J 35:715–718, 2003.
134. Bischofberger AS, Konar M, Posthaus H, et al: Ocular angiosarcoma in a pony—MRI and histopathological appearance, Equine Vet Educ 20:340–347, 2008.
135. Knottenbelt DC, Kelly DF: The diagnosis and treatment of periorbital sarcoid in the horse: 445 cases from 1974 to 1999, Vet Ophthalmol 3:169–191, 2000.
136. Hayton S, Lafreniere R, Jerry LM, et al: Ocular melanoma in Alberta: a 38 year review pointing to the importance of tumor size and tumor histology as predictors of survival, J Surg Oncol 42:215–218, 1989.
137. Deprez M, Uffer S: Clinicopathological features of eyelid skin tumors. A retrospective study of 5504 cases and review of literature, Am J Dermatopathol 31:256–262, 2009.
138. Ragland WL, Keown GH, Spencer GR: Equine sarcoid, Equine Vet J 2:2–11, 1970.
139. Genetzky RM, Biwer RD, Myers RK: Equine sarcoids: causes, diagnosis, and treatment, Compend Contin Educ Vet 5:S416–S420, 1983.
140. Murphy JM, Severin GA, Lavach JD, et al: Immunotherapy in ocular equine sarcoid, J Am Vet Med Assoc 174:269, 1979.
141. Lavach JD, Sullins KE, Roberts SM, et al: BCG treatment of periocular sarcoid, Equine Vet J 17:445–448, 1985.
142. Theon AP, Pascoe JR: Iridium-192 interstitial brachytherapy for equine periocular tumours: treatment results and prognostic factors in 115 horses, Equine Vet J 27:117–121, 1995.
143. Marti E, Lazary S, Antczak DF, et al: Report of the first international workshop on equine sarcoid, Equine Vet J 25:397–407, 1993.
144. Martens A, De Moor A, Demeulemeester J, et al: Histopathological characteristics of five clinical types of equine sarcoid, Res Vet Sci 69:295–300, 2000.
145. Angelos J, Oppenheim Y, Rebhun W, et al: Evaluation of breed as a risk factor for sarcoid and uveitis in horses, Anim Genet 19:417–425, 1988.
146. Mohammed HO, Rebhun WC, Antczak DF: Factors associated with the risk of developing sarcoid tumours in horses, Equine Vet J 24:165–168, 1992.
147. Knottenbelt DC, Matthews JB: A positive step forwards in the diagnosis of equine sarcoid, Vet J 161:224–226, 2001.
148. Ragland WL, Keown GH, Gorham JR: An epizootic of equine sarcoid, Nature 1399:1966.
149. Ragland WL, Spencer GR: Attempts to relate bovine papilloma virus to the cause of equine sarcoid: immunity to bovine papilloma virus, Am J Vet Res 29:1363–1366, 1968.
150. Voss JL: Transmission of equine sarcoid, Am J Vet Res 30:183–191, 1969.
151. Ragland WL, McLaughlin CA, Spencer GR: Attempts to relate bovine

papilloma virus to the cause of equine sarcoid: horses, donkeys and calves inoculated with equine sarcoid extracts, Equine Vet J 2:168–172, 1970.
152. England J, Watson RE, Jr, Larson KA: Virus-like particles in an equine sarcoid cell line, Am J Vet Res 34:1601–1603, 1973.
153. Nasir L, McFarlane ST, Torrontegui BO, et al: Screening for bovine papillomavirus in peripheral blood cells of donkeys with and without sarcoids, Res Vet Sci 63:289–290, 1997.
154. Nasir L, Reid SW: Bovine papillomaviral gene expression in equine sarcoid tumours, Virus Res 61:171–175, 1999.
155. Carr EA, Theon AP, Madewell BR, et al: Expression of a transforming gene (E5) of bovine papillomavirus in sarcoids obtained from horses, Am J Vet Res 62:1212–1217, 2001.
156. Martens A, De Moor A, Ducatelle R: PCR detection of bovine papilloma virus DNA in superficial swabs and scrapings from equine sarcoids, Vet J 161:280–286, 2001.
157. Chambers G, Ellsmore VA, O'Brien PM, et al: Sequence variants of bovine papillomavirus E5 detected in equine sarcoids, Virus Res 96:141–145, 2003.
158. Chambers G, Ellsmore VA, O'Brien PM, et al: Association of bovine papillomavirus with the equine sarcoid, J Gen Virol 84:1055–1062, 2003.
159. Olsen C, Cook R: Cutaneous sarcoma-like lesions of the horse caused by the agent of bovine papilloma, Proc Soc Exp Biol Med 77:281–284, 1951.
160. Angelos JA, Marti E, Lazary S, et al: Characterization of BPV-like DNA in equine sarcoids, Arch Virol 119:95–109, 1991.
161. Martens A, De Moor A, Demeulemeester J, et al: Polymerase chain reaction analysis of the surgical margins of equine sarcoids for bovine papilloma virus DNA, Vet Surg 30:460–467, 2001.
162. Otten N, von Tscharner C, Lazary S, et al: DNA of bovine papillomavirus type 1 and 2 in equine sarcoids: PCR detection and direct sequencing, Arch Virol 132:121–131, 1993.
163. Bucher K, Szalai G, Marti E, et al: Tumour suppressor gene p53 in the horse: identification, cloning, sequencing and a possible role in the pathogenesis of equine sarcoid, Res Vet Sci 61:114–119, 1996.
164. Argyle D, Ellsmore V, Gault EA, et al: Equine telomeres and telomerase in cellular immortalisation and ageing, Mech Ageing Dev 124:759–764, 2003.
165. Lazary S, Gerber H, Glatt PA, et al: Equine leucocyte antigens in sarcoid-affected horses, Equine Vet J 17:283–286, 1985.
166. Gerber H, Dubath M, Lazary S: Association between predisposition to equine sarcoid and MHC in multiple-case families. In Powell D, editor: Equine infectious diseases, Lexington, 1998, The University Press of Kentucky, pp 272–277.
167. Brostrom H: Equine sarcoids. A clinical and epidemiological study in relation to equine leucocyte antigens (ELA), Acta Vet Scand 36:223–236, 1995.
168. Ding Q, Bramble L, Yuzbasiyan-Gurkan V, et al: DNA-PKcs mutations in dogs and horses: allele frequency and association with neoplasia, Gene 283:263–269, 2002.
169. Wyman M, Rings MD, Tarr MJ, et al: Immunotherapy in equine sarcoid: a report of two cases, J Am Vet Med Assoc 171:449–451, 1977.
170. Webster CJ, Webster JM: Treatment of equine sarcoids with BCG, Vet Rec 116:131–132, 1985.
171. Owen RA, Jagger DW: Clinical observations on the use of BCG cell wall fraction for treatment of periocular and other equine sarcoids, Vet Rec 120:548–552, 1987.
172. Klein WR, Rutten VP, Steerenberg PA, et al: The present status of BCG treatment in the veterinary practice, In Vivo 5:605–608, 1991.
173. Kinnunen RE, Tallberg T, Stenback H, et al: Equine sarcoid tumour treated by autogenous tumour vaccine, Anticancer Res 19:3367–3374, 1999.
174. Komaromy AM, Andrew SE, Brooks DE, et al: Periocular sarcoid in a horse, Vet Ophthalmol 7:141–146, 2004.
175. Otten N, Marti E, Soderstrom C, et al: Experimental treatment of equine sarcoid using a xanthate compound and recombinant human tumour necrosis factor alpha, Zentralbl Veterinarmed A 41:757–765, 1994.
176. Tamzali Y, Teissie J, Rols M: First horse sarcoid treatment by electrochemotherapy: preliminary experimental results. 49th Annual Convention of the American Association of Equine Practitioners, New Orleans. Nov 2003.
177. Theon AP, Pascoe JR, Carlson GP, et al: Intratumoral chemotherapy with cisplatin in oily emulsion in horses, J Am Vet Med Assoc 202:261–267, 1993.
178. Theon AP, Pascoe JR, Galuppo LD, et al: Comparison of perioperative versus postoperative intratumoral administration of cisplatin for treatment of cutaneous sarcoids and squamous cell carcinomas in horses, J Am Vet Med Assoc 215:1655–1660, 1999.
179. Fortier LA, Mac Harg MA: Topical use of 5-fluorouracil for treatment of squamous cell carcinoma of the external genitalia of horses: 11 cases (1988–1992), J Am Vet Med Assoc 25:1183–1185, 1994.
180. Hewes CA, Sullins KE: Use of cisplatin-containing biodegradable beads for treatment of cutaneous neoplasia in equidae: 59 cases (2000–2004), J Am Vet Med Assoc 229:1617–1622, 2006.
181. Wilson D, Peyton L, Wolf G: Immediate split-thickness autogenous skin grafts in the horse, Vet Surg 16:167–171, 1987.
182. Palmer S: Carbon dioxide laser removal of verrucous sarcoid from the ear of a horse, J Am Vet Med Assoc 195:1125–1127, 1989.
183. Farris HE, Fraunfelder FT, Mason CT: Cryotherapy of equine sarcoid and other lesions, Vet Med Sm Anim Clin 325–329, 1965.
184. Joyce JR: Cryosurgery for removal of equine sarcoids, Vet Med Sm Anim Clin 70:200–203, 1975.
185. Lane JG: The treatment of equine sarcoids by cryosurgery, Equine Vet J 9:127–133, 1977.
186. Houlton JEF: Treatment of periocular equine sarcoids, Eq Vet J Suppl 2:117–122, 1983.
187. Harris H, Fraunfelder FT, Mason CT: Cryotherapy of equine sarcoid and other lesions, Vet Med Sm Anim Pract 71:325–329, 1976.
188. Neumann SM, Kainer RA, Severin GA: Reaction of normal equine eyes to radio-frequency current-induced hyperthermia, Am J Vet Res 43:1938–1944, 1982.
189. Grier RL, Brewer WG, Jr, Paul SR, et al: Treatment of bovine and equine ocular squamous cell carcinoma by radiofrequency hyperthermia, J Am Vet Med Assoc 177:55–61, 1980.
190. King TC, Priegs DR, Gum GG, et al: Therapeutic management of ocular squamous cell carcinoma in the horse: 43 cases (1979–1989), Eq Vet J 23:449–452, 1991.
191. Ford MM, Champagne ES, Giuliano EA, et al: Radiofrequency hyperthermia as a treatment for equine periocular sarcoids-10 cases [abstract], Vet Ophthalmol 5:290, 2002.
192. Lewis RE: Radon implant therapy of squamous cell carcinoma and equine sarcoid, Proc Am Assoc Equine Pract 10:217–233, 1964.
193. Walker M, Adams W, Hoskinson J, et al: Iridium-192 brachytherapy for equine sarcoid: one and two year remission rates, Vet Radiol 32:206–208, 1991.
194. Byam-Cook KL, Henson FM, Slater JD: Treatment of periocular and non-ocular sarcoids in 18 horses by interstitial brachytherapy with iridium-192, Vet Rec 159:337–341, 2006.
195. Frauenfelder HC, Blevins WE, Page EH: ^{222}Rn for treatment of periocular fibrous connective tissue sarcomas in the horse, J Am Vet Med Assoc 180:310–312, 1982.
196. Turrel J, Stover S, Gyorgyfalvy J: Iridium-192 interstitial brachytherapy of equine sarcoid, Vet Radiol Ultrasound 26:20–24, 1985.
197. Wyn-Jones G: Treatment of periocular tumours of horses using radioactive gold-198 grains, Equine Vet J 11:3–10, 1979.
198. Hilmas DE, Gillette EL: Radiotherapy of spontaneous fibrous connective-tissue sarcomas in animals, J Natl Cancer Inst 56:365–368, 1976.
199. Slatter DH, Nelson A, Smith G: Ocular sequelae of high-dose periocular gamma irradiation in a horse, Eq Vet J Suppl 2:110–111, 1983.
200. Strafuss AC: Squamous cell carcinoma in horses, J Am Vet Med Assoc 168:61–62, 1976.
201. Gelatt KN: Corneolimbal squamous cell carcinoma in a horse, Vet Med Sm Anim Clin 70:53, 1975.
202. Dubielzig RR: Tumors of the eye. In Meuten DJ, editor: Tumors in domestic animals, ed 4, Ames, 2002, Iowa State Press, pp 739–754.
203. Dugan SJ, Roberts SM, Curtis CR, et al: Prognostic factors and survival of horses with ocular/adnexal squamous cell carcinoma: 147 cases (1978–1988), J Am Vet Med Assoc 198:298–303, 1991.
204. Gelatt KN, Myers VS, Jr, Perman V, et al: Conjunctival squamous cell carcinoma in the horse, J Am Vet Med Assoc 165:617–620, 1974.
205. Ellis DR: Treatment of squamous cell carcinoma in a horse, Vet Rec 159:462–463, 2006.
206. Giuliano EA, MacDonald I, McCaw DL, et al: Photodynamic therapy for the treatment of periocular squamous cell carcinoma in horses: a pilot study, Vet Ophthalmol 11 Suppl 1:27–34, 2008.
207. Walker M, Goble D, Geiser D: Two-year non-recurrence rates for equine ocular and periorbital squamous cell carcinoma following radiotherapy, Vet Radiol 27:146–148, 1986.
208. Dugan SJ: Ocular neoplasia, Vet Clin North Am Equine Pract 8:609–626,

1992.
209. Hendrix DVH: Equine ocular squamous cell carcinoma, Clin Tech Equine Pract 4:87–94, 2005.
210. Kaps S, Richter M, Philipp M, et al: Primary invasive ocular squamous cell carcinoma in a horse, Vet Ophthalmol 8:193–197, 2005.
211. Sandmeyer LS, Panizzi L, Grahn BH: Diagnostic ophthalmology. Squamous cell carcinoma, Can Vet J 49:309–310, 2008.
212. McCowan C, Stanley RG: Pigmented squamous cell carcinoma of the conjunctiva of a horse, Vet Ophthalmol 7:421–423, 2004.
213. Vestre WA, Turner TA, Carlton WW: Conjunctival hemangioma in a horse, J Am Vet Med Res 180:1481–1482, 1982.
214. Turner LM, Whitley RD, Hager D: Management of ocular trauma in horses. Part 2: orbit, eyelids, uvea, lens, retina and optic nerve, Mod Vet Pract 341–347, 1986.
215. Rebhun WC, Del Piero F: Ocular lesions in horses with lymphosarcoma: 21 cases (1977–1997), J Am Vet Med Assoc 212:852–854, 1998.
216. Rebhun WC, Bertone A: Equine lymphosarcoma, J Am Vet Med Assoc 184:720, 1984.
217. Goodrich L, Gerber H, Marti E, et al: Equine sarcoids, Vet Clin North Am Equine Pract 14:607–623, vii, 1998.
218. Peiffer R, Wilcock B, Dubielzig R, et al: Fundamentals of veterinary ophthalmic pathology. In Gelatt KN, editor: Veterinary ophthalmology, ed 3, Philadelphia, 1999, Lippincott Williams & Wilkins, pp 355–426.
219. Perez J, Mozos E, Martin MP, et al: Immunohistochemical study of the inflammatory infiltrate associated with equine squamous cell carcinoma, J Comp Pathol 121:385–397, 1999.
220. Junge RE, Sundberg JP, Lancaster WD: Papillomas and squamous cell carcinomas of horses, J Am Vet Med Assoc 185:656–659, 1984.
221. Kim DY, Cho HS, Schommer S, et al: A novel equine papillomavirus as a possible etiology of equine ocular squamous cell carcinoma [abstract], Vet Pathol 46:1074, 2009.
222. Pazzi KA, Kraegel SA, Griffey SM, et al: Analysis of the equine tumor suppressor gene p53 in the normal horse and in eight cutaneous squamous cell carcinomas, Cancer Lett 107:125–130, 1996.
223. Teifke JP, Lohr CV: Immunohistochemical detection of P53 overexpression in paraffin wax-embedded squamous cell carcinomas of cattle, horses, cats and dogs, J Comp Pathol 114:205–210, 1996.
224. Rassnick KM, Njaa BL: Cyclooxygenase-2 immunoreactivity in equine ocular squamous-cell carcinoma, J Vet Diagn Invest 19:436–439, 2007.
225. Gallo O, Masini E, Bianchi B, et al: Prognostic significance of cyclooxygenase-2 pathway and angiogenesis in head and neck squamous cell carcinoma, Hum Pathol 33:708–714, 2002.
226. McInnis CL, Giuliano EA, Johnson PJ, et al: Immunohistochemical evaluation of cyclooxygenase expression in corneal squamous cell carcinoma in horses, Am J Vet Res 68:165–170, 2007.
227. Elce YA, Orsini JA, Blikslager AT: Expression of cyclooxygenase-1 and -2 in naturally occurring squamous cell carcinomas in horses, Am J Vet Res 68:76–80, 2007.
228. McCalla TL, Moore CP, Collier LL: Immunotherapy of periocular squamous cell carcinoma with metastasis in a pony, J Am Vet Med Assoc 200:1678–1681, 1992.
229. Theon AP, Pascoe JR, Meagher DM: Perioperative intratumoral administration of cisplatin for treatment of cutaneous tumors in Equidae, J Am Vet Med Assoc 205:1170–1176, 1994.
230. Rayner SG, Van Zyl N: The use of mitomycin C as an adjunctive treatment for equine ocular squamous cell carcinoma, Aust Vet J 84:43–46, 2006.
231. Gelatt KN: Blepharoplastic procedures in horses, J Am Vet Med Assoc 151:27–44, 1967.
232. García Sánchez GA, Piñón Cabrera AE: Ablation with carbon dioxide laser as a treatment for ocular squamous cell carcinoma in horses, Veterinaria México 37:391–398, 2006.
233. English RE, Nasisse MP, Davidson MG: Carbon dioxide laser ablation for treatment of limbal squamous cell, J Am Vet Med Assoc 196:439–442, 1990.
234. Beard WL, Wilkie DA: Partial orbital rim resection, mesh skin expansion, and second intention healing combined with enucleation or exenteration for extensive periocular tumors in horses, Vet Ophthalmol 5:23–28, 2002.
235. Joyce JR: Cryosurgical treatment of tumors of horses and cattle, J Am Vet Med Assoc 168:226–229, 1976.
236. Hilbert BJ, Farrel RK, Grant BD: Cryotherapy of periocular squamous cell carcinoma in the horse, J Am Vet Med Assoc 170:1305, 1977.
237. Schoster J: Using combined excision and cryotherapy to treat limbal squamous cell carcinoma, Vet Med 357–365, 1992.
238. Harling D, Peiffer RL, Cook C: Excision and cryosurgical treatment of five cases of squamous cell carcinoma in the horse, Equine Vet J Suppl 2:105–109, 1983.
239. Mosunic CB, Moore PA, Carmicheal KP, et al: Effects of treatment with and without adjuvant radiation therapy on recurrence of ocular and adnexal squamous cell carcinoma in horses: 157 cases (1985–2002), J Am Vet Med Assoc 225:1733–1738, 2004.
240. Gavin P, Gillette E: Interstitial radiation therapy of equine squamous cell carcinomas, Vet Radiol Ultrasound 19:138–141, 1978.
241. Chahory S, Clerc B, Devauchelle P, et al: Treatment of a recurrent ocular squamous cell carcinoma in a horse with iridium-192 implantation, J Equine Vet Sci 22:503–506, 2002.
242. Wilkie DA, Burt J: Combined treatment of ocular squamous cell carcinoma, using radiofrequency hyperthermia and interstitial ^{198}Au implants, J Am Vet Med Assoc 196:1831–1833, 1990.
243. Dougherty TJ, Gomer CJ, Henderson BW, et al: Photodynamic therapy, J Natl Cancer Inst 90:889–905, 1998.
244. Moskal TL, Dougherty TJ, Urschel JD, et al: Operation and photodynamic therapy for pleural mesothelioma: 6-year follow-up, Ann Thorac Surg 66:1128–1133, 1998.
245. Nseyo UO, DeHaven J, Dougherty TJ, et al: Photodynamic therapy (PDT) in the treatment of patients with resistant superficial bladder cancer: a long-term experience, J Clin Laser Med Surg 16:61–68, 1998.
246. Giuliano EA, Ota J, Tucker SA: Photodynamic therapy: basic principles and potential uses for the veterinary ophthalmologist, Vet Ophthalmol 10:337–343, 2007.
247. Ota J, Giuliano EA, Mullen SF, et al: Xenotransplantation of cryopreserved equine squamous cell carcinoma to athymic nude and SCID mice, Res Vet Sci 83:355–359, 2007.
248. Ota J, Giuliano EA, Cohn LA, et al: Local photodynamic therapy for equine squamous cell carcinoma: evaluation of a novel treatment method in a murine model, Vet J 176:170–176, 2008.
249. Morgan EJ, Whetstine JL, Giuliano EA, et al: Application of a fluorescence assay for the quantification of the photodynamic agent Photofrin in horses, Appl Spectrosc 61:450–454, 2007.
250. Barnes LD, Giuliano EA, Ota J, et al: The effect of photodynamic therapy on squamous cell carcinoma in a murine model: evaluation of time between intralesional injection to laser irradiation, Vet J 180:60–65, 2008.
251. Giuliano EA, Whestine JL, Tucker SA: Application of a fluorescence assay to determine the stability of verteporfin in Domoso® and sterile water over time [abstract], Vet Ophthalmol 11:427, 2008.
252. Giuliano EA, Ota J, Klauss G, et al: Equine eyelid melanoma treated with surgical resection and local photodynamic therapy [abstract], Vet Ophthalmol 8:429, 2005.
253. Fleury C, Berard F, Balme B, et al: The study of cutaneous melanomas in Camargue-type gray-skinned horses (1): clinical-pathological characterization, Pigment Cell Res 13:39–46, 2000.
254. Ohmuro K, Okada K, Satoh A, et al: Morphogenesis of compound melanosomes in melanoma cells of a gray horse, J Vet Med Sci 55:677–680, 1993.
255. Fleury C, Berard F, Leblond A, et al: The study of cutaneous melanomas in Camargue-type gray-skinned horses (2): epidemiological survey, Pigment Cell Res 13:47–51, 2000.
256. Seltenhammer MH, Simhofer H, Scherzer S, et al: Equine melanoma in a population of 296 grey Lipizzaner horses, Equine Vet J 35:153–157, 2003.
257. Moore CP, Collins BK, Linton LL, et al: Conjunctival malignant melanoma in a horse, Vet Ophthalmol 3:201–206, 2000.
258. Valentine BA: Equine melanocytic tumors: a retrospective study of 53 horses (1988 to 1991), J Vet Intern Med 9:291–297, 1995.
259. MacGillivray KC, Sweeney RW, Del Piero F: Metastatic melanoma in horses, J Vet Intern Med 16:452–456, 2002.
260. Smith SH, Goldschmidt MH, McManus PM: A comparative review of melanocytic neoplasms, Vet Pathol 39:651–678, 2002.
261. Roels S, Tilmant K, Van Daele A, et al: Proliferation, DNA ploidy, p53 overexpression and nuclear DNA fragmentation in six equine melanocytic tumours, J Vet Med A Physiol Pathol Clin Med 47:439–448, 2000.
262. Goetz T, Ogilvie G, Keegan K, et al: Cimetidine for treatment of melanomas in three horses, J Am Vet Med Assoc 196:449–452, 1990.
263. McCauley CT, Hawkins JF, Adams SB, et al: Use of a carbon dioxide laser for surgical management of cutaneous masses in horses: 32 cases (1993–2000), J Am Vet Med Assoc 220:1192–1197, 2002.
264. Rodriguez F, Forga J, Herraez P, et al: Metastatic melanoma causing

spinal cord compression in a horse, Vet Rec 142:248–249, 1998.
265. Patterson-Kane JC, Sanchez LC, Uhl EW, et al: Disseminated metastatic intramedullary melanoma in an aged grey horse, J Comp Pathol 125:204–207, 2001.
266. Tarrant J, Stokol T, Bartol J, et al: Diagnosis of malignant melanoma in a horse from cytology of body cavity fluid and blood, Equine Vet J 33:531–534, 2001.
267. Malatestinic A: Bilateral exophthalmos in a Holstein cow with lymphosarcoma, Can Vet J 44:664–666, 2003.
268. Dobson JM, Blackwood LB, McInnes EF, et al: Prognostic variables in canine multicentric lymphosarcoma, J Small Anim Pract 42:377–384, 2001.
269. D'Agostino JJ, Brightman AH: Bilateral lymphosarcoma of the nictitating membrane in a Quarter Horse, J Equine Vet Sci 24:489–491, 2004.
270. Murphy CJ, Lavoie JP, Groff J, et al: Bilateral eyelid swelling attributable to lymphosarcoma in a horse, J Am Vet Med Assoc 194:939–942, 1989.
271. Glaze MB, Gossett KA, McCoy DJ, et al: A case of equine adnexal lymphosarcoma, Equine Vet J Suppl 83–84, 1990.
272. Kelley LC, Mahaffey EA: Equine malignant lymphomas: morphologic and immunohistochemical classification, Vet Pathol 35:241–252, 1998.
273. Stoppini R, Gilger B, Malarkey D, et al: Bilateral nodular lymphocytic conjunctivitis in a horse, Vet Ophthalmol 8:129–134, 2005.
274. Moore CP, Grevan VL, Champagne ES, et al: Equine conjunctival pseudotumors, Vet Ophthalmol 3:57–63, 2000.
275. Bolton JR, Lees MJ, Robinson WF, et al: Ocular neoplasms of vascular origin in the horse, Equine Vet J Suppl 73–75, 1990.
276. Hacker DV, Moore PF, Buyukmihci NC: Ocular angiosarcoma in four horses, J Am Vet Med Assoc 189:200–203, 1986.
277. Hargis AM, McElwain TF: Vascular neoplasia in the skin of horses, J Am Vet Med Assoc 184:1121–1124, 1984.
278. Moore PF, Hacker DV, Buyukmihci NC: Ocular angiosarcoma in the horse: morphological and immunohistochemical studies, Vet Pathol 23:240–244, 1986.
279. Gearhart PM, Steficek BA, Peteresen-Jones SM: Hemangiosarcoma and squamous cell carcinoma in the third eyelid of a horse, Vet Ophthalmol 10:121–126, 2007.
280. Sansom J, Donaldson D, Smith K, et al: Haemangiosarcoma involving the third eyelid in the horse: a case series, Equine Vet J 38:277–282, 2006.
281. Fatemi-Nainie S, Anderson LW, Cheevers WP: Identification of a transforming retrovirus from cultured equine dermal fibrosarcoma, Virology 120:490–494, 1982.
282. Kunze DJ, Schmidt GM, Tvedten HW: Sebaceous adenocarcinoma of the third eyelid of a horse, Am Anim Hosp Assoc 3:452–455, 1979.
283. Baril C: Basal cell tumour of third eyelid in a horse, Can Vet J 14:66–67, 1973.
284. Johnson GC, Miller MA, Floss JL, et al: Histologic and immunohistochemical characterization of hemangiomas in the skin of seven young horses, Vet Pathol 33:142–149, 1996.
285. Herrera HD, Duchene AG, Croxatto JO, et al: Intravascular papillary endothelial hyperplasia of the conjunctiva in a horse, Vet Ophthalmol 6:269–272, 2003.
286. Stoppini R, Gilger BC, Malarkey DE, et al: Bilateral nodular lymphocytic conjunctivitis in a horse, Vet Ophthalmol 8:129–134, 2005.
287. Huntington PJ, Coloe PJ, Bryden JD, et al: Isolation of a *Moraxella* sp. from horses with conjunctivitis, Aust Vet J 64:118–119, 1987.
288. Dalgleish R, Love S, Pirie HM, et al: An outbreak of strangles in young ponies, Vet Rec 132:528–531, 1993.
289. McChesney AE, Becerra V, England JJ: Chlamydial polyarthritis in a foal, J Am Vet Med Assoc 165:259–261, 1974.
290. Borchers K, Wolfinger U, Ludwig H, et al: Virological and molecular biological investigations into equine herpes virus type 2 (EHV-2) experimental infections, Virus Res 55:101–106, 1998.
291. PN C, O'Rielly JL, Ficorilli N, et al: Isolation of equine herpesvirus type 2 (equine gammaherpesvirus 2) from foals with keratoconjunctivitis, J Am Vet Med Assoc 205:329–331, 1994.
292. Studdert MJ: Equine herpesviruses. 4. Concurrent infection in horses with strangles and conjunctivitis, Aust Vet J 47:434–436, 1971.
293. Craig MI, Barrandeguy ME, Fernandez FM: Equine herpesvirus 2 (EHV-2) infection in Thoroughbred horses in Argentina, BMC Vet Res 1:9, 2005.
294. Holyoak GR, Giles RC, McCollum WH, et al: Pathological changes associated with equine arteritis virus infection of the reproductive tract in prepubertal and peripubertal colts, J Comp Pathol 109:281–293, 1993.
295. Jones TC: Clinical and pathologic features of equine viral arteritis, J Am Vet Med Assoc 155:315–317, 1969.
296. Wood JL, Chirnside ED, Mumford JA, et al: First recorded outbreak of equine viral arteritis in the United Kingdom, Vet Rec 136:381–385, 1995.
297. McChesney AE, England JJ, Rich LJ: Adenoviral infection in foals, J Am Vet Med Assoc 162:545–549, 1973.
298. Cello RM: Ocular onchocerciasis in the horse, Equine Vet J 3:148–154, 1971.
299. Giangaspero A, Tieri E, Otranto D, et al: Occurrence of *Thelazia lacrymalis (Nematoda, Spirurida, Thelaziidae)* in native horses in Abruzzo region (central eastern Italy), Parasite 7:51–53, 2000.
300. Heyde RR, Seiff SR, Mucia J: Ophthalmomyiasis externa in California, West J Med 144:80–81, 1986.
301. Gasthuys FM, van Heerden M, Vercruysse J: Conjunctival habronemiosis in a horse in Belgium, Vet Rec 154:757–758, 2004.
302. Silva RA, Arosemena NA, Herrera HM, et al: Outbreak of trypanosomosis due to *Trypanosoma evansi* in horses of Pantanal Mato-grossense, Brazil, Vet Parasitol 60:167–171, 1995.
303. Laha R, Bera AK, Panja P, et al: Clinical and haemato-biochemical studies in natural trypanosomosis of equines, Indian J Anim Sci 74:339–340, 2004.
304. Wyn-Jones G: Treatment of equine cutaneous neoplasia by radiotherapy using iridium-192 linear sources, Equine Vet J 15:361–365, 1983.
305. Frauenfelder HC, Blevins WE, Page EH: 90Sr for treatment of periocular squamous cell carcinoma in the horse, J Am Vet Med Assoc 180:307–309, 1982.
306. Rebhun WC: Treatment of advanced squamous cell carcinomas involving the equine cornea, Vet Surg 19:297–302, 1990.

Chapter 5

Diseases and Surgery of the Cornea

Alison B. Clode
With contributions from Andy Matthews

Corneal disease is a frequent problem encountered in equine ophthalmology practice, with potentially devastating effects on both vision and globe retention. Horse owners may notice relatively nonspecific signs—a cloudy cornea, blepharospasm, epiphora—that may signal primary corneal disease or may be secondary to intraocular disease. This chapter summarizes corneal anatomy and physiology, corneal diseases, and treatment.

CLINICAL ANATOMY AND PHYSIOLOGY

ANATOMY

Grossly, the normal equine cornea measures 29.7 to 34.0 mm horizontally and 23.0 to 26.5 mm vertically in an adult,[1,2] and 20.5 to 26.6 mm horizontally and 19.5 to 24.0 mm vertically in younger horses (Fig. 5-1).[2,3] In Miniature horses, mean horizontal and vertical diameters measure 25.8 mm and 19.4 mm, respectively, and increase with age up to 7 and 5 years, respectively.[4] Corneal diameter also increases with age in normal Rocky Mountain horses.[2] Compared to other mammals, the equine cornea is relatively flat, with a mean corneal curvature in Rocky Mountain horses measured at 20.59 ±1.72D,[2] versus a curvature of 16.46 ± 1.5D calculated for normal adult horses of other breeds.[5] The large change in refractive index at the air/cornea interface makes the cornea the major refractive structure of the eye. In vivo corneal thickness measurements in normal horses, obtained via ultrasonic pachymetry, are greater peripherally than centrally, with the central cornea measuring 770 µm[2] and 793 µm.[6] Following enucleation, the mean central corneal thickness of normal horses measured 893 µm, being significantly thicker dorsally and ventrally relative to centrally, medially, and laterally.[7] Mean central corneal thickness in normal Miniature horses was 785.6 µm.[4] In healthy Rocky Mountain horses, the corneal thickness increases with age,[2] whereas no variation in corneal thickness has been noted with age, gender, or endothelial cell density in Miniature horses or horses of other breeds.[4,7]

Histologically, the cornea comprises three primary layers of alternating lipophilicity: the superficial epithelium (lipophilic), central stroma (hydrophilic), and deep endothelium (lipophilic) (Fig. 5-2). The stratified squamous epithelium, consisting of 8 to 12 layers of nonkeratinized squamous cells, wing cells, and basal cells, is anchored to its basement membrane by hemidesmosomes. Anchoring fibrils attached to the hemidesmosomes penetrate the basement membrane to end in anchoring plaques in the anterior stroma, creating a stable epithelium/basement membrane/anterior stromal adhesion complex.[8] The poorly

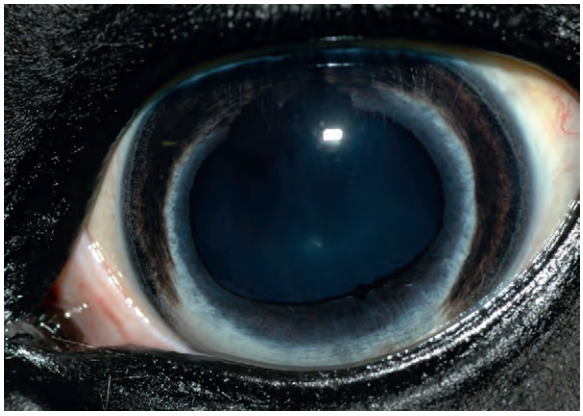


Figure 5-1. Clinical photograph of a normal equine eye, demonstrating the ocular clarity of the cornea.

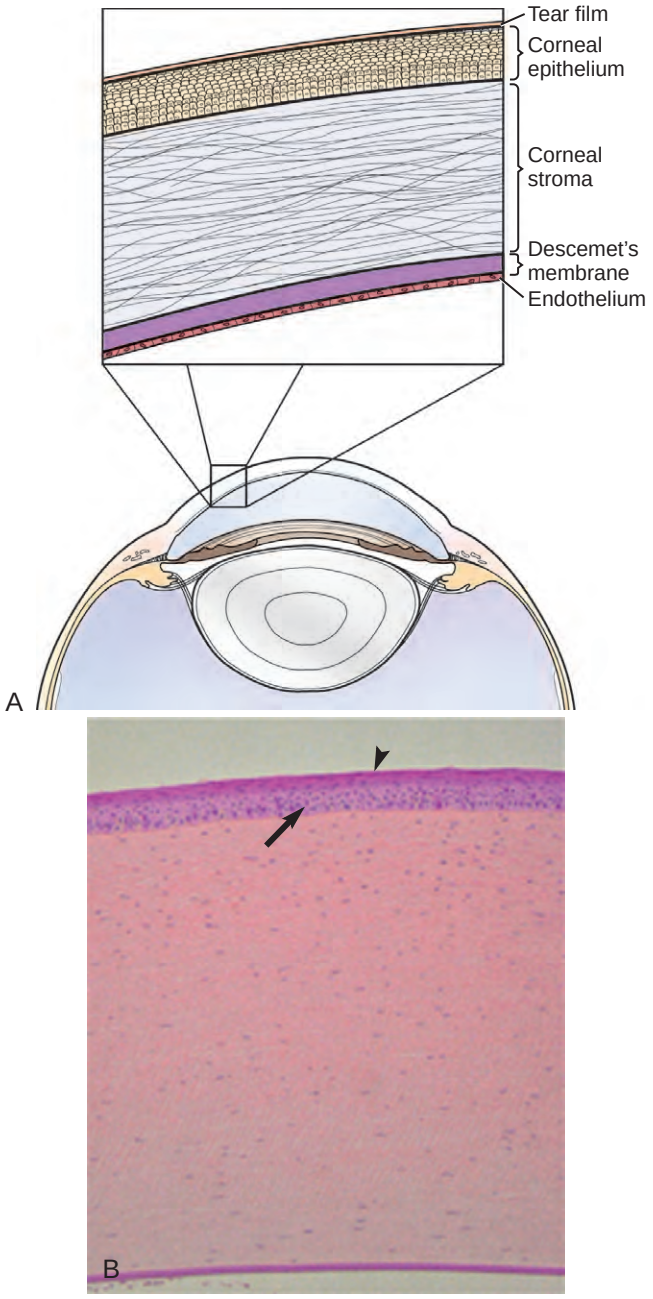


Figure 5-2. **A,** Diagram of equine cornea. Enlarged inset demonstrates relative proportions of corneal epithelium, stroma, and Descemet's membrane/endothelium. **B,** Histologic image of a normal equine cornea (H&E ×40). Note columnar basal epithelial cell layer *(arrow)* with nonkeratinized stratified squamous surface cells *(arrowhead)*. Also note the sparse, scattered stromal cells (keratocytes) among the collagen lamellae comprising the stroma. The eosinophilic posterior layer is Descemet's membrane, with a few associated endothelial cells (the remaining cells were artifactually lost during tissue processing).

cellular stroma, which is 90% of the corneal thickness, is composed of water (75% to 80%), regularly arranged collagen fibers, and a proteoglycan matrix with the glycosaminoglycans (GAGs) dermatan sulfate, chondroitin sulfate, and keratan sulfate.[8] Arrangement of GAGs within the cornea varies by region and depth, with greater levels of chondroitin-4 sulfate in the deep cornea relative to the superficial regions, which have a higher proportion of chondroitin-6 sulfate.[9] This variation may impact corneal water retention and wound healing, ultimately affecting corneal clarity.[9] Deep to the stroma is Descemet's membrane, the basement membrane of the innermost endothelial layer. Due to continued secretion throughout life, Descemet's membrane is thicker in older individuals.[8] The endothelium is a single layer of closely interdigitating hexagonal cells that forms a physical barrier between the cornea and aqueous humor and also utilizes an active pumping mechanism to keep water and solutes out of the cornea (Fig. 5-3).[8] The efficiency of the barrier and pump functions is determined by endothelial cell size, shape, and density, as well as the presence of certain cofactors (i.e., calcium, glutathione, bicarbonate) within the aqueous humor.[8] Mean endothelial cell density in normal horses is 3155 cells/mm^2, showing no variation with gender but declining with increasing age.[7] Interestingly, no correlation was noted between endothelial cell density and corneal thickness in this study, seemingly counter to the effect of endothelial cell density on barrier and pump functions.[7] In this study, however, the measured thickness included Descemet's membranes of variable thicknesses and did not include any corneas with endothelial cell loss below the critical value of 400 to 700 cells/mm^2 necessary for effective endothelial function.[7,8]

PHYSIOLOGY

NUTRITION

Oxygen is supplied to the cornea by the external atmosphere and precorneal tear film, with lesser amounts provided by the aqueous humor and limbal blood vessels.[8] When the eyelids are closed, the palpebral conjunctiva provides smaller amounts of oxygen.[8] Glucose, amino acids, and vitamins are predominantly obtained from the aqueous humor, with smaller amounts from the precorneal tear film and limbal blood vessels.[8] Additional glucose may be obtained from subepithelial glycogen stores in times of increased demand such as wound healing, either via aerobic or anaerobic (glycolysis) metabolism.[8]

MICROFLORA

The normal corneal and conjunctival surface microflora are primarily gram-positive bacteria and fungal organisms, but gram-negative organisms are present as well (Tables 5-1

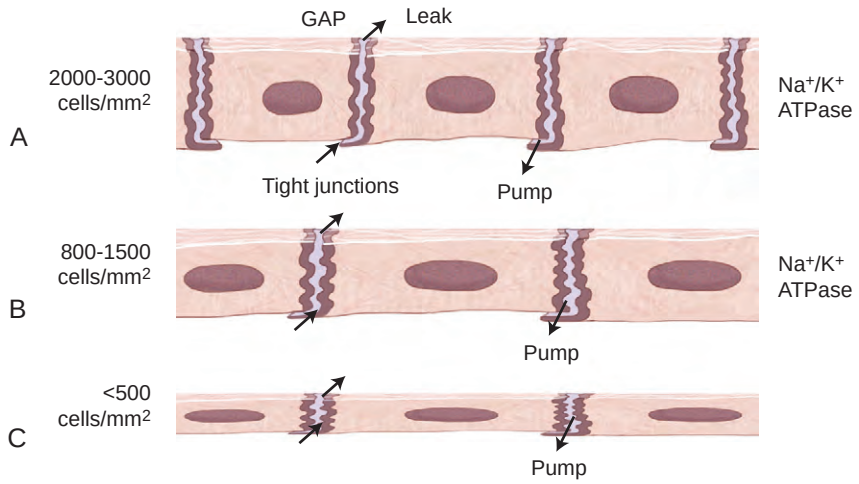


Figure 5-3. Corneal endothelium, a single layer of closely interdigitating hexagonal cells that forms a physical barrier between the cornea and aqueous humor, utilizes an active pumping mechanism to keep water and solutes out of the cornea. Diagram of corneal endothelial cells demonstrates location of the Na^+/K^+-ATPase pump and tight junction locations. **A,** Normal concentration of endothelial cells. **B,** Reduced concentration of endothelial cells. **C,** Low concentration of endothelial cells and resulting leakage of aqueous humor into the corneal stroma.

Table 5-1 | **Gram-Positive Bacterial Isolates from Conjunctival/Corneal Samples from Healthy Horses (2003-2005)**

AUTHOR COUNTRY (STATE) ORGANISM % (NUMBER/TOTAL)	ANDREW ET AL.[13] US (FL)	GEMENSKY-METZLER ET AL.[14] US (OH)
Actinomyces	6 (135/137)	
Bacillus	17 (398/2357)	32
Corynebacterium	29 (689/2357)	4
Dermatophilus	<1 (3/2357)	
Diphtheroid		10
Enterococcus		2
Lactobacillus	<1 (1/2357)	
Micrococcus	2 (53/2357)	8
Rhodococcus	<1 (5/2357)	
Staphylococcus	22 (513/2357)	52
Streptococcus	4 (87/2357)	36
Streptomyces	<1 (19/2357)	66
Unidentified	<1 (6/2357)	

Table 5-2 | **Gram-Negative Bacterial Isolates from Conjunctival/Corneal Samples from Healthy Horses (2003-2005)**

AUTHOR COUNTRY (STATE) ORGANISM % (NUMBER/TOTAL)	ANDREW ET AL.[13] US (FL)	GEMENSKY-METZLER ET AL.[14] US (OH)
Achromobacter		
Acinetobacter		18
Actinobacillus		2
Alcaligenes	<1 (2/2357)	
Citrobacter		8
Enterobacter		14
Escherichia	<1 (1/2357)	24
Klebsiella	<1 (5/2357)	
Moraxella	10 (225/2357)	28
Neisseria		
Pasteurella	<1 (4/2357)	
Proteus	<1 (1/2357)	
Pseudomonas	<1 (1/2357)	8
Sphingomonas	<1 (1/2357)	
Stenotrophomonas	<1 (2/2357)	
Unidentified		

to 5-3). Consistent with previous reports,[10-12] recent evaluations of horses in the United States identified *Staphylococcus* spp. (22% to 50%),[13,14] *Bacillus* spp. (17% to 32%),[13,14] and *Corynebacterium* spp. (29%),[13] as common isolates, in addition to a possible increasing prevalence of *Streptomyces* spp. (66%).[14] The most common gram-negative isolates from horses in the United States are *Moraxella* spp. (28%), *Escherichia* spp. (24%), *Acinetobacter* spp. (18%), and *Enterobacter* spp. (14%).[14] Fungal organisms isolated from normal horses in the greatest frequency include *Aspergillus* spp., *Cladosporium* spp., *Alternaria* spp., and *Penicillium* spp.[12,14-16]

INNERVATION

The highly sensitive cornea receives much of its innervation via the ophthalmic branch of cranial nerve (CN) V (trigeminal nerve). As determined in other species, ciliary nerve branches enter the limbus at the level of the midstroma and course toward the superficial cornea, where they form anterior stromal and subepithelial plexi.[8] Termination of the nerve fibers occurs in the superficial layers of the epithelium,[17] so deeper corneal layers are comparatively poorly innervated.[8] In normal adult horses, corneal sensitivity, quantified using the corneal touch threshold measured by Cochet-Bonnet esthesiometry, is greatest in the central, ventral, and lateral quadrants relative to the nasal and dorsal quadrants.[18,19] In sick foals, corneal sensitivity is significantly decreased in all quadrants relative to normal foals and adults.[18] Pharmacologic corneal anesthesia is important in the diagnosis and treatment of surface ocular disease. Evaluation of the duration of effect of topical ocular proparacaine (0.5%) in normal horses indicated that a single 0.2-mL instillation significantly decreased corneal sensitivity within 5 minutes, with peak effect lasting 25 minutes.[20]

Table 5-3 | **Fungal Isolates from Conjunctival/Corneal Samples from Healthy Horses (2003-2005)**

AUTHOR COUNTRY (STATE) PERCENTAGE OF ISOLATE (NUMBER/TOTAL)	ROSA ET AL.[15] BRAZIL	ANDREW ET AL.[13] US (FL)	GEMENSKY-METZLER ET AL.[14] US (OH)
Acremonium		5 (25/541)	
Alternaria		2 (11/541)	6
Aspergillus	37 (75/204)	6 (30/541)	78
Candida		<1 (3/541)	
Cephalosporium			2
Cladosporium	6 (13/204)	8 (44/541)	32
Chrysosporium		8 (44/541)	
Curvularia		<1 (3/541)	2
Drechslera		1 (7/541)	
Epicoccum		1 (6/541)	
Eurotium	2 (4/204)		
Fonsecaea		<1 (1/541)	
Fusarium	<1 (1/204)	1 (8/541)	2
Geotrichum	1 (2/204)	<1 (2/541)	
Gliocladium		<1 (1/541)	
Gliomastix	<1 (1/204)		
Mucor	2 (5/204)		4
Nigrospora		<1 (2/541)	
Paecilomyces		1 (6/541)	
Papulaspora		<1 (1/541)	
Penicillium	29 (60/204)	5 (29/541)	2
Phialophora		<1 (2/541)	
Pseudallescheria		<1 (1/541)	
Rhizopus	1 (2/204)	5 (25/541)	
Scedosporium		<1 (2/541)	2
Scopulariopsis	18 (37/204)	2 (10/541)	6
Sporothrix		<1 (2/541)	
Stemphylium			4
Syncephalastrum	2 (5/204)		
Torulopsis		<1 (2/541)	
Trichcladium		<1 (2/541)	
Trichoderma	21 (43/204)		
Trichophyton		<1 (2/541)	
Trichosporon		<1 (2/541)	
Tripospermum		<1 (1/541)	
Verticillium	<1 (1/204)	<1 (1/541)	
Wallemia		<1 (1/541)	
Wangiella		<1 (2/541)	
Unidentified	11 (23/204)	49 (263/541)	

The extensive corneal innervation serves two main functions: protection of the eye and stimulation of wound healing. Activation of nociceptive fibers by mechanical, thermal, and chemical stimuli is extremely important to corneal and overall ocular protection, while neuropeptides such as substance P and calcitonin gene-related peptide may exert a trophic influence, stimulating epithelial healing.[21] The importance of these functions may be particularly evident in animals with decreased corneal innervation, potentially predisposing them to development of ulcers (i.e., neurotrophic ulcers) and delaying appropriate wound healing.

CORNEAL IMMUNOLOGY

Andy Matthews

The cornea is an immunologically privileged tissue, anatomically contiguous with two immunologically privileged sites, the ocular surface and the anterior chamber. Immune privilege (IP) is an evolutionary adaptation that downregulates the immune-driven ocular inflammatory response to protect vulnerable structures and preserve vision. It is counterbalanced by the threat of unchecked infection due to inadequate immunoresponsiveness. Corneal IP is governed primarily by normal endothelial cell function,[22] in addition to the absence of blood and lymphatic vessels, the expression of complement regulatory proteins in the aqueous humor and on corneal cells, the expression of Fas ligand on corneal cells, and the relative paucity of professional antigen-presenting cells (APC) constitutively expressing MHC class II antigen (e.g., dendritic cells and Langerhans cells).[23-25] Proinflammatory cytokines, in particular interleukin 1 (IL-1) and tumor necrosis factor α (TNF-α), are responsible for activation and recruitment of these APCs into the cornea and inducing expression of MHC II antigen on native corneal cells, ultimately resulting in loss of corneal IP. Loss of corneal IP, coupled with corneal lymphangiogenesis in the presence of inflammation, permits lymphocyte trafficking into afferent lymphatics,[26,27] creating an effectively "normal" adaptive immune response in inflamed or injured corneas. Corneal allograft rejection and exacerbation of herpetic keratitis in humans may be explained in part by this immunopathogenesis. For more information on ocular surface immunology, please see a recent review article in *Veterinary Clinics of North America*.[28]

WOUND HEALING

EPITHELIUM

The epithelium prevents microbial invasion of the cornea and limits fluid uptake by the hydrophilic stroma.[8] Superficial epithelial cells lost in a constant cycle of apoptotic shedding are replaced by anterior migration of cells generated by the mitotically active basal layer, which is in turn replaced by centripetal migration of limbal stem cells.[8] With a basal mitotic rate of 10% to 15% per day, the entire epithelium turns over every 7 days.[29]

When epithelial cells are lost through corneal abrasion or ulceration, without damage to the underlying basement membrane, basal epithelial cell mitosis ceases, cells lining the wound edge retract and thicken, and epithelial cell/basement membrane hemidesmosomal attachments are disrupted (Fig. 5-4).[8] Centripetal amoeboid migration of surrounding basal cells along a protein scaffolding overlying the basement membrane ultimately (i.e., within hours of injury) results in coverage of the wound bed, at which time basal cell mitosis resumes, restoring the epithelium to its normal structure.[30] In contrast to wounds limited to the epithelial cell layers, those in which the basement membrane is damaged reepithelialize relatively rapidly; however, complete healing may take months owing to necessary reformation of basement membrane and associated adhesion complexes.[31] In horses, experimentally induced corneal ulcers in which the epithelium, basement membrane, and anterior third of the stroma were surgically removed had a median time to reepithelialization of 11 days, or a rate of 0.6 mm/day.[32]

STROMA

Healing of corneal stromal wounds is significantly more complex, beginning with infiltration of polymorphonuclear cells at the wound edge within hours of injury, followed soon after by monocytes (see Fig. 5-4).[8] Surrounding stromal keratocytes undergo fibroblastic transformation, proliferate, and begin to synthesize collagen and extracellular matrix components such as proteoglycans. Fibronectin is also produced following wounding, stimulating cell adhesion and migration, protein synthesis, and fibroblast migration, ultimately promoting wound healing.[33] Remodeling of the stroma by reformation of cell processes and gap junctions and reorganization of collagen fibrils is initially associated with decreased corneal transparency, but continued remodeling over months to years restores normal tensile strength and variable degrees of transparency.[33]

ENDOTHELIUM

In contrast to the remarkable healing and regenerative capacities of the corneal epithelium and stroma in response to injury, that of the endothelium is much more limited. Loss of endothelial cells due to injury/disease, surgical trauma, or aging, leads to replacement by enlargement and migration of adjacent endothelial cells rather than replication. Overall cell number is reduced, leading to abnormally large (polymegathism) and abnormally shaped (pleomorphism) endothelial cells. Tight junctions are maintained among cells during this migration, and following wound closure, sodium/potassium–adenosine triphosphate (Na^+/K^+-ATPase) pump sites are increased, maintaining the effective barrier and pump functions of the endothelium,[34] provided the cell density is greater than the critical density of 400 to 700 cells/mm^2.[35]

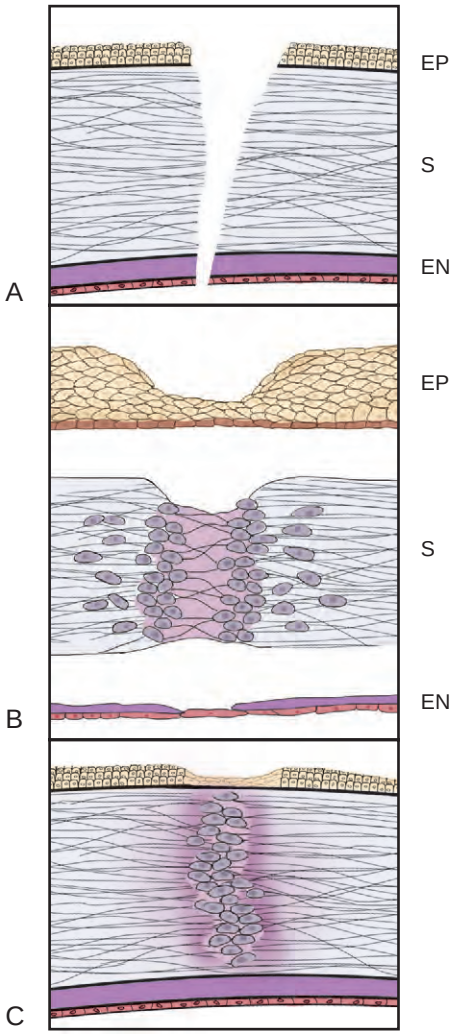


Figure 5-4. Diagram of corneal epithelial wound healing. Healing of a full-thickness corneal wound. **A,** Full-thickness corneal wound. **B,** Epithelium (EP): Cells peripheral to wound edge migrate within hours of injury. Mitosis of epithelial cells begins within 24 to 36 hours of injury. Stroma (S): Fibrin matrix is secreted into wound. Leukocytes and fibroblasts proliferate and migrate to wound edge. Fibroblasts undergo mitosis with subsequent collagen secretion. Endothelium (EN): Cells at wound edge enlarge and migrate to cover defect. Migrated cells thin and flatten. **C,** Wound modification: Epithelium differentiates to stratified squamous layer within 2 weeks. Macrophages remove cellular debris in stroma. Stromal fibroblasts synthesize collagen that is disorganized, reducing corneal transparency. Endothelium is incapable of mitosis.

GROWTH FACTORS

As in other tissues, healing of corneal wounds is enhanced by peptide growth factors, which, following local and systemic production, reach the avascular cornea via the aqueous humor, tears, and limbal blood vessels. Epidermal growth factor (EGF), platelet-derived growth factor (PDGF), transforming growth factor β (TGF-β), connective tissue growth factor (CTGF), keratinocyte growth factor (KGF), insulin-like growth factor (IGF), and hepatocyte growth factor (HGF) perform varied functions, such as promotion or inhibition of corneal epithelial cell proliferation or migration, keratocyte proliferation, and

Table 5-4 | **Growth Factors of the Equine Cornea**

GROWTH FACTOR	IN VITRO OR IN VIVO EVALUATION (SAMPLE)[REF]	STUDY RESULTS	PRESUMED FUNCTION
Connective tissue growth factor (CTGF)	In vivo (tear fluid)[42]	Higher in normal eyes than eyes with melting ulcers	Fibroblast proliferation Collagen production
Epidermal growth factor (EGF)	In vitro (cultured equine epithelial cells and keratocytes)[40]	Increased epithelial cell and keratocyte proliferation	Increase wound healing
Platelet-derived growth factor (PDGF)	In vitro (cultured equine epithelial cells and keratocytes)[40]	Increased epithelial cell and keratocyte proliferation	Increase wound healing
Transforming growth factor β_1 (TGF-β_1)	In vitro (cultured equine epithelial cells and keratocytes)[40]	Decreased epithelial cell and keratocyte proliferation	Decrease or increase wound healing
Epidermal growth factor (EGF)	In vivo (topical administration of human EGF to horses with surgically-induced corneal ulcers)[41]	No significant increase in healing; dose-dependent increase in corneal vascularization, edema, pigmentation	Increase wound healing, but with significant inflammation
Opioid growth factor (OGF) and receptor (OGFr)	In vitro (normal equine cornea)[47]	OGF and OGFr present in normal corneal epithelium	OGF inhibits epithelial wound healing; blockade of OGF/OGFr may enhance healing

inflammatory cell influx (Table 5-4).[36] The complex and incompletely understood interactions and potential species differences among growth factors make definitive statements about their functions difficult. In other species, EGF has been documented to increase normal cell turnover, promote vascularization, and stimulate healing of epithelial and endothelial wounds.[37] PDGF enhances tissue repair by influencing inflammatory reactions, vascularization, proliferation, chemotaxis, and extracellular matrix production.[38] TGF-β increases collagen synthesis, possibly due to increasing production of CTGF, which stimulates fibroblast and collagen production[39]; however, it also inhibits epithelial cell proliferation and keratocyte migration,[36] producing varied effects on overall corneal wound healing.

Evaluation of growth factors in horses has been more limited. Using cultured equine epithelial cells and keratocytes, increased proliferation of epithelial cells and keratocytes in response to EGF and PDGF was noted, while TGF-β decreased proliferation of both.[40] Use of high-dose (50 mcg/mL) and low-dose (5 mcg/mL) EGF in horses with experimentally induced corneal ulcers identified a trend toward more rapid healing in the high-dose group. However, both doses of EGF were associated with increased corneal edema, vascularization, melanosis, and scarring, side effects which likely negate any potential benefit of administration of EGF as performed in that study.[41] Additionally, CTGF has been identified in the tear fluid of both normal and ulcerated equine eyes, with lower levels in ulcerated eyes postulated to be associated with exhausted production of CTGF by lacrimal and third eyelid glands, and/or increased utilization of CTGF by ocular surface receptors.[42]

Opioid growth factor (OGF) works in a receptor-mediated fashion in normal corneal homeostasis as a tonic inhibitor of cell division.[43] Experimental studies in rats, rabbits, and human corneal cell cultures have identified an increased rate of reepithelialization following administration of or incubation with the strong OGF inhibitor, naltrexone.[44-46] OGF and its receptor have been immunohistochemically localized to the equine corneal epithelium,[47] but its specific role in the equine cornea related to epithelial wound healing has not been investigated.

Although endogenous growth factors play an important role in healing corneal wounds, further study will determine possible clinical utility of either therapeutic supplementation or inhibition of these growth factors in an effort to enhance corneal wound repair in horses.

PROTEASES

Both maintenance of normal corneal health and repair during disease or wound healing depend upon proteolytic enzymes and their inhibitors for proper tissue turnover.[48-52] In normal corneas, enzyme inhibition balances degradative activity to promote corneal homeostasis. Disease may result in excessive proteolytic activity by enzymes derived from the precorneal tear film, corneal epithelial cells, keratocytes, infiltrating inflammatory cells, and infectious organisms.[49,50,53-57] This excess proteolytic activity manifests as corneal stromal "melting," or keratomalacia.

The two most extensively studied groups of corneal proteinases are the matrix metalloproteinases (MMPs) and the serine proteases, specifically neutrophil elastase (NE).[48] NE, produced by leukocytes, digests collagen types III and IV, laminin, fibronectin, and heparan sulfate[53,58-60] and has been identified in significantly higher levels in the preocular tear film of horses with ulcerative keratitis than in normal controls.[53] MMP-2 and MMP-9 are both gelatinases but appear to play different roles in corneal physiology. Using immunohistochemistry, MMP-2 was found to be constitutively present in healthy equine cornea, primarily in the epithelium and to lesser degrees in the stroma and endothelium, while MMP-9 was not identified in healthy equine cornea.[48] In diseased equine cornea, MMP-2 expression was increased throughout the equine cornea, with concurrent MMP-9 expression also throughout.[48] The use of gelatin zymography to identify proteolytic activity of MMP-2 and -9 documented an increase in total tear film proteolytic activity in ulcerated equine eyes relative to the contralateral healthy eye, with a decrease in activity to that of the contralateral healthy eye by the day of ulcer healing.[61] These findings support the role of MMP-2 in corneal homeostasis, becoming locally activated in times of minor wound repair,[57,62] whereas MMP-9 is expressed by epithelial cells and PMNs following more extensive corneal wounding.[62-64] Control of this proteolytic activity therefore constitutes a significant component of therapy in such conditions.

SEQUELAE TO CORNEAL WOUNDING

Secondary to healing of corneal wounds, the primary clinical sign noted is corneal opacification due to vascularization, pigmentation, and/or edema.

VASCULARIZATION

The avascularity of normal cornea is important for maintaining optical clarity; however, many disease processes promote corneal vascularization in an effort to augment healing (Fig. 5-5). Inflammatory cells incited by the initial injury and inflammatory mediators from the cyclooxygenase and lipoxygenase pathways stimulate angiogenesis from the perilimbal blood vessels.[8,65,66] Depending upon the disease process, and potentially the species involved, growth factors implicated in stimulating angiogenesis include basic fibroblast growth factor (bFGF),[67] vascular endothelial growth factor (VEGF),[67] and TGF-β,[68] which may exert an inhibitory effect.[69] The interactions among various cytokines, growth factors, and other components of the inflammatory process have yet to be fully elucidated.

PIGMENTATION

Chronic ocular surface irritation induces pigment migration onto the corneal surface from limbal and perilimbal tissues (Fig. 5-6).[70] Histologically, migrating superficial pigment is located within the basal epithelial cells. Stromal pigment is associated with deeper wounds involving inflammatory cells and granulation tissue. Endothelial pigment may come from uveal tissue in anterior segment dysgenesis, persistent pupillary membranes, ruptured iris cysts, anterior synechiae, chronic uveitis, or uveal melanoma.[70] Pigmentation may not progress once the inciting cause is eliminated, but it is also unlikely to regress.

EDEMA

In the healthy cornea, stromal water content is maintained at a stable 78% primarily by the endothelium, with contributions from the epithelium and stromal proteoglycans.[8] The lipophilic epithelium limits fluid uptake from the precorneal tear film, while sulfation, diameter, and spacing of stromal proteoglycans determine the water retention and transparency properties of the stroma.[8] Far more important to the maintenance of stable corneal hydration, and therefore transparency, are the barrier and pump functions of the endothelium. Active endothelial pumping mechanisms for ions, amino acids, and sugars create osmotic gradients which ultimately lead to movement of 6 to 8 mL/hr of water from the stroma to the AH.[8]

In a cornea with healthy epithelium, stroma, and endothelium, corneal thickness (as determined by corneal hydration) is constant up to an intraocular pressure (IOP) of 50 mm Hg, after which point edema and increased thickness result.[71] When corneal thickness increases due to fluid imbibition associated with underlying epithelial or endothelial dysfunction, smaller increases in IOP lead to significantly greater increases in corneal fluid uptake. For this reason, a slightly elevated IOP in the presence of preexisting mild corneal edema may lead to an apparently disproportionately greater increase in corneal thickness. The clinical manifestations of this increased stromal hydration include loss of corneal transparency (Figs. 5-7 and 5-8) and decreased visual function, as well as bullous keratopathy with predisposition to corneal ulceration (Fig. 5-9).

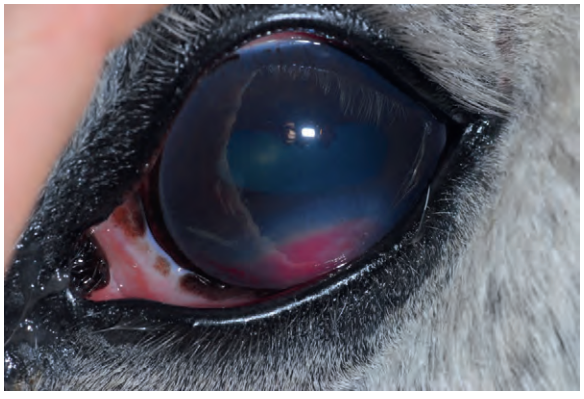


Figure 5-5. Clinical photograph of corneal vascularization in a 9-year-old Trakehner mare. Note the individual straight, superficial vessels extending from the dorsal limbus and the prominent sweep of stromal vessels covering a stromal abscess adjacent to the ventral limbus.

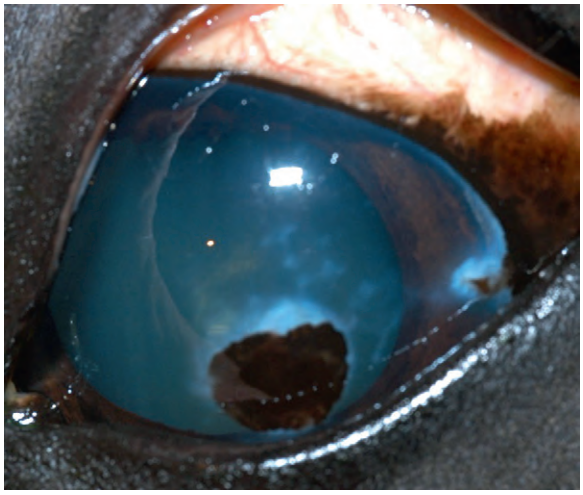


Figure 5-6. Clinical photograph of corneal pigmentation, located ventrolateral paraxially. This horse had a conjunctival graft placed previously, which was harvested from an area of pigmented conjunctiva.

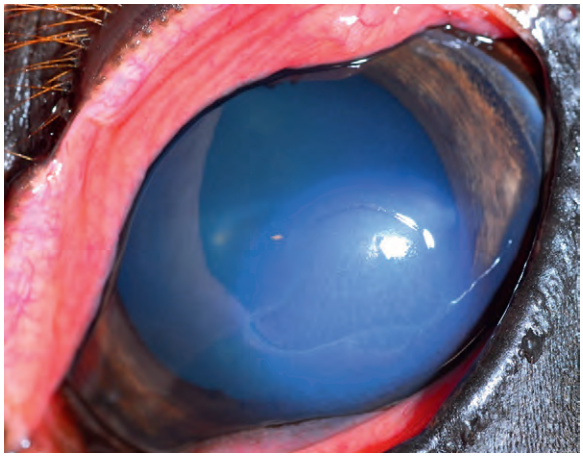


Figure 5-7. Clinical photograph of a corneal ulceration with focal edema in a 12-year-old Saddlebred gelding. Ulcer has not been stained with fluorescein dye, but epithelial margins are visible, and edema extends just beyond ulcerated region.

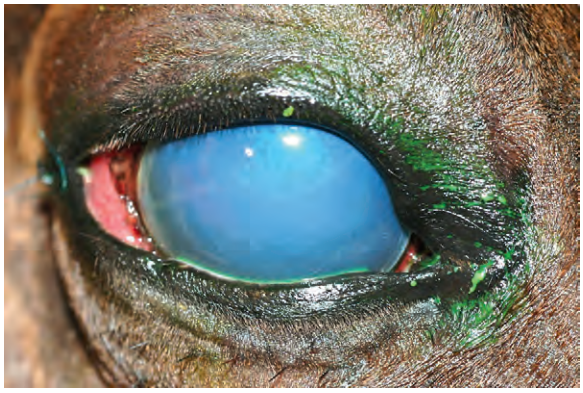


Figure 5-8. Clinical photograph of diffuse (endothelial) corneal edema. This horse had glaucoma secondary to uveitis and had a gonioimplant placed, which is just visible within the anterior chamber at 8 o'clock.

Figure 5-10. Bilateral megalocornea and megaloglobus in a young foal. Significant exposure keratitis has developed, indicated by corneal vascularization and opacification. (Photograph courtesy Dr. David Wilkie.)

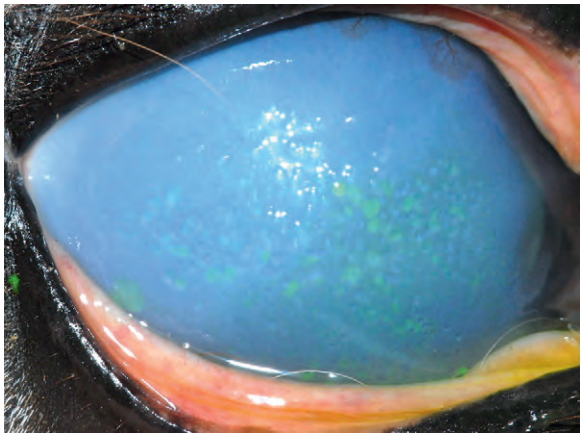


Figure 5-9. Clinical photograph of diffuse (endothelial) corneal edema and associated bullous keratopathy in a 15-year-old Appaloosa mare. Note the multifocal areas of fluorescein dye retention, indicating ruptured bullae interspersed among multifocal bullae that have not yet ruptured.

IMPACT OF CORNEAL DISEASE ON THE EQUINE INDUSTRY

Corneal disease is a common reason for horses to be presented for evaluation of signs of ocular pain, alteration in the appearance of the cornea, or development of vision deficits. Rapid assessment of problems and appropriate treatment are vital to the maintenance of a clear visual axis as well as ocular comfort. The very common nature of corneal disease in the horse makes it a significant problem for individual horses and the equine industry in general.

CONGENITAL DISEASES

MEGALOCORNEA/CORNEAL GLOBOSA

PREVALENCE

Megalocornea, an abnormally large cornea present at birth, appears most commonly in Rocky Mountain horses as a component of a syndrome of multiple congenital ocular anomalies (MCOA) in which temporal iridal, ciliary, and retinal cysts, iridal hypoplasia, cataracts, and retinal dysplasia may also be present.[72] A previous study identified 43 of 71 horses with multiple ocular anomalies as affected with megalocornea, all bilaterally[73]; a separate report describes two unilaterally affected foals.[74] A recent study measuring corneal size and thickness suggests that the corneal appearance may in fact be corneal globosa, or an abnormally shaped cornea, rather than true enlargement.[73] Horses with the Silver (also known as *Chocolate*) coat color are more frequently affected.[72,73,75]

CLINICAL APPEARANCE

Affected horses have a clear cornea with normal central topography, grossly observable increased optical corneal diameter, short radius of corneal curvature, and a globular, protruding corneal contour (Fig. 5-10).[73] The anterior chamber in these horses is excessively deep, while the lens-iris diaphragm appears normal (Fig. 5-11). Additionally, affected individuals may have macropalpebral fissure, miosis, congenital cataract, uveal or peripheral retinal cysts, and retinal anomalies (dysplasia, detachment).

DIFFERENTIAL DIAGNOSES

Congenital or neonatal glaucoma with coinciding buphthalmia may present similarly to megalocornea, but glaucoma is more frequently unilateral and associated with an elevated IOP (unlike megalocornea). Exophthalmia due to a space-occupying retrobulbar mass may appear similar to an abnormally large-appearing globe, but resistance to retropulsion will not be present with megalocornea.

PATHOGENESIS

Megalocornea in association with multiple anterior segment anomalies is an embryologic defect, the development of which is poorly understood. In humans, optic cup growth may be decreased, resulting in successive waves of migration of mesenchymal tissue over an excessive large, broad ciliary region, ultimately producing an enlarged corneal diameter.[76] This abnormal growth may originate with a neuroectodermal abnormality within the anterior optic cup.[76,77] Pedigree analysis of Rocky and Kentucky Mountain horses suggests either a dominant mode of inheritance with incomplete penetrance and linkage to coat color,[72] or a codominant mode of inheritance

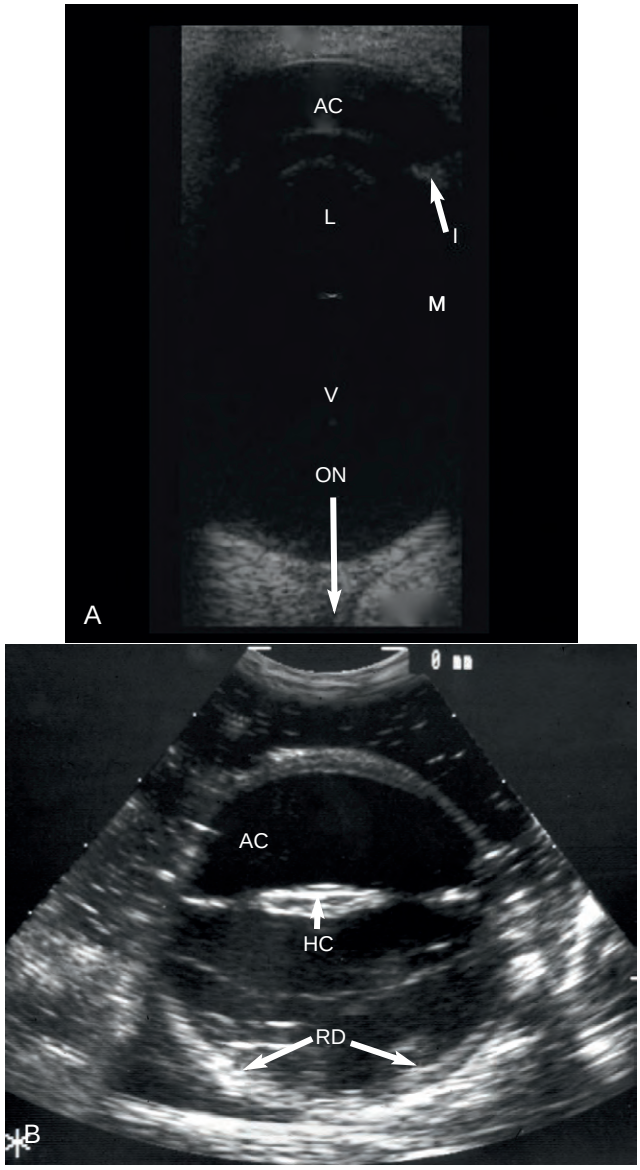


Figure 5-11. A, B-mode ultrasonographic image of a normal equine eye, showing appropriate proportions for anterior chamber length (AC), lens size (L), and vitreal chamber length (VC) (7.5-MHz probe). **B,** B-mode ultrasonography of one eye of the foal in Fig. 5-12. In comparison with Fig. 5-11, *A*, note the deep anterior chamber (AC), hypermature cataract (HC), and retinal detachment (RD). (**A,** Photograph courtesy Dr. Marc Cronau.)

involving the MCOA locus on the ECA6q gene.[75] Further, it is suggested that individuals with more severe clinical manifestations are homozygous for the mutation involving the ECA6q gene, while those with less severe signs are heterozygous.[75]

TREATMENT

No treatment is necessary, and the condition is nonprogressive.

PROGNOSIS

The corneal changes in affected individuals do not determine the overall prognosis as much as the associated ocular anomalies, such as lens and retinal abnormalities.

MICROCORNEA

PREVALENCE

Microcornea, or congenitally small cornea, is infrequently reported in horses; however, severely affected individuals with corneal diameters of less than 10 mm and marked visual impairment have been described.[78] Microphthalmos or other ocular anomalies may also be present.[79] It is not uncommon for horses to have the appearance of an undersized cornea with an otherwise normal globe, without visual impairment.[79]

CLINICAL APPEARANCE

In individuals with normally sized globes and palpebral fissures, microcornea allows increased visualization of the sclera. When accompanied by microphthalmos and micropalpebral fissure, a proportionally normal amount of sclera is visible.[80] Cataracts and coloboma of the iris, lens, or optic nerve have also been reported in horses with microcornea.[79,80]

DIFFERENTIAL DIAGNOSES

Phthisis bulbi, or a shrunken globe associated with chronic inflammation or previous globe rupture, is the primary differential diagnosis for microcornea. The corneas of phthisical eyes are frequently but not always scarred and more opaque than the generally clear cornea of individuals affected with microcornea.

PATHOGENESIS

An early developmental deficiency in the optic vesicle may result in microcornea with microphthalmos, whereas a later failure of normal growth and expansion of the optic cup with premature or delayed optic vesicle/ectoderm contact may produce microcornea.[80]

TREATMENT

Microcornea is nonprogressive, and no treatment is necessary.

PROGNOSIS

Horses with microcornea alone may have normal functional vision. Individuals with additional ocular anomalies may have visual deficits associated with those lesions (i.e., cataract, optic nerve coloboma).

DERMOIDS

PREVALENCE

Corneal dermoids, or choristomas, are nonprogressive, unilateral or bilateral, congenital lesions consisting of epithelial and dermis-like components found in an abnormal location.[81] They have been reported in a group of related Quarter Horses in association with iridal hypoplasia and cataracts,[82] and in a Standardbred colt with no other ocular anomalies.[83]

CLINICAL APPEARANCE

As a congenital defect, corneal dermoids are generally noticed shortly after birth. They frequently arise at the dorsal limbus[82] and are variably pigmented and potentially haired corneal masses (Fig. 5-12). Irritation may be caused if large lesions impair eyelid closure or if hairs from the lesion cause trichiasis.

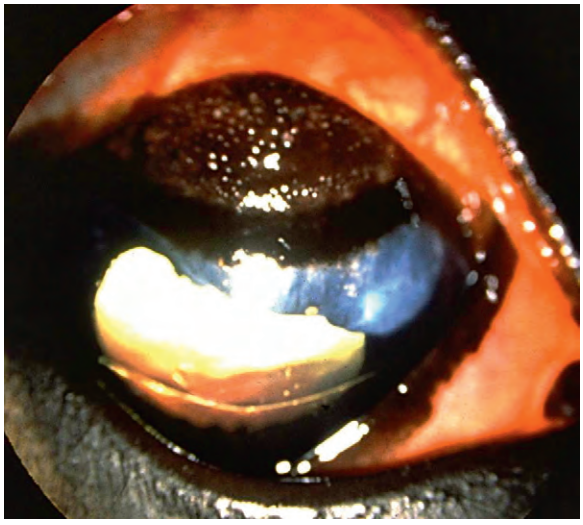


Figure 5-12. Clinical photograph of corneal dermoid located at the dorsal limbus. Note pigmentation, hair, and skin typical of a corneal dermoid. (Photograph courtesy Dr. David Wilkie.)

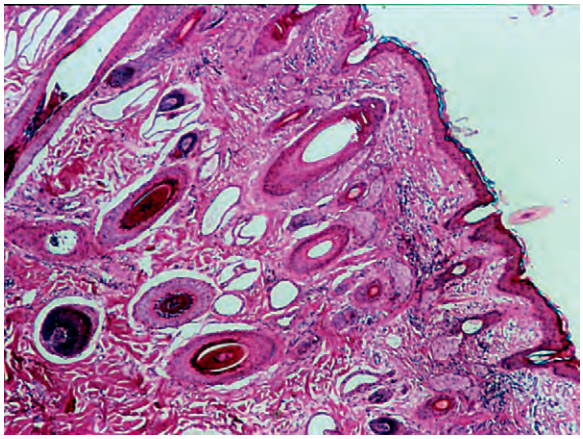


Figure 5-13. H&E-stained section of corneal specimen demonstrating hair follicles and adnexal structures typical of a corneal dermoid (×20).

Table 5-5 | **Appropriate Medical Therapy for an Uncomplicated, Superficial Corneal Ulcer**

DRUG CLASS	EXAMPLE(S)	FORMULATION(S)	DOSE/FREQUENCY
Prophylactic antibiotic	Neomycin/polymyxin B/gramicidin; oxytetracycline; erythromycin; chloramphenicol	Ointment Solution	¼-inch strip q6-8h 0.1-0.2 mL q6-8h
Therapeutic mydriatic cycloplegic	Atropine	Ointment Solution	¼-inch strip q24-48h 0.1-0.2 mL q24-48h
Systemic NSAID	Flunixin meglumine	Paste Solution	1.1 mg/kg PO or IV q12h

DIFFERENTIAL DIAGNOSES

Variation in the presence of pigment and hairs, the overall appearance of a dermoid, and the age at which the lesion is noticed affect possible differential diagnoses. Other types of neoplasia, reactive lymphoid hyperplasia, nodular episcleritis, and parasitic granulomas should be considered. Definitive diagnosis is based on clinical appearance and histopathologic evaluation, which identifies keratinized stratified squamous epithelium (versus the nonkeratinized epithelium of the cornea) overlying an irregular dermis with hair follicles, sweat glands, and sebaceous glands (Fig. 5-13).[84] At the axial margin, collagen within the dermis blends with that of the corneal stroma, and the epidermis becomes contiguous with the corneal epithelium. The presence of cartilage or bone within a dermoid is rare.

PATHOGENESIS

Although the pathogenesis is unknown, abnormal differentiation of a group of cells early in development may be involved. Alternately, defective induction of surface ectoderm by the optic vesicle, producing skin rather than corneal epithelium, may be involved.[85]

TREATMENT

Most corneal dermoids are superficial, and removal by keratectomy provides complete resolution. Postoperative care is as for an uncomplicated superficial ulcer (Table 5-5), including prophylactic topical antibiotic administration until the keratectomy site has reepithelialized, and topical atropine and systemic analgesics (nonsteroidal antiinflammatory drugs [NSAIDs]) if reflex anterior uveitis is present. Dermoids may extend into the stroma, so thorough evaluation with magnification and surgical removal with appropriate instrumentation and magnification is necessary for safe removal.

PROGNOSIS

Dermoids are nonprogressive, and surgical removal is curative.

CORNEAL VASCULARIZATION

PREVALENCE

Congenital corneal vascularization has been reported in a Thoroughbred foal examined at 16 hours of age[86] and in a foal associated with congenital corneal melanosis.[87] Temporary partial corneal vascularization and cloudiness that resolved spontaneously was reported in a group of foals.[88]

CLINICAL APPEARANCE

Clinical signs reported in previous cases of congenital corneal vascularization include bulbar and palpebral conjunctivitis, hyperemia, and vascular congestion.[86] Short, straight, superficial perilimbal vessels extended from the conjunctiva onto the dorsal cornea.[86] No other ocular abnormalities or signs of ocular pain were present.

DIFFERENTIAL DIAGNOSIS

Differential diagnoses for corneal vascularization include causes of corneal irritation: birth trauma, entropion, corneal ulceration, foreign bodies, keratoconjunctivitis sicca (KCS),

neutrophilic keratitis, anterior uveitis, and congenital glaucoma to name a few.

PATHOGENESIS

In the reported cases, pathogenesis is unknown but believed to be associated with late-term intrauterine influences (such as trauma or inflammation). Late in gestation, the eyelids are no longer attached to each other, allowing exposure of the corneas and conjunctiva to amniotic fluid and any irritants within it.[86]

TREATMENT

In the reported cases, no treatment was necessary. Thorough evaluation to rule out other causes of keratitis is appropriate, however, in the event treatment of other conditions may be necessary.

PROGNOSIS

In the reported cases, corneal vascularization spontaneously resolved without complications. In one foal, resolution occurred within 7 days of birth, without treatment.[86]

ACQUIRED DISEASES

ULCERATIVE KERATITIS: NONINFECTIOUS

SUPERFICIAL CORNEAL ULCERATION

PREVALENCE

An uncomplicated superficial ulcer is one without cellular infiltrate or stromal loss that has been present for less than 7 days. Their frequent occurrence in horses is thought to be due in part to the prominence of the equine globe, increasing the propensity for injury.

CLINICAL APPEARANCE

Owing to the extensive sensory innervation of the superficial cornea, horses with ulcers are generally in significant discomfort. Blepharospasm, blepharoedema, epiphora, and conjunctival hyperemia are common. Mild edema may be present in the involved area only, and fluorescein dye uptake will be clearly demarcated (Fig. 5-14). No cellular infiltrate, visible as yellowish opacification of the lesion, is present in an uncomplicated ulcer. As an isolated process, superficial ulceration should not be accompanied by vascularization of the cornea; however, mild secondary anterior uveitis manifesting as miosis, mild aqueous flare, and/or hypotony may be present.

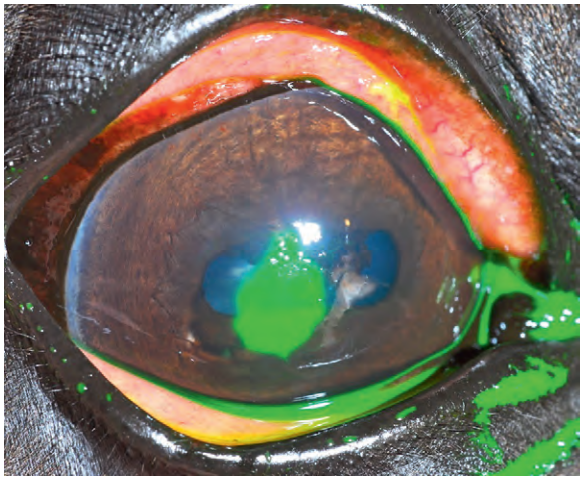


Figure 5-14. Clinical photograph of a superficial corneal ulceration in a 12-year-old Saddlebred gelding, demonstrating retention of fluorescein dye and clearly demarcated epithelial edges.

DIFFERENTIAL DIAGNOSIS

Differential diagnoses for superficial ulcers without cellular infiltrate include nonhealing (indolent) ulcers, herpesvirus keratitis, self-trauma-induced ulcerations, and ulcerations secondary to adnexal abnormalities (i.e., congenital or acquired eyelid defects, trichiasis, conjunctival foreign bodies). It is important to consider infiltrative ulcerative diseases prior to arriving at a diagnosis of an uncomplicated ulcer, however, considering the risk of undetected bacterial or fungal infections.

PATHOGENESIS

Corneal ulcerations generally occur secondary to trauma, either exogenous (i.e., sticks, fences, hay, foreign bodies) or endogenous (i.e., entropion, trichiasis). Provided the inciting cause is eliminated and infection is avoided, simple loss of the corneal epithelium should heal within 5 to 7 days. As detailed previously, healing occurs through a process of cessation of basal cell mitosis, migration of a sheet of cells to cover the wound bed, and restoration of mitotic activity to regenerate normal epithelial architecture.[8] In humans, this process is completed at a rate of 60 to 80 µm/hr, corresponding to healing a 6-mm defect within 48 hours.[8] Horses reepithelialize at a rate of 0.6 mm/day.[32] If the basement membrane is damaged, complete healing may be prolonged as reestablishment of basement membrane and associated adhesion complexes must occur.

TREATMENT

The primary components of therapy for an uncomplicated superficial ulcer are topical antibiotic therapy as prophylaxis for infection, a therapeutic mydriatic-cycloplegic to treat the secondary anterior uveitis that occurs with corneal ulceration, and a systemic NSAID for the uveitis and analgesia (see Table 5-5). An appropriate topical ophthalmic antibiotic should be broad-spectrum and minimally epithelial-toxic, such as neomycin/polymyxin B/bacitracin, erythromycin, or oxytetracycline ointments. Tetracyclines have anti-MMP activity, which may help stabilize the protein matrix involved in healing an epithelial wound, and therefore may have added benefit in treatment of superficial ulcerations beyond their antibacterial effect.[89,90] Topical antibiotics are administered ideally every 6 to 8 hours, while the therapeutic mydriatic-cycloplegic is generally needed once every 24 to 48 hours.

PROGNOSIS

Provided the underlying cause is identified and corrected, and infection is avoided, uncomplicated superficial ulcers should heal within 7 days. If these criteria are not met and the ulcer does not heal or worsens, it is no longer considered an uncomplicated ulceration.

NONHEALING CORNEAL ULCERATION

PREVALENCE

Nonhealing corneal ulcers are refractory to healing in the absence of a persistent underlying cause or infection.[91-93] Their

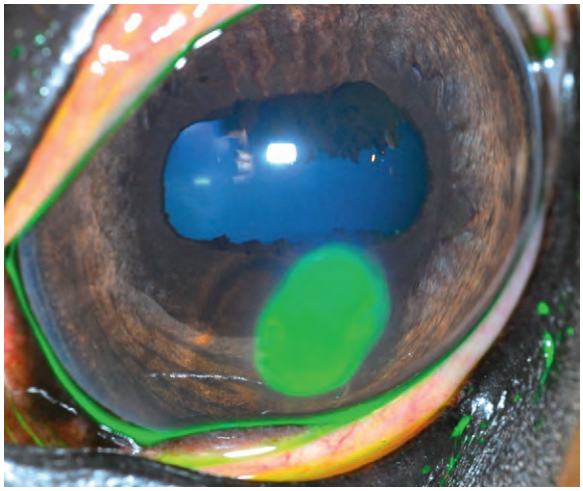


Figure 5-15. Clinical photograph of a nonhealing corneal ulcer. Note the loose epithelial edges under which fluorescein dye is migrating, typical of a nonhealing corneal ulcer.

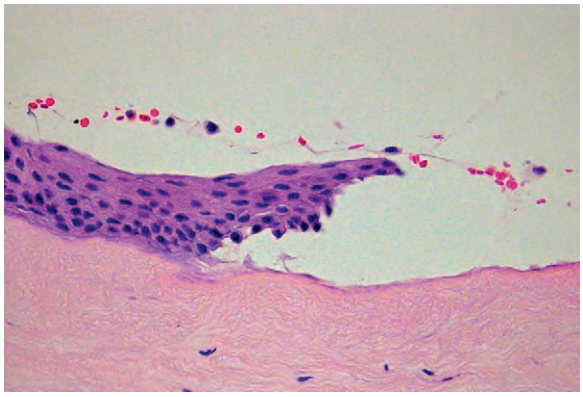


Figure 5-16. Histologic image of a superficial keratectomy sample from a horse with a nonhealing ulcer (H&E ×400). Note nonadherent epithelial "lip" with irregular basement membrane in ulcerated area.

prevalence is unknown, but numerous reports of such ulcers exist in veterinary literature.[91-96] The reported mean ages have been 12 years in a group of 10 horses[95] and 13.7 years in a group of 23 horses,[93] although affected horses have ranged from 2 to 38 years.[91,94,96] No gender or breed predilection has been identified, with breeds affected including Thoroughbreds, Quarter Horses, Arabians, Warmbloods, Appaloosas, and others.[91,93,95,96]

CLINICAL APPEARANCE

Nonhealing ulcers are chronic, with mean duration prior to referral reported from 17 days[93] to 54 days.[95] Variable signs of discomfort are present, independent of duration. Involvement is limited to the corneal epithelium, and neither ongoing mechanical trauma nor evidence of infection is present. Nonadherent epithelial edges, identified by leakage of fluorescein underneath the epithelium surrounding a well-defined area of ulceration, are a consistent finding (Fig. 5-15).[93,95] Mild superficial edema without clinically evident cellular infiltration may be present. Corneal vascularization is present in as many as 34.8% of cases, independent of duration.[93,95] Signs of mild reflex anterior uveitis, such as miosis or aqueous flare, may be present.

DIFFERENTIAL DIAGNOSES

As with any corneal ulcer, it is important to identify and eliminate the underlying cause, as well as rule out infection. Underlying causes to consider include eyelid abnormalities (entropion, ectropion, trichiasis), qualitative or quantitative tear film abnormalities, and preexisting corneal disease (degeneration, dystrophy, bullous keratopathy). Cytology and bacterial (aerobic, anaerobic) and fungal cultures should be performed to rule out infection. Histopathology may be performed on corneal biopsy specimens, with discontinuous, disorganized, hyperplastic epithelium, increased numbers of stromal fibroblasts, variable vascularization, and variable presence of inflammatory cells reported previously in affected horses (Fig. 5-16).[93] Changes reported via light and electron microscopic evaluation of corneal specimens in affected dogs include the presence of an epithelial lip and epithelial dysmaturation, a periodic acid Schiff (PAS)-positive superficial stromal acellular hyalinized zone beneath an absent or discontinuous epithelial basement membrane, variable (generally mild) leukocytic cellular infiltration, and variable stromal spindle cell proliferation.[97]

PATHOGENESIS

While not investigated in horses, the pathogenesis of nonhealing ulceration has been evaluated in dogs.[97-99] The basement membrane discontinuity and superficial stromal hyaline membrane identified in dogs with nonhealing ulcers are not present in dogs with chronic corneal wounds, indicating that extracellular matrix and anterior stromal abnormalities may inhibit the formation of adhesion complexes critical for attachment of the healing epithelium.[97] Also in dogs with nonhealing ulcers, alterations in corneal innervation develop in the stroma surrounding the lesion, possibly as an attempt to aide healing.[99]

MEDICAL TREATMENT

Medical therapy for a nonhealing ulcer follows the same principles as for an uncomplicated superficial ulcer (see Table 5-5). Topical prophylactic antibiotic administration (every 6 to 8 hours), topical therapeutic mydriatic-cycloplegic administration (every 12 to 48 hours), and systemic NSAID administration are indicated. Because degradation of the extracellular matrix integral for epithelial migration has been implicated in the pathogenesis of nonhealing ulcers in other species,[100,101] administration of an anticollagenase (i.e., topical tetracycline, topical serum, EDTA) may also be included in the therapeutic regimen.

SURGICAL TREATMENT

Epithelial débridement is the initial therapeutic step, performed to remove nonadherent epithelium, delineate the true margins of the defect, and stimulate migration of surrounding basal cells to assist healing.[102,103] Following an auriculopalpebral nerve block and application of topical ocular anesthetic, dry cotton-tipped applicators are rubbed over the corneal surface, removing abnormal epithelium while leaving normal, healthy epithelium attached (Fig. 5-17). Therapeutic soft contact lenses may be placed to provide comfort and potentially stimulate epithelial cell adhesion.[104] Additional therapies, including thermal cautery, grid keratotomy, and superficial keratectomy, address the underlying anterior stromal abnormality. Multifocal superficial stromal burns created by use of thermal cautery,

Figure 5-17. Clinical photograph demonstrating appropriate technique for débridement of nonadherent epithelial edges. The cotton swab will remove abnormal epithelium, leaving normal (adherent) epithelium intact.

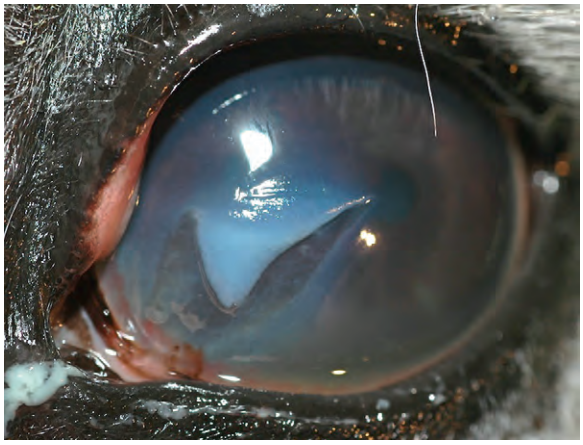


Figure 5-18. Clinical photograph of 24-year-old Arabian gelding with a partial-thickness corneal laceration. Edges of flap have curled under and flap is edematous, giving it a cloudy appearance. Pupil is miotic and anterior chamber is cloudy, indicative of reflex anterior uveitis.

located throughout the ulcer bed and within the surrounding 1 mm of normal epithelium, alter the abnormal anterior stromal hyalinized zone.[91] A grid keratotomy, performed by creating a hatched grid across the entire ulcer bed through any remaining basement membrane, exposes epithelial cells to stromal collagen type I, which is believed to promote more effective cell attachment.[105-107] A grid keratotomy may enable extension and entrapment of subclinical infection into the anterior stroma; it should be performed with caution in geographic regions with a high prevalence of bacterial and fungal keratitis. Superficial keratectomy involves removal of the entire abnormal basement membrane and anterior stroma associated with the defect, allowing the resulting wound to heal by second intention (see Corneal Surgery section for more details).[108,109] Following each of these procedures, medical therapy is indicated as described earlier.

PROGNOSIS

With appropriate combination of medical and surgical therapy, the prognosis for nonhealing ulcers is good. In a study involving 23 horses, those treated with débridement alone healed in a mean of 15.3 days, those treated with a grid keratotomy healed in a mean of 16 days, and those receiving superficial keratectomy healed in 23 days.[93] It is important to note, however, that only 63% of those treated with débridement alone healed, while 78% to 80% of those treated with grid keratotomy or superficial keratectomy healed. In a study of 10 horses receiving grid keratotomy, mean healing time for 7 of the patients was just over 8 days.[95] These horses healed with minimal corneal vascularization or edema, which reportedly resolved. Two of the horses experienced complications attributed to viral keratitis, but no other problems were noted. Thermal cautery resulted in healing of nonhealing ulcers within 2 weeks in two horses with unilateral disease, with no reports of complications.[91]

TRAUMATIC CORNEAL WOUNDS

PREVALENCE

Traumatic corneal wounds, including foreign bodies, partial- and full-thickness lacerations, and iris prolapse, are encountered with relative frequency in horses because of the prominence of their globe and the presence of unavoidable hazards in their environment.[110,111] A study of corneal lacerations in horses identified blunt trauma as the cause in 46.5% (20/43 eyes) versus sharp trauma in 23.3% (10/43 eyes) and undetermined causes in 30.2% (13/43 eyes).[110] Iris prolapse developed in 46.9% of perforations from infected corneal ulcers and from trauma-induced full-thickness corneal lacerations (15 of 32 eyes each). Iris prolapse occurred in 6.2% (2 of 32) of eyes with ruptured deep stromal abscesses.[111] A retrospective study of scleral rupture in three horses identified the rupture at the corneolimbal junction, presumably associated with trauma.[112]

CLINICAL APPEARANCE

Regardless of the depth or extent of the wound, signs of significant ocular pain will be present, including most notably blepharospasm, blepharoedema, enophthalmos, and epiphora. Conjunctival hyperemia may be marked, and conjunctival foreign bodies (palpebral, bulbar, or posterior aspect of third eyelid) may be identified. Fluorescein dye uptake and corneal edema will likely be present surrounding a corneal foreign body (if present) or in association with the corneal wound (Fig. 5-18). If the laceration is full thickness, the globe may be visibly smaller, the wound may be sealed by a fibrin plug or iris (iris prolapse), and the anterior chamber may be shallow (Fig. 5-19). In horses with scleral rupture presumed to be associated with blunt trauma, full-thickness limbal wounds were visible in each of three cases.[112] The degree of associated anterior uveitis varies. Superficial corneal foreign bodies may have minimal anterior uveitis, whereas deep or penetrating foreign bodies or lacerations will be accompanied by significant miosis, flare, hypopyon, and hyphema. Variable involvement of the posterior segment may be present, manifesting as cataract, retinal detachment, or vitreal hemorrhage.[112]

DIFFERENTIAL DIAGNOSES

The main differential diagnosis for corneal laceration is corneal ulceration (which lacerations are a form of), while differential diagnoses for iris prolapse include descemetocele, anterior synechia, neoplasia, corneal foreign body, and corneal sequestrum. Definitive diagnosis of traumatic keratitis is based on thorough

ophthalmic examination, including fluorescein dye application and careful assessment for degree of intraocular involvement. Traumatic corneal wounds, whether partial or full thickness, will likely be accompanied by a greater degree of intraocular inflammation than other diseases such as corneal neoplasia or sequestrum. Ocular ultrasound may also be performed, but extreme caution should be exercised if full-thickness wounds are suspected so as to avoid further damage. If necessary, transpalpebral ultrasound is recommended to avoid contact of lubricant, which is toxic, with intraocular structures. Appropriate sedation and local anesthetic blocks are critical for thorough evaluation of a painful traumatized eye. Corneal cytology and cultures (aerobic bacterial, anaerobic bacterial, and fungal) are recommended if infection is suspected.

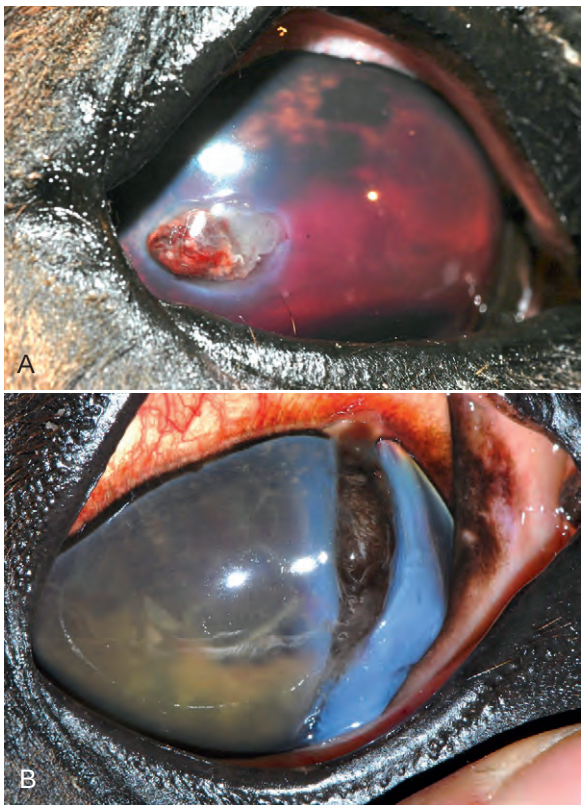


Figure 5-19. **A,** Clinical photograph of a full-thickness corneal perforation in a 6-year-old Paint Horse mare. Wound is sealed with a combination of iris, blood, and fibrin. Significant hyphema and miosis are present, along with the appearance of a shallow anterior chamber, consistent with collapse of the globe. **B,** Clinical photograph of a vertically oriented full-thickness corneal laceration in a 12-year-old Thoroughbred mare. Edges of wound are edematous, and wound is sealed with iris. Pupil is miotic, inflammatory debris is present in anterior chamber, and globe appears small, consistent with globe collapse.

PATHOGENESIS

Corneal and conjunctival foreign bodies may be readily encountered in the environment. If lodged within the conjunctiva or fornices, they may cause continued corneal irritation, resulting in ulceration, vascularization, and possibly infection. If lodged within the cornea, they may cause mild irritation and vascularization, or they may cause more significant irritation, vascularization, anterior uveitis, and infection. Partial- and full-thickness lacerations may result from blunt trauma (i.e., collision with stationary objects or kicks from other horses) or from sharp trauma (i.e., nails, sticks). Owing to the distribution of forces within the eye, blunt trauma may also be associated with lens luxations, retinal detachment, and intraocular hemorrhage, whereas objects producing sharp trauma may penetrate the cornea, iris, and lens (Fig. 5-20). Iris prolapse may result from sharp trauma or rupture of an infected corneal ulcer or stromal abscess (Fig. 5-21).

MEDICAL TREATMENT

If a conjunctival or superficial foreign body is present, it should be removed provided removal can be safely performed without risk of further corneal penetration. To facilitate removal, the horse should be sedated, auriculopalpebral and frontal nerve blocks performed, and topical anesthetic administered. A Kimura platinum spatula or dry cotton swab may be used to remove the foreign body. Corneal cytology and bacterial and fungal cultures should be performed, and topical medical therapy as for a superficial corneal ulcer should be administered (see Table 5-5).

If a deep or full-thickness corneal wound or foreign body is present, the eye should be minimally manipulated to avoid causing more extensive damage as surgical options are

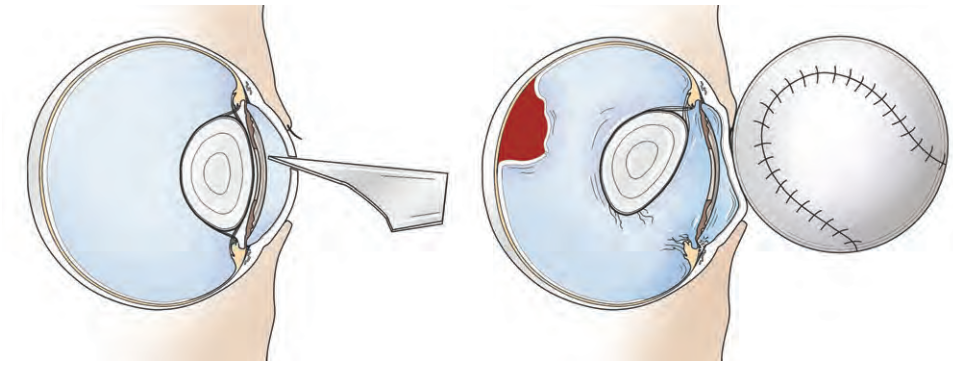


Figure 5-20. Diagram showing effects of sharp versus blunt ocular trauma. Sharp trauma is more likely to severely affect the cornea, anterior chamber, and lens; blunt trauma is more likely to produce severe posterior segment damage.

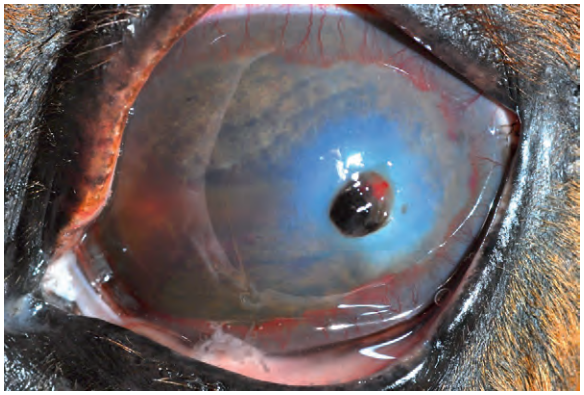


Figure 5-21. Clinical photograph of 13-year-old Quarter Horse gelding with corneal perforation and iris prolapse, with associated miosis, anterior uveitis, and shallow anterior chamber. Note the perilimbal corneal vascularization indicative of a chronic process.

considered. If surgical therapy is not necessary or not practical, medical therapy should be directed toward preventing or eliminating infection, controlling surface and intraocular inflammation, and managing pain. If they can be safely obtained without causing further ocular damage, samples for corneal cytology and bacterial and fungal cultures should be collected prior to administering medications. Topical therapeutic antibiotics (i.e., aminoglycosides, fluoroquinolones) should be administered as often as every 2 to 4 hours in conjunction with systemic antibiotics, as for infectious keratitis (see later section). Topical and oral antifungal agents may be indicated depending on the geographic locale (see later section). Topical therapeutic mydriatic-cycloplegics should be administered as frequently as every 6 to 8 hours, ideally minimizing potentially sight-threatening complications such as posterior synechiae and cataracts that may occur due to severe secondary anterior uveitis. Systemic analgesia should be provided, generally with NSAIDs. Placement of a subpalpebral lavage catheter (see Chapter 2) is indicated to minimize periocular manipulation with administration of medications.

SURGICAL TREATMENT

Surgical treatment to stabilize the corneal surface is indicated for corneal lesions extending deeper than one-third the corneal stromal depth, irregular lesions, and large lesions.[110] Apposition of linear laceration edges may be achieved with primary suturing, and a conjunctival graft may be placed over the laceration to provide greater stabilization and immediate blood supply (Fig. 5-22).[110,111] Full-thickness or irregular lesions may require grafting procedures such as conjunctival, amnion, or autogenous corneal grafts.[111] Surgical repair of an iris prolapse may involve resection of exposed unviable iris or replacement of viable iris into the anterior chamber, followed by closure of the remaining full-thickness wound. For detailed description of surgical procedures, see the surgical portion of this chapter.

PROGNOSIS

The prognosis for eyes with superficial conjunctival or corneal foreign bodies is good, provided the foreign body is removed and infection is avoided. The prognosis for lacerations depends upon depth, length, coinciding intraocular inflammation, and presence or absence of infection. Lacerations greater than

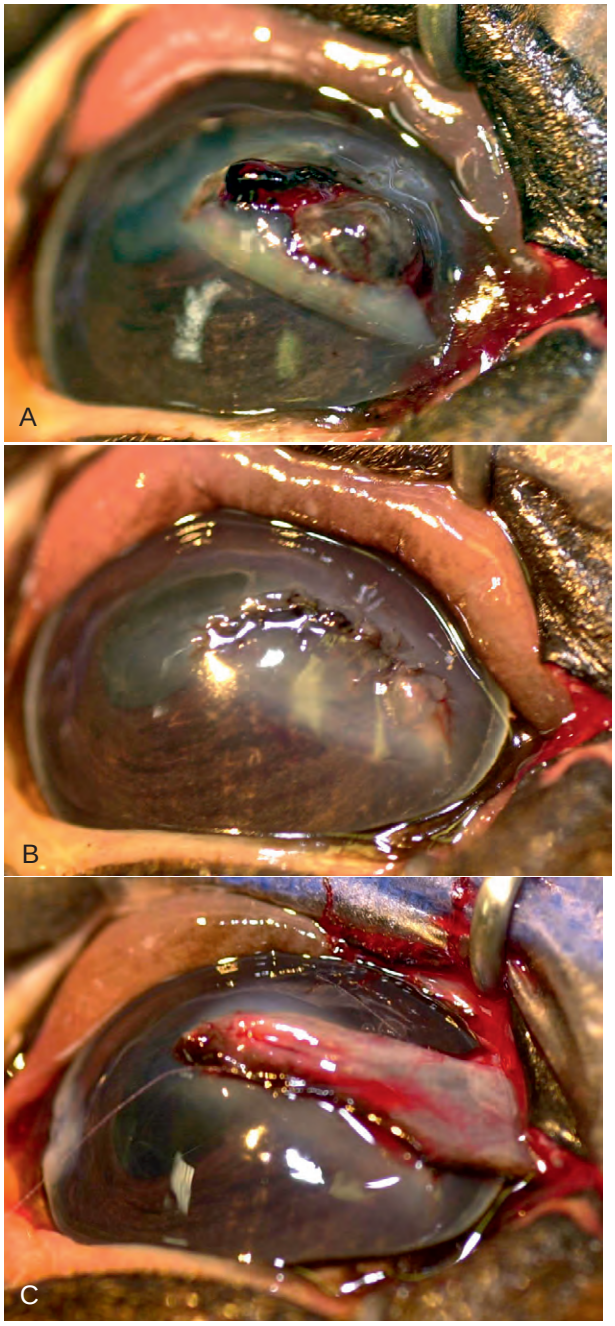


Figure 5-22. A, Large horizontal full-thickness corneal laceration with iris prolapse. **B,** Direct suturing of corneal laceration after replacement of iris prolapse back into anterior chamber. **C,** Placement of a conjunctival graft over laceration repair to provide greater stabilization and immediate blood supply. Horse regained vision in this eye and returned to its previous level of performance.

15 mm in length, those that cross the limbus, and those with keratomalacia or hyphema have a poor prognosis.[111] Additional poor prognostic indicators include long-standing or large wounds, lens capsule rupture, and lens luxation.[110] Iris prolapse resulting from corneal trauma (rather than extension of ulcerative keratitis) has a more favorable prognosis for globe retention (12/15 [80%] versus 10/15 [67%], respectively),[111] but both are associated with a poor prognosis for vision retention.

Only 6/15 (40%) of horses with perforated ulcers and 5/15 (33%) of horses with full-thickness lacerations retained vision.[111] All three globes with corneolimbal rupture necessitated enucleation.[112]

EOSINOPHILIC KERATITIS/ KERATOCONJUNCTIVITIS

PREVALENCE

Eosinophilic keratitis or keratoconjunctivitis (EK), rarely identified in the horse, has been reported in a Quarter Horse,[113] five Thoroughbreds, and two Arabians.[114] In the report of seven cases, the majority (5/7 horses) had bilateral EK, with younger horses apparently predisposed (mean age 3 years, range 1 to 5 years).[114]

CLINICAL APPEARANCE

Horses with EK may initially present with nonspecific signs of mild to severe blepharospasm, chemosis, conjunctival hyperemia, epiphora, and caseous mucoid discharge, although the degree of pain may be variable.[113-115] The corneal lesions appear as whitish necrotic plaques, frequently overlying superficial corneal ulceration, typically beginning in the peripheral cornea and extending to the axial cornea (Fig. 5-23). Concurrent KCS and lacrimal adenitis may be present.[116,117]

DIFFERENTIAL DIAGNOSIS

Differential diagnoses for EK include other infiltrative, potentially ulcerative corneal diseases: fungal, bacterial, parasitic *(Onchocerca cervicalis)*, or viral (equine herpesvirus 2 [EHV-2]) keratitis; immune-mediated (lymphoplasmacytic) keratitis; neoplasia (squamous cell carcinoma [SCC], mastocytoma); calcium or lipid deposition; or fibrosis. Diagnosis is most readily made based on corneal cytology, which demonstrates abundant eosinophils accompanied by smaller numbers of mast cells, lymphocytes, plasma cells, and neutrophils (Fig. 5-24).[113,114] Histopathologic evaluation of the plaques reveals subepithelial foci of fragmented and degenerated collagen fibers infiltrated by eosinophils and neutrophils, with smaller numbers of lymphocytes, plasma cells, and macrophages (Fig. 5-25).[113] A brightly eosinophilic, acellular, granular material may surround the plaques.[113] No evidence of parasitic microfilaria has been identified.[114]

PATHOGENESIS

Although eosinophils are characteristically identified as part of a response to allergic or parasitic stimuli, the pathogenesis of EK remains unknown. Environmental irritants or allergens, fomites, organisms, improper management practices, or seasonal changes may initiate EK.[114,116] Mild eosinophilic infiltration has inconsistently been identified in conjunction with

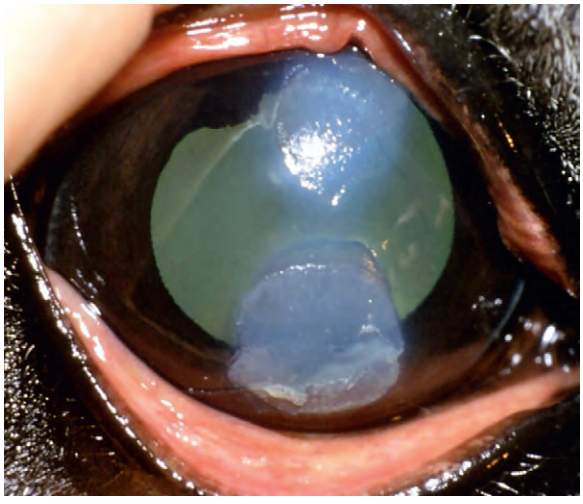


Figure 5-23. Clinical photograph of eosinophilic keratitis. Two paracentral, ulcerated, infiltrated lesions are present.

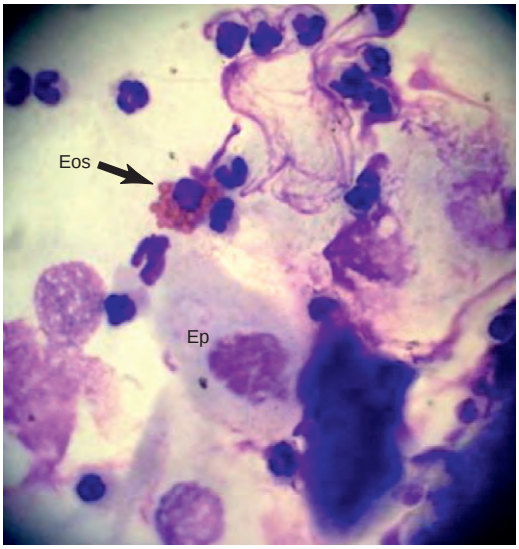


Figure 5-24. Cytologic sample obtained from cornea of a horse with eosinophilic keratitis. An eosinophil (Eos) *(arrow)* is present among epithelial cells (Ep) and other inflammatory cells. (Photograph courtesy Dr. Ann Dwyer.)

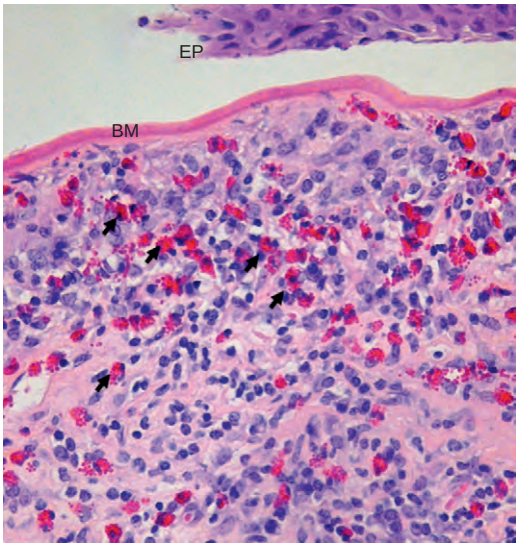


Figure 5-25. Histologic image of superficial keratectomy sample obtained from a horse with eosinophilic keratitis. Note numerous pink eosinophils *(arrows)* interspersed among mixed inflammatory cells. Epithelial basement membrane (BM) appears thickened, and overlying epithelium (EP) is nonadherent (H&E, ×400).

parasitic keratoconjunctivitis,[118] suggesting a possible association in some but not all affected individuals. It has been proposed that an allergic or inflammatory reaction to long-term use of ivermectin as an anthelmintic may also be involved.[114] Mast cell degranulation induced by any of the above factors may recruit eosinophils to the cornea,[114] where eosinophil granule proteins may perpetuate inflammation and inhibit wound healing via cytotoxicity, further mast cell degranulation, and neutrophil activation, as well as by deleteriously affecting epithelial cell morphology and viability.[119] Feline herpesvirus 1 is detected with greater frequency in cats with eosinophilic keratitis than in cats without (76% versus 5.9% polymerase chain reaction [PCR]-positive, respectively),[120] but such evaluation of a possible role of equine herpesvirus in equine EK has not been performed.

MEDICAL TREATMENT

Targeted treatment of the underlying immune component of EK is necessary to achieve resolution, with topical corticosteroids being the treatment of choice, frequently for a prolonged period of time (Table 5-6).[114] Corticosteroid use in the presence of concurrent corneal ulceration increases the risk of secondary infection, but such infection rarely develops in horses with EK. Prophylactic antibiotics should be administered in conjunction with topical steroids. Topical NSAIDs have been reported to increase the severity of EK, possibly by NSAID-induced potentiation of inflammation mediated by leukotriene B4, a major regulator of eosinophilic disease in the horse.[121] Systemic NSAIDs and corticosteroids may be indicated both to control the disease process and provide analgesia. In consideration of the frequent detection of mast cells with eosinophilic disease, topical mast cell stabilizers may also be indicated. Topical cyclosporin 1.5% solution has been evaluated in cats with eosinophilic keratitis and resulted in improvement of lesions within 3 weeks in 31 of 35 cats (88.6%) and no response in the remaining four cats.[122] No similar evaluation of cyclosporin or related immunomodulating drugs has been performed in horses; their use should therefore be subject to caution.

SURGICAL TREATMENT

Superficial keratectomy may shorten the course of the disease, possibly owing to removal of eosinophil granule major basic protein.[123]

PROGNOSIS

EK frequently requires long-term therapy to achieve complete resolution but has an overall good prognosis. Potential recurrence rates are unknown.

SEQUESTRUM

PREVALENCE

Corneal sequestra are rare in the horse, with four cases reported in the veterinary literature, all of which were from Europe.[96,124] Affected breeds include an Arabian, a Shetland pony, a Standardbred, and a Thoroughbred.

CLINICAL APPEARANCE

Affected individuals commonly present with a history of blepharospasm and superficial corneal erosions of weeks to months' duration, with variable epiphora. One case developed in association with keratoconjunctivitis sicca and had a correspondingly dry cornea with mucoid discharge (Fig. 5-26).[124] The sequestrum in that case was clinically similar to those reported in cats, manifesting as a dark brown discoloration of the cornea within a superficial ulceration. In contrast, the bed of the erosion in the other three cases had a grayish opalescent hue.[96] Faint fluorescein dye staining was present in all cases, and vascularization and cellular infiltration were variable.

DIFFERENTIAL DIAGNOSIS

Differential diagnoses include nonhealing ulcer, infectious keratitis (especially fungal plaque), corneal foreign body, band keratopathy, corneal degeneration, and iris prolapse. Cytology and culture and sensitivity should be performed to assess for possible infection. Histopathologic evaluation identifies intensely eosinophilic necrotic corneal stroma, with a superficial Masson's trichrome–positive acellular zone (Fig. 5-27).[124] The case clinically similar to feline sequestra stained negative for PAS and elastin,[124] while the other three cases were PAS and elastin positive.[96]

PATHOGENESIS

As with feline corneal sequestra, the cause of equine sequestra is unknown. A common factor appears to be chronic superficial corneal irritation without significant evidence of infection,

Table 5-6 | **Medical Therapy for Eosinophilic Keratitis/Keratoconjunctivitis**

DRUG CLASS	EXAMPLE(S)	FORMULATION	DOSAGE	OTHER POINTS
Topical corticosteroid	Neomycin/polymyxin/ dexamethasone 0.1%; prednisolone acetate 1%	Ointment Solution Suspension	¼-inch strip q6-8h 0.1-0.2 mL q6-8h	Slowly (over weeks) decrease frequency as lesions improve
Topical therapeutic mydriatic cycloplegic	Atropine	Ointment Solution	¼-inch strip q12-48h 0.1-0.2 mL q12-48h	Frequency depends upon degree of mydriasis achieved between doses
Topical mast cell stabilizers	Olopatadine	Solution	0.1-0.2 mL q6-8h	Slowly decrease frequency as lesions improve
Topical prophylactic antibiotic	See Table 5-5			Used in presence of corneal ulcer
Systemic NSAID	Flunixin meglumine	Paste Solution	1.1 mg/kg PO or IV q12h	
Systemic corticosteroid	Prednisolone	Tablet	0.5 to 1.0 mg/kg PO q12-24h, taper	

Figure 5-26. Enucleated left globe demonstrating corneal ulceration and brown pigmentation of corneal stroma. (Courtesy McClellan Veterinary Ophthalmology, 2000.)

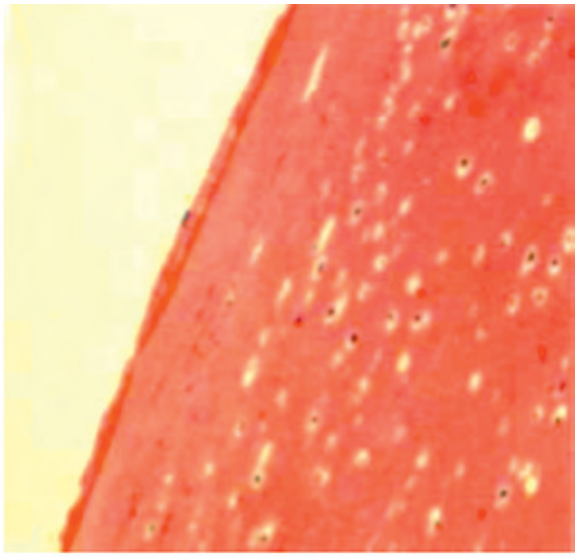


Figure 5-27. Histologic image of superficial axial cornea, demonstrating absence of keratocytes but scattered neutrophils and pyknotic nuclei within the desiccated stroma (H&E ×200). (Courtesy McClellan Veterinary Ophthalmology, 2000.)

producing focal corneal necrosis. Three equine cases differed from the feline disease in that they showed only superficial pigmentation and vascularization,[96] whereas the necrotic region of the fourth case was darkly pigmented and vascularized,[124] as is more typical in the feline form of the disease. The composition of the dark brown discoloration is unknown insofar as Fontana staining for melanin was negative.[124] Proposed theories for the origin of color of feline sequestra include melanin,[125] mineral,[126] iron, copper, and other metals,[125-127] or precorneal tear film components,[128] although no definitive identification has yet been determined.

MEDICAL TREATMENT

Medical therapy as for superficial corneal ulcerations (see Table 5-5) is indicated, but no resolution of sequestration occurred in any cases with medical therapy alone.

SURGICAL TREATMENT

Three horses received superficial keratectomies, leading to resolution without recurrence.[96] The keratectomies extended to one-fourth stromal depth and 1 mm beyond the peripheral edges of the lesion. They were treated postoperatively with a temporary tarsorrhaphy, topical broad-spectrum antibiotics, oral phenylbutazone, and topical atropine. Financial constraints led to enucleation of the fourth horse.[124]

PROGNOSIS

The three cases receiving therapy showed no recurrence for follow-up times ranging from 14 to 36 months.[96]

INDUCED KERATOPATHY: RADIATION THERAPY

PREVALENCE

Few reports exist documenting adverse effects on the equine cornea following radiation therapy administrated to target ocular and periocular tumors. Beta irradiation (strontium-90 [^{90}Sr]) of the cornea following surgical removal of a limbal SCC presumably led to progressive bullous keratopathy and ulceration in a Paint horse,[129] and high-dose gamma irradiation (radioactive gold [^{198}Au]) of a periorbital fibrosarcoma was linked with ulcerative keratitis.[130] Keratitis and corneal ulceration were reported in 6.9% of 115 horses treated with iridium-192.[131]

CLINICAL APPEARANCE

The keratopathy associated with ^{90}Sr application began 10 weeks after the surgical procedure and radiation application, manifesting initially as diffuse edema that progressed over the subsequent 8 weeks to involve 90% of the cornea and include bullae. The eye was not painful, nor did it manifest inflammation over the 1 year of follow-up. A melting ulcer and an iris prolapse were also reported in two horses following treatment with ^{90}Sr, although definite links between the therapy and detrimental side effects were not drawn.[132] Treatment with high-dose gamma radiation induced a central superficial ulcer and multifocal, punctate, fluorescein-negative epithelial defects in the ventral cornea.[130] Additional lesions included iris swelling, miosis, and focal retinal atrophy.

DIFFERENTIAL DIAGNOSIS

Differential diagnoses for radiation-induced corneal damage include other causes of corneal edema (e.g., corneal ulceration, endothelial degeneration, uveitis, glaucoma) and other causes of corneal ulceration and epithelial defects (e.g., trauma, foreign body, infection). A thorough history and ocular exam evaluating for other causes of corneal disease should indicate whether or not a connection between corneal disease and radiation therapy exists.

PATHOGENESIS

Radiation classically has greater effects on rapidly dividing cells, inducing DNA damage via creation of free radicals, ulti-

mately inhibiting neoplastic growth. With its relatively rapid turnover capacity, the corneal epithelium is sensitive to the effects of ocular and periocular radiation therapy. Mechanisms of cell damage include radiolysis of cellular water and decreased renewal of enzyme systems, DNA synthesis, and cellular membrane repair.[133] Effects may be greater in individuals with predisposing factors adversely affecting corneal health, such as deficient tear production, difficulty blinking, or preexisting ulceration.[130]

TREATMENT

Treatment is based on clinical presentation. Topical antimicrobials and lubricants are indicated when ulceration is present, in addition to systemic analgesics (NSAIDs) as necessary (see Table 5-5). If corneal edema is significant and/or accompanied by development of bullae, use of topical hyperosmotic 5% sodium chloride ointment may be indicated.

PROGNOSIS

As evidenced in the ^{90}Sr-treated horse that developed severe irreversible corneal edema, the prognosis for vision in eyes with radiation-induced damage is poor.[129] Additionally, progression of ulcerative disease necessitated enucleation in one horse,[132] indicating a potentially poor prognosis for globe retention in association with radiation damage.

TEAR-DEFICIENCY SYNDROMES

PREVALENCE

Tear-deficiency syndromes, both quantitative (KCS) and qualitative, are much less common in the horse than in the dog. Reported cases have involved predominantly younger horses (1 to 6 years of age), including Thoroughbred, Quarter Horse, Oldenburg, and German Warmblood breeds.[134-139] There is a single report involving a 19-year-old Shetland pony.[124]

CLINICAL APPEARANCE

Clinical manifestations of tear-deficiency syndromes include blepharospasm, conjunctivitis, and mucopurulent ocular discharge in the absence of epiphora.[134] The corneal epithelium will frequently have a hazy, lackluster appearance that may be accompanied by superficial vascularization, recurrent ulceration, and pigmentation.[134,139] Corneal ulcerations that either recur or manifest delayed healing are common.[134-137] Schirmer tear test (STT) I values, representing both basal and reflex tearing, may be markedly decreased from the normal range of 12.72[140] to 24.8[141] mm wetting/min.[134,136-138] Depending upon the underlying cause of the tear-deficiency syndrome, additional clinical signs may be present, such as facial nerve paralysis (ear droop, decreased palpebral reflex, deviation of the muzzle),[135,137] anisocoria,[137] facial swelling,[135] or ocular surface masses.[138]

DIFFERENTIAL DIAGNOSES

Differential diagnoses for deficient quantity or quality of tear film production include conditions that extensively damage the lacrimal tissue or periocular innervation provided by the trigeminal (sensory) or facial (motor) nerves. Lacrimal tissue damage may be associated with inherited or acquired conformational eyelid defects, infectious or immune-mediated blepharitis,[134,135] or extensive eyelid or third eyelid neoplasia. Damage to periocular innervation is frequently associated with direct or compressive nerve injury from fractures to the mandibular ramus or stylohyoid bone and associated inflammation.[135,137]

PATHOGENESIS

Congenital or acquired eyelid conformational defects (e.g., coloboma, laceration, ectropion/entropion, neoplasia) may sufficiently damage lacrimal gland tissue in the dorsolateral or third eyelid, inhibiting gland function or effective spreading of the tear film.[142] Direct damage to the lacrimal gland may also be associated with inflammatory disease or toxins.[142] One horse was diagnosed with KCS secondary to eosinophilic granulomatous dacryoadenitis, possibly secondary to parasite *(Thelazia lacrimalis)* infestation and their subsequent death following anthelmintic administration.[138] Eosinophilic infiltration of the glandular tissue in another horse was also reported, possibly associated with an adverse drug reaction or parasitic infection.[134] Locoweed poisoning leads to vacuolation of glandular tissue and possibly KCS as well.[143] In contrast to the dog, systemic administration of sulfonamides does not appear to cause KCS in the horse.[144]

Innervation of the lacrimal gland is provided by the parasympathetic nervous system, with preganglionic fibers originating in the parasympathetic nucleus of the facial nerve. While not definitively known, it is suspected that they travel initially as part of the facial nerve, then branch off as the major petrosal nerve to the pterygopalatine ganglion, where they diverge and travel with the zygomatic branch of CN V to reach the lacrimal gland (Fig. 5-28).[142,145] Damage anywhere along this pathway, or damage to the afferent arm provided by CN V, may produce KCS. Neurologic dysfunction has been reported to result following fracture of the ramus of the mandible, with direct trauma to the facial nerve resulting in facial nerve paralysis initially, and presumed ascending perineural inflammation producing KCS.[135] Fracture of the stylohyoid bone has also produced facial nerve paralysis and associated KCS.[137] Topical parasympatholytic therapy, such as atropine therapy for anterior uveitis, may transiently decrease tear production.[134]

MEDICAL TREATMENT

Treatment of tear-deficiency syndromes involves use of tear-replacement and tear-stimulant medications. Tear-replacement therapy, such as ointments or gels containing hyaluronate solutions,[146] may need to be administered as frequently as every 2 to 6 hours, which may be impractical in horses. Lacrimostimulant medications that increase tear production by suppressing the inflammatory response that impairs gland function and improving conjunctival mucin stores (topical cyclosporin, tacrolimus) are recommended for immune-mediated KCS in dogs. Topical 2% cyclosporin has been administered twice daily to horses with KCS and has improved clinical signs,[134,136] but controlled studies of efficacy and safety in horses have not been performed. Pilocarpine, which provides direct neurologic stimulation to the gland, is administered orally to dogs with neurogenic KCS and has been administered topically to horses at 0.125%, 0.25%, and 4% concentrations, producing mixed results.[134,136-138] Topical prophylactic antibiotic therapy and systemic NSAIDs should be provided in the presence of corneal ulceration, and treatment of any coinciding condition (e.g., fracture) should be treated appropriately.

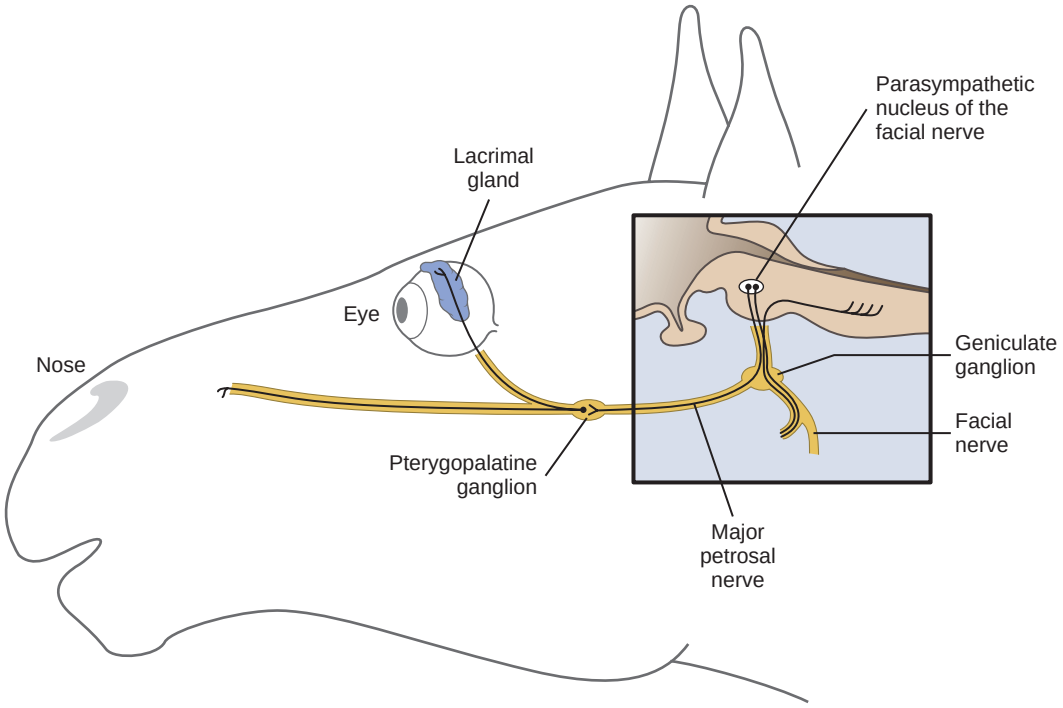


Figure 5-28. Diagram of suspected pathway of lacrimal gland innervation in the horse.

SURGICAL TREATMENT

Parotid duct transposition, in which salivary secretions are used to lubricate the ocular surface, has been successfully performed in one horse.[147] However, the suggestion has been made that bilateral surgery may impair the digestive capability of the horse and therefore should be avoided.[138] A partial temporary or permanent tarsorrhaphy may be needed in some cases to protect the cornea, especially in eyes with facial nerve dysfunction. Enucleation has also been performed in cases when treatment is not feasible.[124]

PROGNOSIS

Inflammatory dacryoadenitis has a poor long-term prognosis, considering the need to continue treatment presumably for the lifetime of the animal. Administration of 2% cyclosporin in two horses, one with eosinophilic dacryoadenitis confirmed on histopathology, led to improvement in clinical signs over the short term, but one horse was lost to follow-up within weeks, and the other was euthanatized owing to the need for continued treatment.[134,136] Administration of pilocarpine (0.125% to 4%) produced mixed results.[134,136-138] KCS resulting from traumatic fractures has a good prognosis; resolution of inflammation associated with the fracture coincided with improvement in clinical signs, allowing discontinuation of therapy.[135,137]

CHEMICAL BURNS

PREVALENCE

Chemical burns are infrequently reported in horses, but considering environmental, stabling, and handling variables, they likely occur more than noted in the literature. The single case report in the literature involves a mare with presumed organophosphate fly-wipe contact.[148]

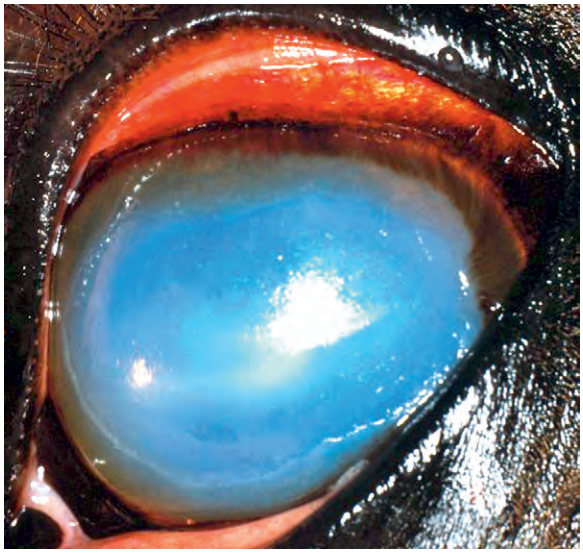


Figure 5-29. Clinical photograph of the left eye of a 16-year-old Thoroughbred mare with ulcerative chemical keratitis induced by accidental contact with formalin.

CLINICAL APPEARANCE

As in any species, clinical signs of chemical burns are nonspecific, consisting primarily of varying degrees of blepharospasm, epiphora, chemosis, and conjunctival hyperemia (Fig. 5-29).[149,150] Corneal opacification is frequent, either due to edema associated with ulceration or keratomalacia associated with collagenase activity. Corneal ulceration may be extensive, and involvement of the adnexa/periocular area may be present.

DIFFERENTIAL DIAGNOSES

If ulceration is superficial, differential diagnoses include sterile nonhealing ulcers or immune-mediated keratitis. If ulceration is more extensive and associated with keratomalacia, differential diagnoses should include infected (bacterial, fungal) or sterile melting ulcers. Other differentials to consider include calcific band keratopathy, corneal degeneration, or stromal abscesses. The history and possible associated lesions (e.g., periocular damage) may help rule out certain diagnoses.

PATHOGENESIS

Acidic (pH < 7.0) chemical burns coagulate epithelial surface proteins, creating a barrier to further penetration of the agent into the cornea or intraocular environment.[149] In contrast, alkali (pH > 7.0) burns denature epithelial surface proteins, severely impairing barrier function and allowing penetration into the deeper cornea and intraocular environment, causing a relatively greater degree of damage.[150] Additional factors pertinent to the agent that play a role in ocular damage include its concentration and temperature and the force with which it contacts the cornea.[149] The neutrophilic inflammatory response is very detrimental, occurring initially 12 to 24 hours after injury then again at 21 days.[151]

MEDICAL TREATMENT

The most important aspect of treatment of corneal burns is immediate, copious, prolonged irrigation.[149] Specific solutions able to neutralize both acid and alkali burns have been formulated,[150] but time is critical, and readily available eye wash, lactated ringer's solution (LRS), or even tap water are more clinically useful. Care should be taken to ensure that all quadrants of the cornea, as well as all aspects of the conjunctiva and fornix, are irrigated. Following irrigation, a prophylactic topical antibiotic, topical mydriatic-cycloplegic, and oral NSAID should be administered to prevent infection and provide analgesia to the compromised ocular surface (see Table 5-5).[149,150] Anticollagenase agents, such as tetracyclines, serum, or ethylenediamine tetraacetic acid (EDTA), may be administered to minimize collagenolysis.[115] Citrate and ascorbic acid have shown use in humans with ocular burns as free-radical scavengers and inhibitors of proteolysis.[149] A mainstay of therapy in human patients with ocular burns is the use of topical corticosteroids,[149,150] but this is not recommended in equine patients, considering the potential for secondary infection and delayed epithelialization in the presence of corneal ulceration.

SURGICAL TREATMENT

In severe cases that do not heal with medical therapy alone, surgical stabilization or reconstruction of the ocular surface may be necessary. Removal of necrotic tissue and placement of conjunctival pedicle grafts, amniotic membrane transplants, or full-thickness corneal grafts (penetrating keratoplasty) may be indicated.

PROGNOSIS

The prognosis for recovery from a chemical corneal burn depends upon the degree of damage of limbal epithelial cells,[149] which serve as the source for regenerating epithelial cells. Treatment may be prolonged, and scarring may be pronounced.

ULCERATIVE KERATITIS: INFECTIOUS

HERPESVIRUS KERATITIS

PREVALENCE

As with herpesvirus in other species, EHV-2 has a high overall seropositivity rate (90%)[152]; however, its association as a causative agent of keratitis in the horse is not clearly defined. A positive correlation was identified in one case series in which PCR of ocular swabs were positive in 12 of 27 horses with ocular disease versus only 2 of 21 horses without.[153] The opposite was found in another study, in which PCR of ocular swabs detected EHV-2 in 4 of 48 (8.3%) of horses with ocular disease and 22 of 77 (28.6%) without.[154] An additional earlier report identified 35 of 80 foals with ocular disease suspected as being related to EHV-2.[155]

CLINICAL APPEARANCE

EHV-2 affects both adult horses and foals and may produce signs of ocular pain, particularly epiphora and blepharospasm.[116,153,155,156] A common clinical manifestation is superficial ulceration (fluorescein positive) or erosion (rose bengal positive) in a multifocal punctate or dendritic pattern (Fig. 5-30). However, a similar pattern of corneal opacification without stain retention may also be present (Fig. 5-31).[116,155-157] Variable degrees of corneal edema and vascularization may

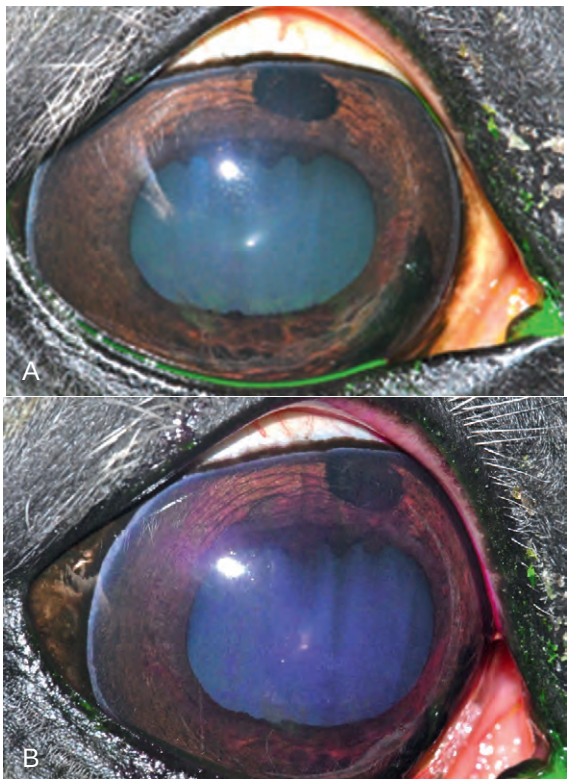


Figure 5-30. **A,** Clinical photograph of the right eye of a 13-year-old Thoroughbred mare with suspected equine herpes virus 2 keratitis, stained with fluorescein dye. Note roughened appearance of cornea, with faint superficial vascularization. **B,** Clinical photograph of same eye in **(A)** following application of rose bengal vital dye. Note the lacy network of dye retention, not present following fluorescein dye application. A focal region of iridal hyperpigmentation is present between 12 and 1 o'clock.

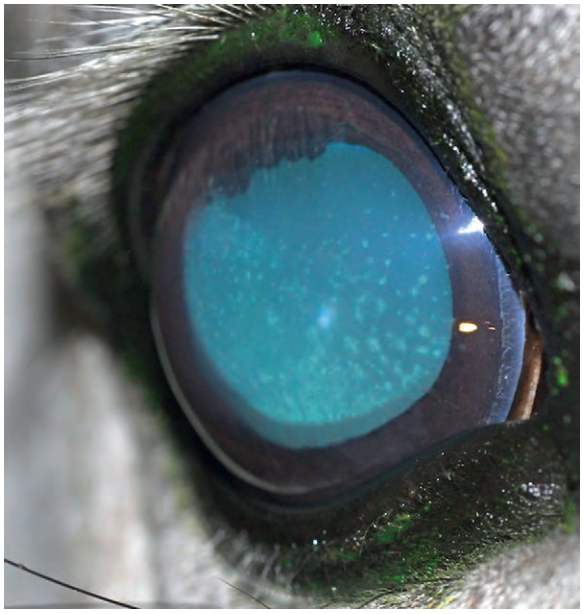


Figure 5-31. Clinical photograph of an 11-year-old Thoroughbred mare with nonulcerative multifocal superficial punctate keratopathy, possibly consistent with equine herpes virus 2 infection.

result.[116] Clinical manifestations of disease caused by EHV-1 are distinctly different and demonstrate nervous system involvement (blindness, strabismus, optic neuritis, exposure keratitis, etc).

DIFFERENTIAL DIAGNOSES

The primary differential diagnosis for ocular disease caused by EHV-2 is early fungal keratitis, which may manifest as multifocal corneal opacification that is either fluorescein positive or negative but stains rose bengal positive.[158] Other diseases to consider include other causes of corneal ulceration (e.g., trauma, foreign body, KCS), as well as nonulcerative corneal opacification (e.g., immune-mediated keratitis, nonulcerative keratouveitis, calcific band keratopathy, corneal degeneration). Confirmation of a diagnosis of herpetic keratitis/keratoconjunctivitis is difficult to obtain because of the high overall prevalence of seropositivity in the equine population and the uncertain connection between identification of EHV-2 in ocular locations and the presence of disease. Diagnosis therefore depends primarily upon ruling out other causes of corneal disease, in conjunction with a positive response to therapy. Virus isolation, electron microscopy, and molecular biology techniques have been used previously to confirm exposure to or infection with EHV-2.[155]

PATHOGENESIS

EHV-2 is a gamma herpesvirus that produces lifelong infections characterized by variable periods of disease recrudescence and latency. Gamma herpesviruses establish latency in lymphocytes, and EHV-2 has also been identified as latent in the trigeminal and ciliary ganglia.[154,159,160] Latency within the trigeminal ganglia may be associated with both surface ocular and other disease processes in which EHV-2 has been implicated (e.g., rhinitis, bronchiolitis, tracheitis, and pneumonia), inasmuch as the ocular and nasal mucosa are both innervated by branches of the trigeminal nerve.[155,159] Reactivation is most likely during periods of stress such as breeding or transport, but the exact mechanism by which EHV-2 causes disease is uncertain.

TREATMENT

While the pharmacokinetic and toxicity patterns for some antiviral drugs have been evaluated in horses, in vitro or in vivo efficacy specifically for EHV-2 has not.[161-164] In other species, topical antivirals are virostatic, with no efficacy versus latent virions,[165] and often must be administered at a high frequency (i.e., minimum 4 to 6 times/day). Treatment of horses with 1% trifluridine and 0.5% idoxuridine has been reported.[156,157] Additionally, topical NSAID administration may be useful in controlling inflammation associated with herpesvirus keratitis.[116] Oral L-lysine supplementation is recommended in other species to control recrudescence of herpetic diseases; it acts by competitively inhibiting the incorporation of arginine into the viral genome, thereby decreasing viral replication. Such supplementation as therapy for herpesvirus has not been evaluated in horses; however, anecdotal evidence suggests that clinical signs may be decreased in horses receiving 10 to 30 g of L-lysine orally once daily.[116] In the presence of corneal ulceration, prophylactic topical antibiotic and oral analgesic therapy (NSAID) is indicated, along with a topical therapeutic mydriatic-cycloplegic agent if reflex anterior uveitis is also present. Administration of a topical corticosteroid is generally not recommended, because immunosuppression may allow increased viral replication.[155]

PROGNOSIS

Considering the recrudescing nature of herpesvirus infections, the prognosis for complete resolution of possible herpetic keratitis/keratoconjunctivitis is variable. Considering that most cases are relatively mild, however, clinical signs are usually successfully managed, and an overall comfortable and visually functional globe is maintained.

BACTERIAL ULCERATIVE KERATITIS

PREVALENCE

Infection of corneal ulcers with bacteria is frequently encountered in horses. In one evaluation of 38 eyes from 37 horses with ulcerative keratitis, only 6 had no bacterial growth.[166] Isolation of either bacteria and/or fungal organisms from horses with undefined extraocular disease identified positive cultures in 98/123 eyes (79.7%), with *Streptococcus* spp. (43.9%), *Staphylococcus* spp. (24.2%), and *Pseudomonas* spp. (13.8%) most frequently identified.[167] In 41 eyes of horses with ulcerative keratitis in the northeast United States, bacteria or fungal organisms were identified on cytology samples from 23/36 eyes (64%) and cultured from 22/39 eyes (56%), eight of which were *Pseudomonas* spp.[168] While *Staph*, *Strep*, and *Pseudomonas* spp. are the most common isolates, numerous other organisms have been reported as either known or presumed pathogenic (Tables 5-7 and 5-8),[166,167,169-181] including anaerobic bacteria, frequently *Clostridium* spp., in 18/140 horses (12.9%) with corneal ulcers, often with coinciding aerobic bacterial growth.[182]

CLINICAL APPEARANCE

Bacterial keratitis frequently results in nonspecific clinical signs such as blepharospasm, epiphora, ocular discharge,

Table 5-7 | **Number of Presumed Pathogenic, Gram-Negative Bacterial Isolates Identified in Horses With Ulcerative Bacterial Keratitis**

AUTHOR ORGANISM GENUS (RESPIRATION, MORPHOLOGY)	UTTER ET AL., 2009[168]	LEDBETTER AND SCARLETT, 2008[182]	KELLER AND HENDRIX, 2005[169]	LASSALINE ET AL., 2005[183]	SAUER ET AL., 2003[170]	REBHUN ET AL., 1999[172]	SWEENEY AND IRBY, 1996[184]	MOORE ET AL., 1995[171]
Acinetobacter (A, bacilli)	6		3		2			3
Actinobacillus (FA, rod)			1					2
Aeromonas (FA, bacilli)						1		
Burkholderia (A, rod)					1			
Enterobacter (FA, rod)	3				2			
Escherichia (FA, rod)			1		5			4
Flavobacterium (FA, rod)					2			
Fusobacterium (AN, rod)		1						
Klebsiella (FA, rod)			1					1
Moraxella (A, diplococci)					1			3
Neisseria (A, diplococci)			1					
Ochrobactrum (A, coccobacillus)					1			
Pantoea (FA, rod)			1					
Pasteurella (FA, pleomorphic)					2			1
Proteus (FA, rod)			1					
Providencia (FA, rod)								2
Pseudomonas (A, rod)	5		6	3	15		70	14
Salmonella (FA, rod)								
Serratia (FA, rod)			2		3			
Non-fermenting rods			4					

AUTHOR ORGANISM GENUS (RESPIRATION, MORPHOLOGY)	ADAMSON AND JANG, 1985[173]	MCLAUGHLIN ET AL., 1983[167]	MOORE ET AL., 1983[166]	DIVERS AND GEORGE, 1982[174]	REBHUN, 1981[175]	GELATT 1974[176]
Acinetobacter (A, bacilli)		1	6			
Actinobacillus (FA, rod)						
Aeromonas (FA, bacilli)						
Burkholderia (A, rod)						
Enterobacter (FA, rod)		8	9		1	
Escherichia (FA, rod)		5	2		1	
Flavobacterium (FA, rod)		1				
Fusobacterium (AN, rod)						
Klebsiella (FA, rod)		3	4			
Moraxella (A, diplococci)		3				
Neisseria (A, diplococci)		1				
Ochrobactrum (A, coccobacillus)						
Pantoea (FA, rod)						
Pasteurella (FA, pleomorphic)		3	1			
Proteus (FA, rod)		4	1			
Providencia (FA, rod)			1			
Pseudomonas (A, rod)		17	10	1		1
Salmonella (FA, rod)	1					
Serratia (FA, rod)						
Nonfermenting rods						

A, Aerobe; *AN*, anaerobe; *FA*, facultative anaerobe.

photophobia, and corneal opacification,[185,186] which are initially indistinguishable from other ocular diseases, including uncomplicated superficial corneal ulcers. With bacterial infection however, stromal involvement produces marked edema, cellular infiltration, and deepening of the ulcer bed, potentially accompanied by keratomalacia, or "melting" (Figs. 5-32 and 5-33).[185] Anterior uveitis may be severe, manifesting as miosis, flare, hypopyon, and hypotony. If the ulceration was chronic prior to establishment of infection, corneal vascularization may be present (Fig. 5-34). Definitive correlation of a certain clinical appearance with individual agents is not possible, but reports of ulcerative keratitis associated with β-hemolytic *Streptococcus equi* documented severe keratomalacia in 11/11 eyes and marked uveitis in 8/11 eyes.[179] *Pseudomonas* spp. are frequently rapidly progressive and also associated with marked uveitis.[166,184] In humans, anaerobic bacterial infections of the cornea are associated with a characteristic clinical appearance of gaseous stromal bubbles and a frothy coagulum in the ulcer bed.[187,188] These characteristics were not consistently noted in horses with anaerobic infections, but

Table 5-8 | **Number of Presumed Pathogenic, Gram-Positive Bacterial Isolates Identified in Horses With Ulcerative Bacterial Keratitis**

AUTHOR ORGANISM GENUS (RESPIRATION, MORPHOLOGY)	UTTER, ET AL., 2009[168]	LEDBETTER AND SCARLETT, 2008[182]	KELLER AND HENDRIX 2005[169]	SAUER ET AL., 2003[170]	SANCHEZ ET AL., 2001[180]	BROOKS ET AL., 2000[179]	CULLEN AND GRAHN, 2000[177]
Actinomyces (FA, rod)		2					
Bacillus (A, rod)							
Clostridium (AN, rod)		16					
Corynebacterium (FA, rod)	3		2	1			
Diplococcus							
Enterococcus (FA, cocci/diplo)				1			
Eubacterium (AN, rod)		1					
Listeria (FA, rod/bacilli)					1		
Micrococcus (A, cocci)				1			
Nocardia (A, rod)							
Peptostreptococcus (AN, cocci)		1					
Propionibacterium (AN, rod)		1					
Staphylococcus spp. (FA, cocci)				2			
Coagulase-positive *Staphylococcus* (i.e., *S. aureus*) (cocci)	2		3	4			
Coagulase-negative *Staphylococcus* (i.e., *S. epidermidis*)			3	1			
Streptococcus spp. (FA, cocci)				1			
α-Hemolytic *Streptococcus* spp. (i.e., *S. pneumoniae*)	1		1				
β-Hemolytic *Streptococcus* spp. (i.e., *S. equi zooepidemicus*)	5		18	15		11	1
Nonhemolytic *Streptococcus* spp.			2				
Nutritionally variant streptococci							
Macrococcus			1				
Actinomyces (FA, rod)		2					
Bacillus (A, rod)					13		
Clostridium (AN, rod)	2						
Corynebacterium (FA, rod)		5			4	1	
Diplococcus					1		
Enterococcus (FA, cocci/diplo)							
Eubacterium (AN, rod)							
Listeria (FA, rod/bacilli)							
Micrococcus (A, cocci)							
Nocardia (A, rod)					1		
Peptostreptococcus (AN, cocci)							
Propionibacterium (AN, rod)							
Staphylococcus spp. (FA, cocci)		16			17	5	
Coagulase-positive *Staphylococcus* (i.e., *S. aureus*) (cocci)							
Coagulase-negative *Staphylococcus* (i.e., *S. epidermidis*)							
Streptococcus spp. (FA, cocci)					22		
α-Hemolytic *Streptococcus* spp. (i.e., S. pneumoniae)		6					
β-Hemolytic *Streptococcus* spp. (i.e., *S. equi zooepidemicus*)		10			32	3	1
Nonhemolytic *Streptococcus* spp.							
Nutritionally variant streptococci			35	24			
Macrococcus							

A, Aerobe; *AN*, anaerobe; *FA*, facultative aerobe.

in one study all infected ulcers were stromal, and most had keratomalacia.[182]

DIFFERENTIAL DIAGNOSES

Differential diagnoses for bacterial keratitis include other infectious infiltrative ulcerative diseases (fungal keratitis, herpesvirus keratitis, foreign body) and noninfectious infiltrative ulcerative diseases (sterile keratitis, immune-mediated keratitis, eosinophilic keratoconjunctivitis). Nonulcerative conditions should also be considered: stromal abscess, nonulcerative keratouveitis, corneal degeneration, calcific band keratopathy, and corneal neoplasia. Marked ocular discomfort, the clinical appearance of cellular infiltrate (whitish-yellowish corneal opacification), corneal edema, and anterior uveitis typically distinguish infiltrative ulcerative diseases from uninfiltrated (i.e., simple superficial ulcer, nonhealing ulcer). Definitive diagnosis is based on a combination of corneal cytology and bacterial culture and sensitivity. See Chapters 1 and 2 for a

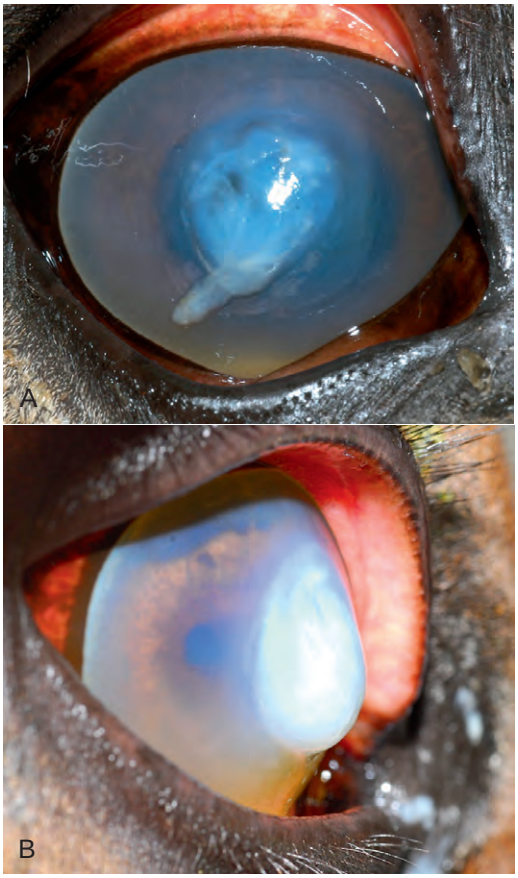


Figure 5-32. **A,** Clinical photograph of 5-year-old Quarter Horse mare with an axial melting corneal ulcer. The malacic cornea is edematous and mildly infiltrated and is sloughing ventrally. Surrounding cornea is edematous, and hypopyon is visible in the ventral anterior chamber. **B,** Clinical photograph of a 14-year-old Quarter Horse gelding with an axial melting corneal ulcer. The malacic cornea is distorting the contour of the globe. Pupil is miotic; yellowish discoloration of ventral anterior chamber is suggestive of hypopyon, consistent with reflex anterior uveitis.

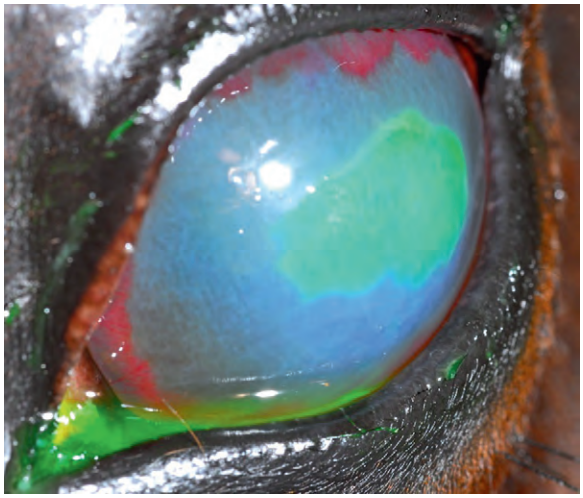


Figure 5-34. Clinical photograph of 7-year-old Arabian gelding with a central superficial corneal ulceration. Extensive perilimbal vascularization and diffuse corneal edema are indicative of a chronic, potentially more severe disease process than is expected with an uncomplicated superficial corneal ulcer.

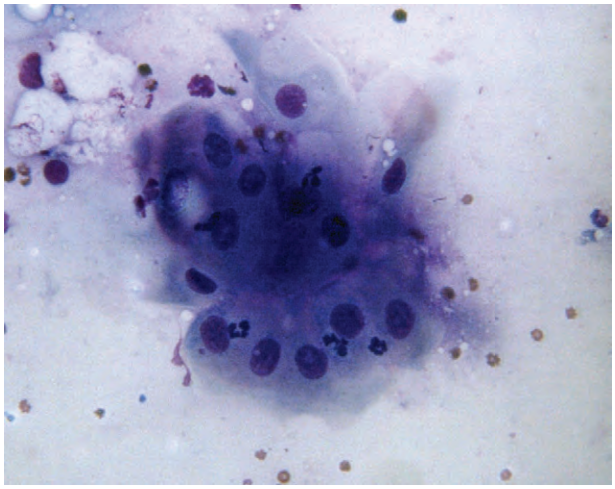


Figure 5-35. Cytology of bacterial and neutrophilic keratitis. There is a central clump of epithelial cells with neutrophils (Diff-Quik Stain ×100).

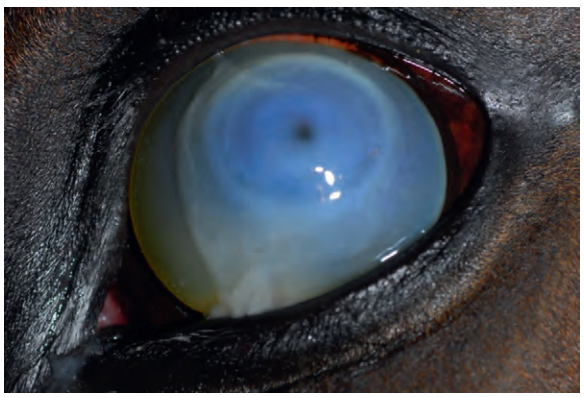


Figure 5-33. Clinical photograph of 4-year-old Hanoverian mare with an extensive melting corneal ulcer, which has progressed to formation of a descemetocele (dark area in center of circular melt). Entire surrounding cornea is edematous, and hypopyon is present in the ventral anterior chamber. Pupil not visible with direct illumination.

description of the technique of collecting and interpreting corneal cultures and cytology. Corneal cytology with Gram or Wright-Giemsa staining may determine the presence of extracellular or intracellular bacteria, in addition to significant inflammatory cell infiltration, providing rapid results that are used to guide therapy (Fig. 5-35). Culture and sensitivity should also be performed to allow more effective management for cases not responding to initial empiric therapy. A study evaluating relative efficacy of cytology, cultures, or both in evaluation of animals with infectious ulcerative keratitis identified 26/48 animals with cytology suggestive of infection and 29/48 with positive cultures.[189]

PATHOGENESIS

The corneal epithelium is an effective barrier to infection by normal resident ocular microflora. In its absence, however, normally nonpathogenic surface ocular bacteria and known pathogenic species adhere to and invade the exposed basement

membrane and stroma, establishing infection and prompting inflammatory cell influx. Overproduction of proteases (relative to antiproteases) by the invading organism, inflammatory cells, epithelial cells, and stromal fibroblasts initiates corneal digestion,[49,50,57,63,190-193] resulting in extensive keratomalacia characteristic of corneal melting. The most significant proteinases include matrix metalloproteinases (MMP)-2 and -9 and neutrophil elastase, which have been identified in increased amounts in the tear film of ulcerated equine eyes.[53] Additionally, total tear film proteolytic activity increases in the presence of ulcers and decreases as ulcers heal.[61] While the described process is not specific to particular bacteria, some bacteria also have individual virulence factors that increase their pathogenicity. Specifically, *Staphylococcus aureus* is able to resist phagocytosis following invasion of tissue[194] and produces the toxins hyaluronidase,[195] alpha toxin,[196,197] and leukocidins.[198] *Pseudomonas aeruginosa* uses pili to adhere to corneal epithelium, facilitating migration to the corneal stroma where it produces exotoxins, endotoxins, and proteases.[199-201] β-Hemolytic *Streptococcus* spp. also produce an exotoxin that facilitates corneal destruction.[202,203] Controlling these processes (discussed later) is vital to controlling the overall disease progression.

Topical antibiotic therapy may predispose to infection by inhibiting growth of normal bacteria which produce substances that exert an inhibitory effect on other microorganisms, and by shifting the bacterial population to predominantly gram-negative organisms.[185] Topical corticosteroid therapy may increase the likelihood of infection by decreasing local immunity[204] and delaying reepithelialization of bacterial ulcers.[205] A recent study evaluating the effect of treatment with topical antibiotics and corticosteroids on the ocular surface microflora in normal equine eyes did not support this theory, however, instead showing only a transient decrease in microflora growth with no increase in gram-negative organisms throughout the course of treatment.[14] In the presence of corneal disease, it is possible that topical therapy may have different effects on microflora population.[14]

Horses with chronic dermatologic disease, ocular trauma, preexisting corneal disease, or previous ocular surgery have a higher risk of developing anaerobic bacterial infections of their corneal ulcers, frequently with concurrent aerobic infection.[182] Predisposing diseases are thought to create a low oxygen tension environment conducive to growth of anaerobic bacteria, whereas aerobic organisms utilize oxygen and produce nutrients, growth factors, energy substrates, and protective enzymes that facilitate growth of anaerobic organisms.[206-208] Once infection is established, anaerobes cause significant corneal pathology by elaborating toxins, metabolites, enzymes, and degradation products and stimulating potentially destructive corneal immune responses.[209-211]

MEDICAL THERAPY

To control infection, inflammation, and pain and decrease unregulated proteolysis, aggressive medical therapy is indicated in cases of confirmed or suspected bacterial keratitis (Table 5-9). Placement of a subpalpebral lavage catheter (see Chapter 2) is appropriate to facilitate frequent administration of multiple medications to a painful eye, with minimal risk to an already compromised cornea.

Topical therapeutic antibiotics, administered every 2 to 6 hours, are selected based on initial cytology results, pending culture and sensitivity results. In general, fluoroquinolones should be considered to be therapeutic antibiotics only, while most other topical antibiotics may be either prophylactic or therapeutic, depending upon both the organism and previous therapy. Variable susceptibility patterns and increasing resistance have been reported across isolate, time, and geographic location for common bacterial pathogens, emphasizing the importance of sensitivity testing in each case. A study of bacteria isolated from horses with ulcerative keratitis in Tennessee from 1993 to 2004 documented susceptibility to ciprofloxacin (5 of 5) and chloramphenicol (17 of 17) for *Streptococcus equi* subspecies *zooepidemicus;* however, resistance was documented to the components of common triple antibiotic preparations (neomycin, polymyxin B, bacitracin) and other aminoglycosides, particularly tobramycin (12 of 13).[169] A similar pattern was reported in two evaluations of *Streptococcus* isolates from Florida,[170] although susceptibility to

Table 5-9 | **Medical Therapy for an Infected Corneal Ulcer: Bacterial**

DRUG CLASS	EXAMPLE(S)	FORMULATION(S)	DOSE	OTHER POINTS
Topical therapeutic antibiotic	Gram-positive: moxifloxacin, chloramphenicol, neomycin, bacitracin	Ointment†	¼-inch strip q2-4h	
	Gram-negative: ciprofloxacin, ofloxacin, aminoglycosides, chloramphenicol,* neomycin, polymyxin B	Solution	0.1-0.2 mL q2-4h	
Topical therapeutic mydriatic-cycloplegic	Atropine	Ointment† Solution	¼-inch strip q12-24h 0.1-0.2 mL q12-24h	Frequency is based on degree of mydriasis achieved between doses
Topical antiprotease	See Table 5-10			
Systemic NSAID	Flunixin meglumine	Paste Solution	1.1 mg/kg PO or IV q12h	
Systemic antibiotic	Trimethoprim sulfamethoxazole (T)	Varies with drug	20-30 mg/kg PO q12h (T)	
	Doxycycline (D)		10-20 mg/kg PO q12h (D)	
	Potassium penicillin (P)		20,000 U/kg IV q6h (P)	
	Gentamicin (G)		4-6.6 mg/kg IM or IV q24h (G)	

*Not effective versus *Pseudomonas* spp.
†Avoid administering a topical ointment if a full-thickness corneal wound is present or may occur.

enrofloxacin was lower.[179] All *Pseudomonas aeruginosa* isolates from Tennessee were sensitive to aminoglycosides (11/11) and fluoroquinolones (6/6),[169] results similar to those in previous reports documenting susceptibilities of *Pseudomonas* spp. to aminoglycosides ranging from 85% to 93%.[171,184] In contrast, a study of isolates from horses in Florida from 1991 to 2000 found a significant increase in resistance of *Pseudomonas* isolates to gentamicin.[170] *Pseudomonas aeruginosa* isolates from human ocular disease have lower in vitro susceptibility to moxifloxacin than ciprofloxacin.[212,213] Considering this accumulated information, identification of gram-positive organisms may indicate topical chloramphenicol or fluoroquinolones as good empiric therapy, while identification of gram-negative organisms may provide indication for aminoglycosides or fluoroquinolones. In the presence of increasing resistance patterns, however, the importance of determining susceptibility patterns for individual isolates cannot be overemphasized. For example, in the 2 decades since the introduction of the fluoroquinolone, ciprofloxacin, increasing in vitro resistance to ciprofloxacin has been identified among gram-positive bacterial isolates from cases of ocular disease in humans.[214-216]

Topical therapeutic mydriatic-cycloplegics (e.g., 1% atropine) are used to control reflex anterior uveitis. Mydriasis decreases the risk of permanent posterior synechia and secondary glaucoma, with the degree of mydriasis correlating to the degree of cycloplegia, an important component of pain relief. In general, more severe corneal disease produces more severe reflex uveitis, which may necessitate treatment as frequently as every 6 hours initially to effectively dilate a miotic pupil and paralyze the ciliary body musculature. As the corneal disease improves, the uveitis will resolve as well (Fig. 5-36). Considering the potential for systemic absorption and subsequent generalized parasympatholytic effects, horses should be closely monitored for signs of gastrointestinal discomfort.[217]

Oral or parenteral antibiotics may also be administered to horses with bacterial keratitis, but the penetration of systemic antibiotics into the cornea, anterior chamber, and preocular tear film is unknown. Drugs able to penetrate to either the intraocular environment or the preocular tear film may be in direct contact with infected corneal tissue, therefore potentially increasing therapeutic efficacy. Corneal vascularization and intraocular inflammation, as present in horses with significant ocular surface disease, may increase drug levels. In addition to its antimicrobial effect, doxycycline has anticollagenolytic and antiinflammatory activity and has been advocated for treatment of ocular surface disease as well as enhancement of corneal repair.[218] Oral administration of doxycycline to horses with uninflamed eyes at a dose of 10 mg/kg twice daily for 5 days did not result in appreciable aqueous or vitreous humor levels in one study,[219] while another study in which normal horses were given 20 mg/kg every 12 hours for 5 doses did find measurable intraocular levels.[220] A third study in which normal horses were administered 20 mg/kg doxycycline once daily found measurable drug levels in the preocular tear film.[221] Other antibiotics (e.g., trimethoprim sulfa, fluoroquinolones) at appropriate doses may also be administered to horses with bacterial keratitis.

Topical antiproteases are administered to control upregulated protease activity. The most commonly used substances include autologous serum, *N*-acetylcysteine, disodium EDTA, tetracyclines, ilomastat, and tetanus antitoxin (Table 5-10). Serum contains α_1-antitrypsin, an endogenous inhibitor of

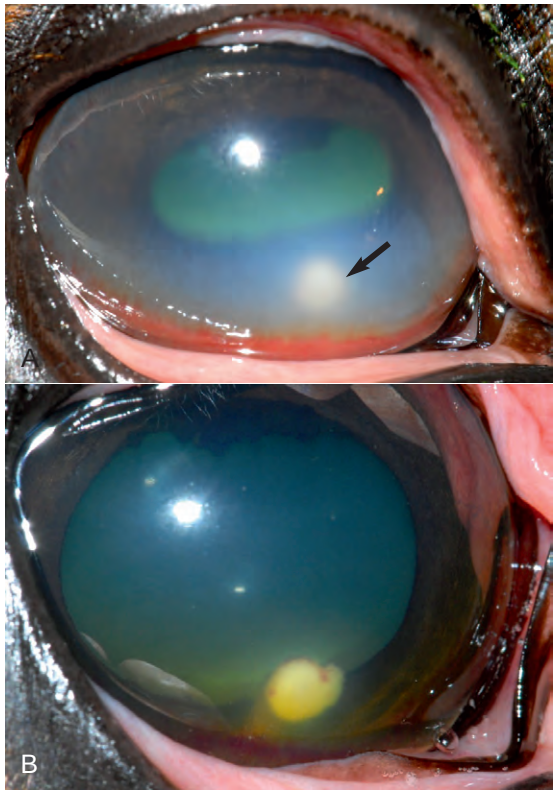


Figure 5-36. A, Clinical photograph of 3-year-old Thoroughbred mare at initial presentation for evaluation of a deep stromal abscess *(arrow)*. Note perilimbal vascularization, moderate corneal edema, and relatively miotic pupil (horse was being treated with topical atropine). **B,** Clinical photograph of same horse following a few days of hospitalization with intensive medical therapy. Vascularization persists, but edema has improved and pupil is mydriatic, indicative of improved control of corneal disease and reflex anterior uveitis.

Table 5-10 | **Antiproteases Commonly Used as Therapy for Infectious Equine Keratitis**

ANTIPROTEASE	MECHANISM OF ACTION	TARGET	ADMINISTRATION
EDTA 0.2%	Zinc and calcium chelation	Matrix metalloproteinases (MMPs)	Topical
Autologous serum	Entrapment of protease		Topical
α_2-macroglobulin		Serine proteases and MMPs	
α_1-antitrypsin		Serine proteases	
Tetracyclines	Zinc and calcium chelation	MMPs	Topical (0.1%) Oral
N-Acetylcysteine 5%-10%	Zinc and calcium chelation	MMPs	Topical
Ilomastat 0.1%	Zinc and calcium chelation	MMPs	Topical

serine proteases, and α_2 macroglobulin, an endogenous inhibitor of serine proteases and MMPs.[50,222,223] *N*-Acetylcysteine inhibits MMPs by chelating calcium and zinc, ions necessary for enzymatic stability and function.[224] Tetracyclines inhibit MMP synthesis and activity, as well as synthesis of other inflammatory mediators (e.g., IL-1, B cells, macrophages).[89,90,225-227] Ilomastat is a synthetic MMP inhibitor,[228] and tetanus antitoxin has been utilized for anticollagenase activity.[229] Comparison of relative efficacy of available anticollagenase substances demonstrates consistently strong antiproteolytic activity for equine serum, EDTA, *N*-acetylcysteine, and tetracyclines. In an in vitro study of tear film from horses with ulcerative keratitis, equine serum and *N*-acetylcysteine decreased total proteolytic activity by 90% and 99%, respectively,[224] and in vitro collagenase activity on corneal tissue samples was decreased by approximately 50%.[53] EDTA and doxycycline decreased total in vitro proteolytic activity by 99% and 96%, respectively.[224] Additional reported techniques include use of heparin[230]; prophylactic subcutaneous vaccination with a combination of *Pseudomonas* spp. protease toxoid, elastase toxoid, and common protective antigen[231]; and intracorneal inoculation of immunoglobulins with antibodies against *P. aeruginosa* protease, elastase, and exotoxin derived from inoculated horses.[232] Due to poor efficacy, toxoid injection and intracorneal inoculation are not currently recommended.

Topical application of growth factors may decrease corneal ulcer healing time by affecting epithelial and keratocyte proliferation, cell migration, and vascular growth.[36] Although epidermal growth factor (EGF) demonstrated favorable effects on epithelial cell and keratocyte proliferation in vitro,[40] evaluation in horses with ulcerative keratitis demonstrated inflammation and scarring sufficient enough to advise against therapeutic use of EGF.[41] Use of other growth factors is not currently advocated; insufficient clinical evaluation has been performed in horses.

Opioid growth factor (OGF) has a demonstrated inhibitory effect on cell division, and blockade of it and its receptor by the strong antagonist naltrexone has been shown to decrease healing time in experimentally created epithelial defects in other species.[45,46] Administration of this or other OGF inhibitors has not been evaluated in the equine eye.

Subconjunctival injections of antibiotics and atropine may be performed if frequent topical application is not possible or if the horse will not tolerate a subpalpebral lavage catheter,[185] but they are not an ideal mode of therapy because of limited subconjunctival space available, the inflammatory response incited, and unpredictable drug bioavailability. This route may lead to high (and therefore ideally therapeutic) corneal drug concentrations, but similar concentrations are likely reached with frequent topical application. Considerable variability in drug properties significantly affects pharmacokinetic parameters; however, relative to topical application, subconjunctival administration of antibiotics results in transiently high corneal drug levels followed by persistent low troughs within 8 hours.[233] This would necessitate injections potentially as frequently as two to three times a day to maintain appropriate drug levels, versus consistent maintenance of drug levels with topical application.[234]

Oral or parenteral antiinflammatory medications are administered for analgesia, with NSAIDs a safer choice than systemic steroids in horses with bacterial keratitis. Steroids may inhibit wound healing and potentiate infection. No studies comparing relative efficacy of various NSAIDs (e.g., phenylbutazone, flunixin meglumine, firocoxib) as ocular analgesics in horses have been performed.

SURGICAL TREATMENT

If medical therapy is delayed or ineffective, surgical therapy may be performed to provide immediate vascular supply (with coinciding provision of fibroblasts, growth factors, and protease inhibitors) and, in some cases, structural support. Indications for surgery include ulcers with greater than 50% stromal loss, ulcers with less than 50% stromal loss but worsening despite appropriate therapy, descemetoceles, and perforated ulcers.[168,185] In addition to depth and infiltration of the ulcer bed, the level of anterior uveitis indicates the degree of control of corneal disease—that is, a superficial bacterial ulcer associated with moderate to severe uveitis suggests worsening or lack of control of corneal infection. Surgical procedures include conjunctival grafts (pedicle, bipedicle, hood, bridge, free island, tarsopalpebral, 360-degree), lamellar corneal grafts (corneoconjunctival transposition, corneoscleral transposition), or grafts with natural (autologous cornea, amnion) or synthetic/biosynthetic (biosys, A-cell) tissues (Fig. 5-37). Details of surgical procedures are described in a later section. Following surgical correction of the ulcer, medical therapy should continue as before, unless a change in antimicrobial selection is indicated.

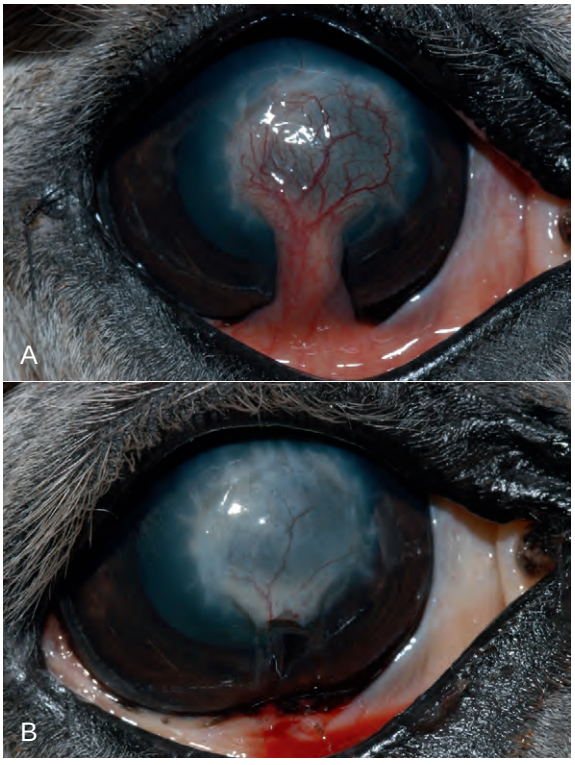


Figure 5-37. Clinical photograph of 14-year-old Quarter Horse gelding with a healed conjunctival graft, approximately 6 weeks postoperative **(A).** Graft remains vascularized and is becoming incorporated into the cornea. Sutures have been resorbed, and the eye is otherwise clear and comfortable. The pedicle of the graft was trimmed at this time **(B).**

PROGNOSIS

The prognosis for retaining a visual, comfortable globe in horses with bacterial keratitis depends upon controlling infection and corneal digestion, as well as coinciding anterior uveitis. A positive visual outcome resulted in 8/11 eyes with β-hemolytic *Streptococcus equi* infection following combination medical and surgical therapy.[179] Of 33 eyes infected with nutritionally variant *Streptococci* spp., 22 healed with vision and one healed without vision following medical therapy, and three healed with vision following surgical therapy.[178] Of 70 eyes with *Pseudomonas* spp.–infected ulcers, 53/70 (76%) retained vision with medical and/or surgical therapy, and the remaining were blind or enucleated.[184]

FUNGAL ULCERATIVE KERATITIS

PREVALENCE

Ulcerative keratomycosis is frequently reported in horses, particularly in warm months and in geographic areas with warm, humid climates,[235-237] with various organisms implicated as pathogenic (Table 5-11).[166,167,171,229,236-254] Of all horses presenting to the University of Florida ophthalmology service from 1987 to 1996, 5.7% (39/684) were diagnosed with fungal keratitis, with 59% culturing *Aspergillus* spp. or *Fusarium* spp.[245] Of 38 eyes with ulcerative keratitis evaluated at the University of Missouri between 1978 and 1981, 15 (40%) were positive for fungal organisms.[166] Of 41 horses with ulcerative keratitis in the northeastern United States from 2000 to 2006, 10 (24%) were diagnosed with keratomycosis, all with *Aspergillus* spp.[168] *Aspergillus* was identified in 4 of 10 horses (40%) with ulcerative keratomycosis in Spain, and *Fusarium*, *Penicillium*, and *Microsporum*, respectively, in each of 3 others.[235] *Aspergillus* spp. and *Fusarium* spp. also predominated in a group of horses with perforating corneal ulcers secondary to infectious keratitis.[111]

Various clinical manifestations of fungal keratitis have been described, which can be broadly grouped into three categories: superficial keratomycosis (including microerosion, superficial ulceration, and plaque formation), stromal ulcerative keratomycosis (including corneal furrowing, melting, and perforation), and stromal abscesses (to be discussed later).[235,244,245,258-260] The various forms of stromal ulcerative keratomycosis appear to be the most common, comprising anywhere from 50% to 80% of

Table 5-11 | **Potentially Pathogenic Fungal Organisms Isolated from Horses with Ulcerative Keratitis**

ORGANISM	NUMBER OF ISOLATES 2000-2009	REFERENCES 2000-2009	NUMBER OF ISOLATES 1990-1999	REFERENCES 1990-1999	NUMBER OF ISOLATES PRIOR TO 1990	REFERENCES PRIOR TO 1990
Alternaria			1	171	5	236,242
Aspergillus	72	255,256,257,168,179,235,258,259	80	171,237,244-249	22	167,236,239-241
Candida	8	256	10	171,244,246,248,250	1	242
Cephalosporium					1	166
Chrysosporium	1	257	1	237		
Cladorrhinum			1	252		
Cladosporium			1	246		
Cryptococcus					2	236
Curunlara			1	237		
Curvularia	2	179,257	1	245		
Cylindrocarpon			6	245,247,251		
Cystodendron			1	245		
Drechslera					1	236
Fusarium	15	235,255-257	23	171,244-248	8	167,229,236,238,240,242
Geotrichum			1	171	1	241
Hanseniaspora			1	246		
Histoplasma	1	254				
Microsporum	3	235,256				
Mucor	2	256	5	246,248	5	236,239,242
Paecilomyces	2	253			2	236
Penicillium	2	235,257	6	171,245-247	6	167,236,242
Pichia	1	256				
Pseudallescheria	1	256	1	246	1	243
Rhizoctonia					1	236
Rhizopus					1	167
Rhodotorula					1	236
Saccharomyces					1	236
Scedosporium	1	256	2	244		
Scopulariopsis	1	257	1	171		
Scytalidium			1	247		
Stemphylium	1	256	1	244		
Torulopsis			2	246,247		
Trichoderma					1	236
Trichophyton			1	237		
Trichosporon	1	256	2	244,248	1	167
Verticillium	1	256				
Unidentified yeast	3	235,256	4	245,247		

cases in various retrospective studies.[235,244,248,258] Superficial ulcerative and stromal abscesses comprise from 17% to 32% and 9% to 33%, respectively, of cases.[244,258]

CLINICAL APPEARANCE

Superficial keratomycosis presenting as microerosions is characterized by multifocal whitish subepithelial opacities staining positively with rose bengal dye, indicative of epithelial devitalization, with or without accompanying ulceration (Figs. 5-38, 5-39).[244,259] Secondary uveitis and signs of ocular pain are variable in affected horses. Superficial ulcerative disease is a slightly more severe presentation and appears as an area of clearly defined epithelial loss with whitish to yellow opacification indicative of cellular infiltration and edema (Fig. 5-40).[229,235,244,251] Signs of ocular pain, secondary uveitis, and corneal vascularization may be variable in affected horses but are generally greater than with microerosions. Alternatively, a whitish-yellow, necrotic plaque of corneal stroma within an area of corneal ulceration ("cake-frosting" appearance), frequently accompanied by significant superficial and stromal corneal vascularization and more prominent pain and anterior uveitis, may be present (Fig. 5-41).[235,243,244,251,258] In these individuals, the ulceration may be superficial, but the necrotic infiltrated region may extend into the stroma.

Stromal keratomycosis may present as either an area of relatively superficial ulceration and infiltration surrounded by a curvilinear region of stromal loss, known as *furrowing* (Fig. 5-42), or as a deeper ulceration (i.e., melting ulcer, descemetocele, or perforated ulcer, with or without iris prolapse [Fig. 5-43]).[244,251,258] The furrow develops at any point in the disease process, frequently occurs rapidly (i.e., over 24 to 48 hours), and generally does not extend around the entire circumference of the infiltrated area. Severe keratomalacia, descemetocele formation, or corneal perforation may succeed the furrow, or they may occur without identifiable preceding furrow formation.[168,235,244,258] Due to the significant corneal disease, ocular pain and anterior uveitis are more severe in individuals with stromal keratomycosis than those with superficial keratomycosis.

DIFFERENTIAL DIAGNOSES

Differential diagnoses for ulcerative fungal keratitis include other infiltrative ulcerative diseases (bacterial keratitis, eosinophilic keratoconjunctivitis, immune-mediated keratitis, herpesvirus keratitis), trauma, corneal degeneration, calcific band keratopathy, and corneal neoplasia. The high degree of variability among clinical presentations mandates a high index of suspicion for fungal keratitis in predisposed geographic regions. In addition, mixed bacterial and fungal infections may be present as frequently as 20% to 33% of the time.[235,245,246] Initial diagnosis is by corneal cytology (Fig. 5-44) and bacterial and fungal cultures, with histopathology and molecular-based techniques (PCR) providing additional confirmation. A study of 48 animals with corneal ulcers receiving cytology and bacterial and fungal cultures identified infection in 35 eyes using cytology, cultures, or both (versus 26 and 29 eyes by cytology or culture alone, respectively).[189] Of 10 eyes with keratomyco-

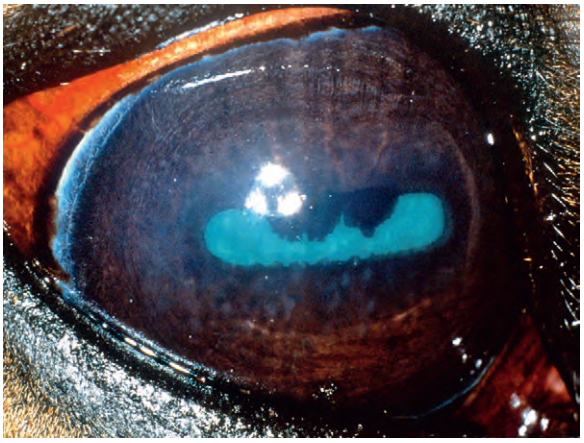


Figure 5-38. Clinical photograph of right eye of a 16-year-old Warmblood mare with superficial punctate ulcerative fungal keratitis. Note multifocal, small (<1 mm) corneal opacities and miotic pupil.

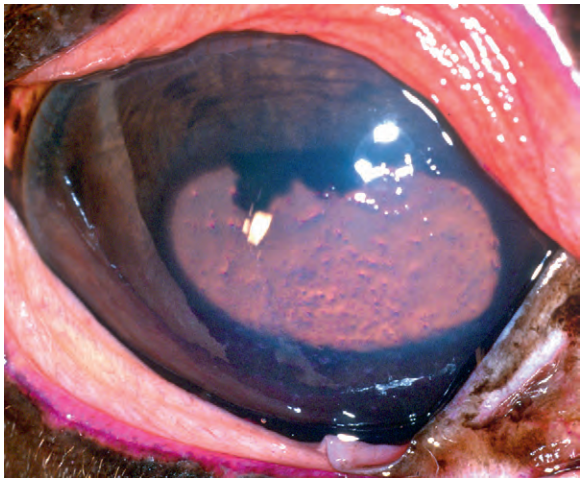


Figure 5-39. Clinical photograph of right eye of a 14-year-old Arabian gelding following application of rose bengal vital dye, demonstrating faint dye retention typical of superficial punctate ulcerative fungal keratitis.

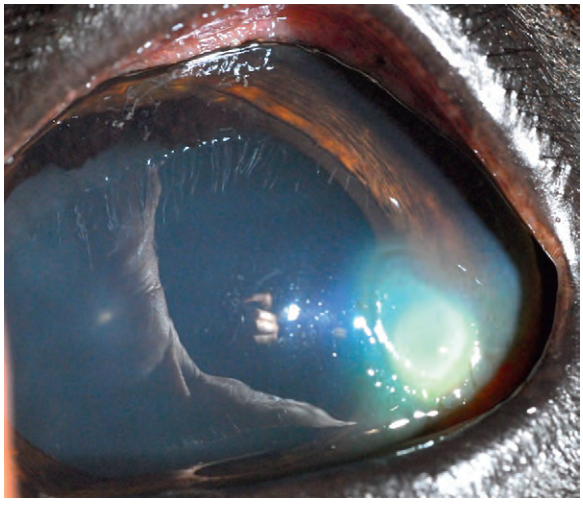


Figure 5-40. Clinical photograph of left eye of a National Spotted Saddle Horse gelding of unknown age with superficial ulcerative fungal keratitis. The yellowish plaque with surrounding area of edema and stromal loss ("furrow") are a typical presentation of fungal keratitis. The horse was being treated with atropine, explaining the mydriasis.

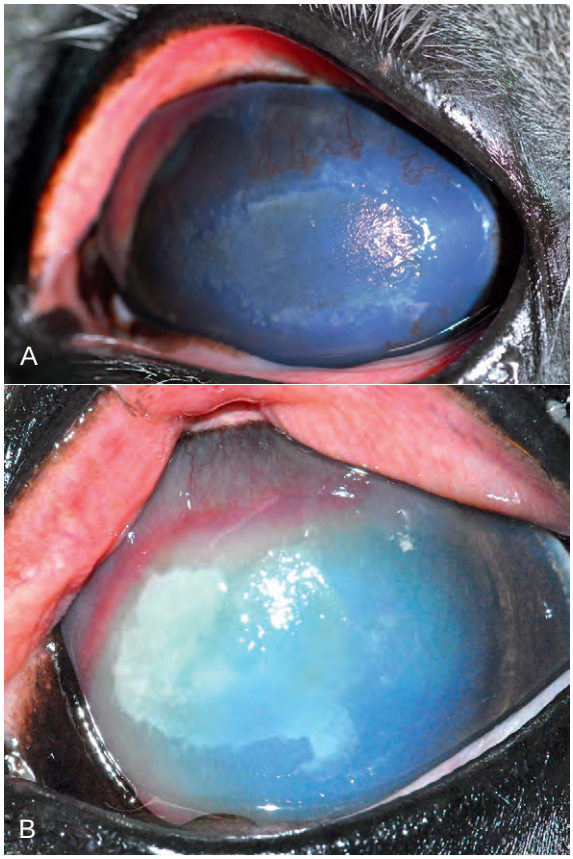


Figure 5-41. **A,** Clinical photograph of left eye of a horse with a superficial fungal plaque. Superficial vascularization encircling the area of cellular infiltration and the gritty, granular appearance of corneal surface are a possible presentation of fungal keratitis. **B,** Clinical photograph of left eye of a horse with a superficial fungal plaque and associated corneal vascularization, edema, and cellular infiltration.

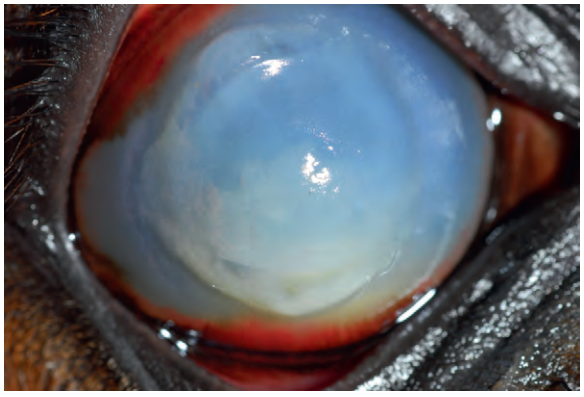


Figure 5-42. Clinical photograph of right eye of a 6-year-old Quarter Horse gelding with ulcerative keratomycosis. Note extensive central corneal edema and cellular infiltration, with a rim of variable degrees of stromal loss ("furrow"). Deep perilimbal vascularization and hypopyon are also present.

sis, infection was diagnosed by cytology in 4/9 eyes and by culture in 8/10.[235] Histopathologic evaluation of specimens collected at the time of surgical therapy for fungal keratitis may identify fungal hyphae (Fig. 5-45),[245] but speciation is not possible by this method alone. PCR has been reported for diagnosing keratomycosis in humans as well as horses[261,262] but currently is not readily available in equine ophthalmology.

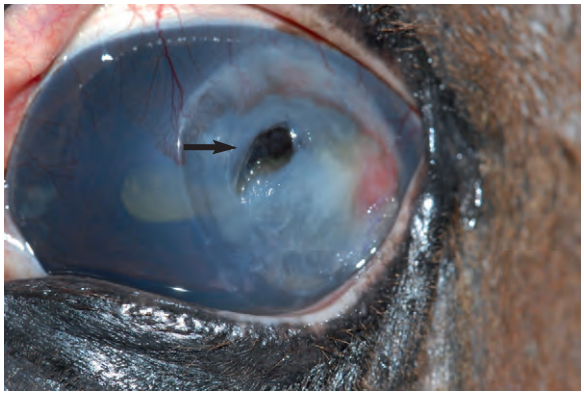


Figure 5-43. Clinical photograph of left eye of a 31-year-old Arabian gelding with a descemetocele *(arrow)* secondary to fungal keratitis. Corneal vascularization, cellular infiltration, and edema are present. Pupil is miotic (horse was being treated with atropine), and cataract is visible.

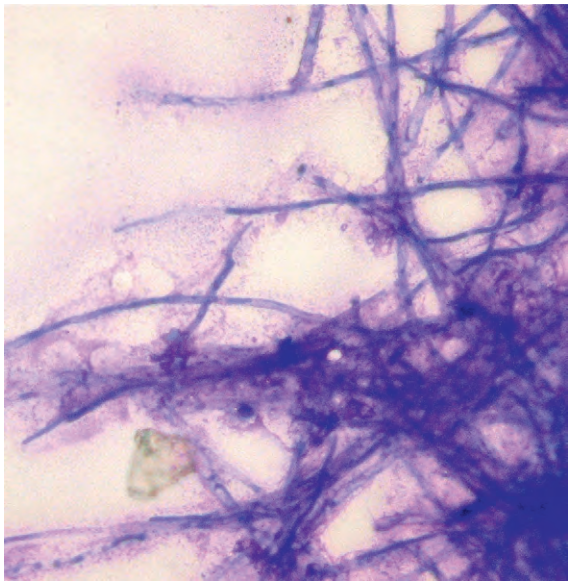


Figure 5-44. Cytologic sample from cornea of a horse with keratomycosis. Parallel cell walls are faintly visible demarcating the edge of individual hyphae (Diff-Quik stain).

PATHOGENESIS

As with bacterial infections, corneal epithelial loss allows ocular surface or environmental fungal organisms to adhere to, invade, and infect the corneal stroma.[115,263,264] Following infection, multiple pathophysiologic mechanisms are suspected as being involved in progression of corneal disease. Release of proteases from fungal organisms, reactive keratocytes, and responding inflammatory cells leads to worsening infection and inflammation, stromal digestion, and reactive anterior uveitis.[55,265] Fungal organisms have been shown inhibit angiogenesis in vitro, thereby interfering with the cornea's ability to heal.[255] Deep stromal involvement is perpetuated by an apparent affinity of fungal organisms for the glycosaminoglycans of the deeper corneal stroma adjacent to Descemet's membrane, as evidenced by their location near and within Descemet's membrane on histopathology specimens (see Fig. 5-45).[115,266,267]

Factors reported to predispose individuals to development of keratomycosis include previous administration of topical

antimicrobial and corticosteroid medications.[14,245,265,268] Normal predominantly gram-positive ocular surface microflora,[10,269] which produce a balance of antibacterial and antifungal substances, shifts to predominantly gram-negative organisms in ulcerative disease.[166] Topical antimicrobial treatment potentially exacerbates this shift and its deleterious effects. Topical corticosteroids may decrease the immune response and inhibit phagocytic activity or directly alter the phenotype of fungi to more pathogenic forms.[265] One study in horses found a greater negative impact of topical antibiotic than corticosteroid therapy in cases of ulcerative keratomycosis, with a greater percentage of horses diagnosed with fungal keratitis receiving antibiotics (82.1%) than corticosteroids (15.4%) prior to referral.[245] The same trend was identified in another study in which 60% (6/10) of horses received topical antibiotics prior to referral for ulcerative keratomycosis, versus topical corticosteroids in 20% (2/10).[235] A prospective study comparing ocular microflora following experimental administration of antibiotic and antibiotic-corticosteroid combination medications to the eyes of normal horses identified no treatment effect, however, documenting an initial decrease in positive fungal cultures in both treated and untreated control eyes.[14] These results suggest that factors in addition to topical medications are involved in establishment of fungal infection.

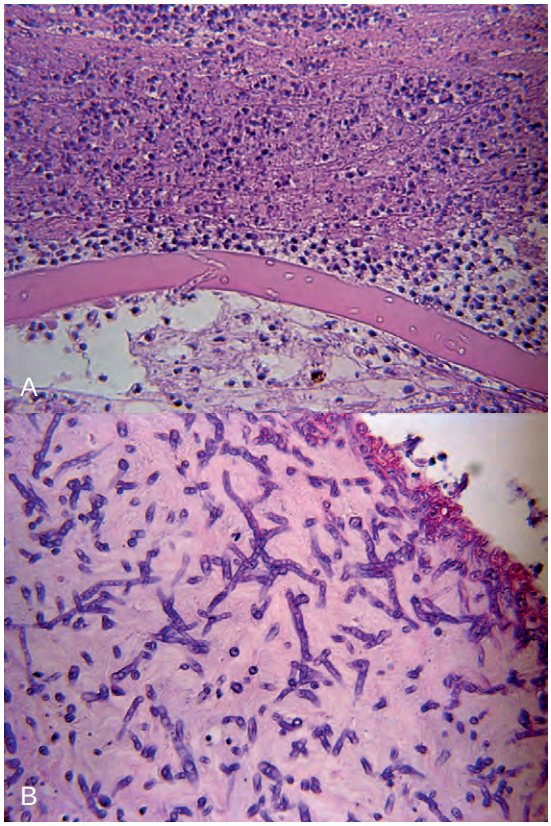


Figure 5-45. A, H&E-stained corneal surgical biopsy specimen showing numerous fungal hyphae in corneal stroma and infiltrating Descemet's membrane. **B,** Higher magnification of H&E-stained corneal surgical biopsy specimen showing fungal hyphae.

MEDICAL TREATMENT

Medical therapy for ulcerative keratomycosis targets fungal organisms, secondary bacterial infections, secondary anterior uveitis, corneal digestion, and ocular pain (Tables 5-12 to 5-14; see Tables 5-9 and 5-10). Prophylactic topical antibiotics are appropriate if bacterial infection is not identified, while therapeutic topical antibiotics, with or without systemic antibiotics, are recommended if concurrent bacterial infection is present. Topical atropine is administered at a frequency necessary to control the reflex anterior uveitis, which is often severe (i.e., every 6 to 12 hours). Systemic NSAIDs are the antiinflammatories of choice for their analgesic capabilities and their comparative safety (versus systemic corticosteroids).

As with all ocular medications, selection of appropriate topical and systemic antifungal agents should follow consideration of certain important principles. Most antifungal drugs are considered fungistatic due to an inability to achieve adequate concentrations in the presence of an intact corneal epithelium.[265,270] When treating ulcerative keratomycosis, however, epithelial loss and the ability to administer topical medications at a high frequency (i.e., every 1 to 2 hours) generally allow much higher drug concentrations to be reached in the cornea and aqueous humor. It has been suggested that starting initial therapy at such an aggressive frequency may result in clinical deterioration due to an intense inflammatory reaction associated with massive death of fungal hyphae,[117] but in each case, this potential must be weighed against the risks of worsening infection in the presence of inadequate therapy. Therapeutic débridement may be performed during the healing phases to increase drug penetration and potentially decrease the number of fungal organisms. Additionally, systemically administered drugs, including antibiotics, antifungals, and antiinflammatories, likely reach greater intraocular levels in the presence of secondary anterior uveitis resulting from corneal disease.

Table 5-12 | **Systemically Administered Antifungal Agents**

CLASS	MECHANISM OF ACTION	EXAMPLES	DOSAGE	OTHER POINTS
Azoles	Inhibit ergosterol synthesis; intracellular accumulation of toxic metabolites; cell membrane damage	Fluconazole	14 mg/kg PO once, then 5 mg/kg PO q24h	Good intraocular penetration, with or without inflammation; spectrum more limited than other azoles
		Itraconazole	1.5 mg/kg IV q24h 5 mg/kg PO q24h	Poor intraocular penetration; if PO administration, use IV solution, as capsules have highly variable absorption
		Voriconazole	3 mg/kg PO q12h	Good intraocular penetration, with or without inflammation; spectrum more limited than other azoles

Table 5-13 | **Topical Ophthalmic Antifungal Agents**

CLASS	MECHANISM OF ACTION	EXAMPLES	FORMULATION AND STORAGE	FREQUENCY*	OTHER POINTS
Polyenes	Cell membrane permeability and leakage; oxidative damage	Natamycin	5% suspension	q2-4h	Only commercially available ophthalmic antifungal; best for ulcerative disease
		Amphotericin B	0.075% to 0.20% solution in sterile water, dark bottle, refrigerate	q2-4h	Best for ulcerative disease; increased epithelial toxicity relative to natamycin
Triazoles	Inhibit ergosterol synthesis; intracellular accumulation of toxic metabolites; cell membrane damage	Fluconazole	0.2% solution	q2-4h	Poorer efficacy versus both yeast and filamentous agents than other azoles
		Itraconazole	1% in 30% DMSO	q2-4h	Good penetration through intact epithelium
		Voriconazole	1% solution in sterile water, refrigerate	q2-4h	Good penetration through intact epithelium
Imidazoles	Inhibit ergosterol synthesis; intracellular accumulation of toxic metabolites; cell membrane damage	Ketoconazole	1%	q2-4h	Best for ulcerative disease; poorer efficacy than other azoles
		Miconazole	1%	q2-4h	Good penetration through intact epithelium
Other	Metal ions bind microbial DNA and inhibit synthesis	Silver sulfadiazine	1% ointment	q12-24h	
	Germicide	Povidone-iodine	2% solution	q24h	

*Suggested initial frequency, depending upon severity of infection and inflammatory response; may be decreased or increased as appropriate for individual case.

Table 5-14 | **Combination Therapy for Infectious Ulcerative Keratitis: Fungal**

DRUG CLASS	EXAMPLES	FORMULATION	DOSE/FREQUENCY	OTHER POINTS
Topical antifungal	Natamycin 5%, voriconazole 1%, miconazole 1%, itraconazole 1%/DMSO 30%	Solution Suspension	0.1- 0.2 mL q2-4h	
Topical prophylactic *or* therapeutic antibiotic*	See Tables 5-5 and 5-9			
Topical therapeutic mydriatic cycloplegic	Atropine	Ointment Solution	¼ -inch strip q12-24h 0.1-0.2 mL q12-24h	Frequency depends on degree of mydriasis achieved between doses
Topical antiprotease	See Table 5-10			
Systemic antifungal	Fluconazole (F)	Tablets	14 mg/kg PO once, then 5 mg/kg PO q24h (F)	Good intraocular penetration but poor spectrum relative to other azoles (F); good intraocular penetration and good spectrum of activity (V)
	Voriconazole (V)	Tablets Suspension Solution	3 mg/kg PO q12h (V)	
Systemic NSAID	Flunixin meglumine	Paste Solution	1.1 mg/kg PO or IV q12h	
Systemic antibiotic	Trimethoprim sulfamethoxazole (T)	Varies with drug	20-30 mg/kg PO q12h (T)	
	Doxycycline (D)		10-20 mg/kg PO q12h (D)	
	Potassium penicillin (P)		20,000 U/kg IV q6h (P)	
	Gentamicin (G)		4-6.6 mg/kg IM or IV q24h (G)	

*Prophylactic antibiotic therapy is indicated as for ulcerative keratitis, with therapeutic antibiotics administered if coinciding bacterial infection suspected or confirmed.

Regardless of the initial therapeutic protocol, treatment for keratomycosis is frequently necessary for weeks to months.[265]

Three general classes of antifungals are currently available: polyenes, azoles, and nucleoside analogs. Polyenes (natamycin, amphotericin B) preferentially bind ergosterol, the cell membrane sterol unique to fungi, increasing cell membrane permeability.[234] They are also able to bind cholesterol, the sterol present in mammalian cell membranes, potentially creating toxicities.[234] Azoles (miconazole, ketoconazole, fluconazole, itraconazole, voriconazole) preferentially bind to a fungal-

specific enzyme in the cytochrome P450 system, inhibiting ergosterol synthesis, increasing membrane permeability, and altering fungal cell enzyme systems.[265] The nucleoside analog, flucytosine, is enzymatically altered within the fungal cell to the cytotoxic principal, fluorouracil.[234]

Polyenes (natamycin and amphotericin B) are broad spectrum, with generally good efficacy versus filamentous and yeast fungal organisms.[265] Natamycin (5%) is the only approved topical ophthalmic antifungal agent currently available, and it is generally believed to have limited epithelial penetration,[271] although studies indicate that it may in fact penetrate an intact corneal epithelium.[272] In vitro analysis of efficacy of natamycin versus isolates from equine keratomycosis reveal variable results relative to azoles[236,247,256] and to silver sulfadiazine.[257] However, the minimum inhibitory concentrations (MICs) of natamycin in combination with tobramycin, cefazolin, and equine serum versus *Aspergillus* and *Fusarium* isolates in vitro were significantly lower than calculated MICs for natamycin alone.[273] In contrast to variable results for filamentous fungi, natamycin has consistently good in vitro efficacy versus yeast isolates.[256] Amphotericin B has poor epithelial penetration following topical administration as well, and at higher concentrations, appears more likely to produce toxic effects to the corneal epithelium.[274] In the presence of a corneal ulcer, topical administration may result in therapeutic corneal levels, but the comparative safety and better spectrum[256] of natamycin makes it preferable. Subconjunctival administration of amphotericin B, which may provide sustained high drug levels, may be performed in cases of refractory keratomycosis, but concern exists regarding potential for local toxic effects.[265] A treatment regimen of 0.2 mL of a 5 mg/mL solution administered subconjunctivally every 48 hours, generally for 3 doses, has been utilized on several horses, with overall favorable results (B.C. Gilger, personal communication) (Fig. 5-46). Systemic administration of amphotericin B for corneal disease is generally not recommended because of the drug's systemic toxicities.

Azoles are available for topical, oral, and intravenous administration. Common agents include fluconazole, miconazole, itraconazole, and voriconazole.[166,171,246,248,275] Miconazole, administered either topically as a 1% solution or subconjunctivally (5 to 10 mg every 24 to 48 hours), has reasonable intraocular penetration as evaluated in other species.[234,246,265] Topically administered itraconazole 1% in 30% dimethyl sulfoxide (DMSO) has good intraocular penetration, as measured by corneal tissue levels in horses with normal corneas, and produced no signs of ocular irritation.[276] Itraconazole may also be administered orally or intravenously, but it was not detectable in the aqueous humor of uninflamed equine eyes.[277] Fluconazole, administered intravenously or orally at 10 mg/kg, demonstrated measurable aqueous humor levels in horses without intraocular inflammation.[278] Breakdown of the blood-ocular barrier with uveitis and significant corneal vascularization may produce measurable intraocular and corneal levels of fluconazole; however, this has not been evaluated in the horse. Topical administration of 1% voriconazole resulted in good intraocular penetration, as measured by aqueous humor levels in normal equine eyes, and produced no signs of ocular irritation.[275] Oral and intravenous administration of a single 4 mg/kg dose of voriconazole also resulted in detectable aqueous humor levels in the absence of intraocular inflammation,[275] while repeated oral dosing of 3 mg/kg every 12 hours maintained potentially therapeutic plasma levels.[279] Relative in vitro efficacy of the agents versus equine keratomycosis isolates has consistently identified a broader spectrum for miconazole and itraconazole relative to fluconazole,[247,256] but comparison with voriconazole or other newer azoles with expanded spectra[280,281] has not been performed in horses. Newer azoles such as posaconazole and ravuconazole have an improved spectrum,[282,283] but their use as topical ocular antifungal agents in the horse has not been evaluated.

Clinical efficacy of antifungal agents is difficult to assess in consideration of the variable presentations, severity at the time of evaluation, previous therapeutics, coinciding infections, and individual variation. Clinical reports of cases treated with topical natamycin,[168,229,243,245,248-251] topical amphotericin B,[250] topical miconazole,[235,245,246,251,284] topical itraconazole,[248] and oral fluconazole[250] demonstrate variable vision and globe retention, but definitive conclusions about individual therapies cannot be made, with the exception being that treatment is long term. Additional considerations include concomitant administration of substances meant to inhibit collagenase activity and enhance antimicrobial efficacy. In vitro evaluation of a novel buffered chelator in conjunction with miconazole, ketoconazole, itraconazole, and natamycin demonstrated significantly reduced MICs for each drug versus filamentous fungal organisms in the presence of the chelator; clinical use of the chelator has not been reported.[285] Serum, EDTA, tetracyclines, and other anticollagenases may be indicated as adjunctive therapy in ulcerative keratomycosis.

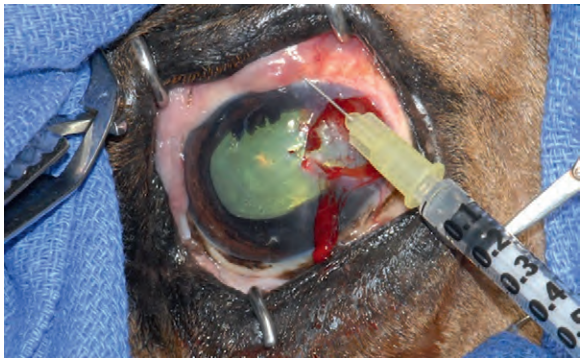


Figure 5-46. Intraoperative photograph of subconjunctival amphotericin B injection, performed following removal of diseased cornea via keratectomy.

SURGICAL TREATMENT

Surgical therapy is performed to remove infectious organisms and inflammatory cells and to stabilize weakened cornea. Specific indications for therapy include stromal loss of greater than one-third corneal thickness (including deep ulcers and descemetoceles), corneal perforation, uncontrolled anterior uveitis, or limited to no response to medical therapy.[168,185,286] Surgical options include superficial or lamellar keratectomy with or without conjunctival,[185,246,251,284,287] amnion,[183] or biosynthetic material[288] grafting procedures; corneoconjunctival transposition[289]; posterior lamellar or deep lamellar endothelial keratoplasty (PLK, DLEK, respectively)[266,290]; or penetrating keratoplasty (PK) with or without coverage by a conjunctival graft (Figs. 5-47 and 5-48).[251,286,291] For detailed review of procedures, see the surgical section later in the chapter.

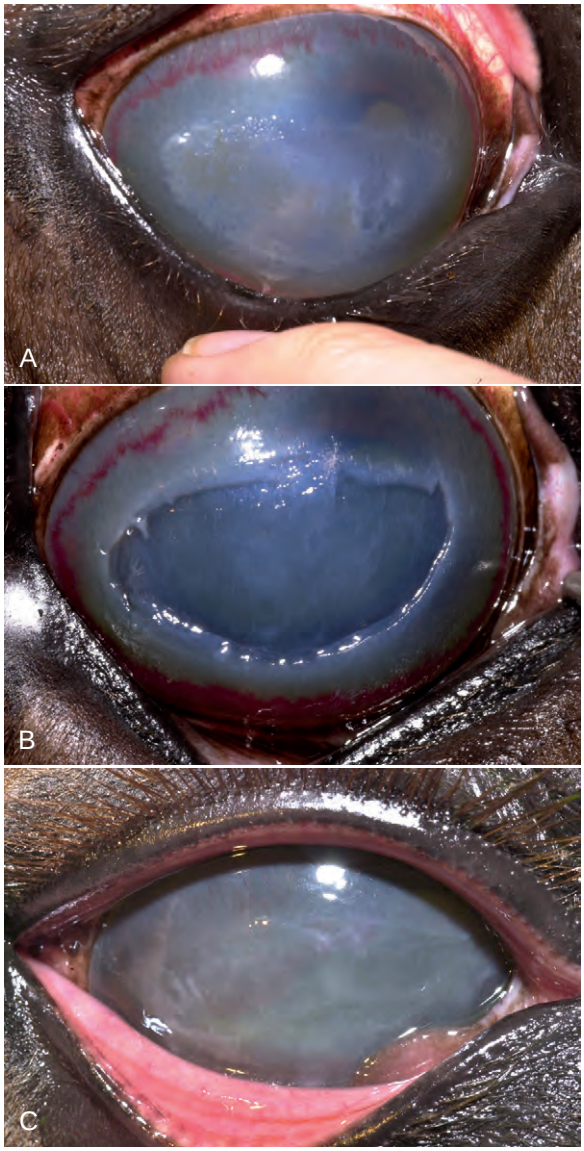


Figure 5-47. **A,** Clinical photograph of right eye of a 7-year-old Saddlebred gelding presenting with a superficial fungal plaque. Perilimbal vascularization, mild diffuse edema, and central discolored granular-appearing area are present, consistent with fungal infiltration. **B,** Clinical photograph of the eye in **(A)** following removal of infected cornea via superficial keratectomy. The bed of the keratectomy site is edematous but free of cells or infectious organisms. **C,** Clinical photograph of the eye in **(A)** and **(B)** 4 weeks after superficial keratectomy. Cornea is moderately fibrotic and vascularized, with no recurrence of cellular infiltration or infection.

PROGNOSIS

The prognosis for ulcerative keratomycosis depends upon aggressive, appropriate therapeutic intervention. In a series of nine horses with keratomycosis, mean treatment duration was 35 days (range 16 to 53 days), resulting in excellent vision in six and globe retention in eight.[248] A favorable visual outcome and globe retention were reported in over 90% and 95%, respectively, of 39 cases of ulcerative keratomycosis receiving either medical or medical and surgical therapy, treated for a mean duration of 48 days (range 31 to 192 days).[245] Ten cases treated for a median of 73 days (range 45 to 120 days) had a favorable visual outcome in 50% and globe retention in 70%.[235] In cases with corneal disease other than ulcerative keratomycosis, PK, PLK, and DLEK resulted in a favorable visual outcome in 77.9%, 98.1%, and 89.9% of 206 eyes, respectively.[291]

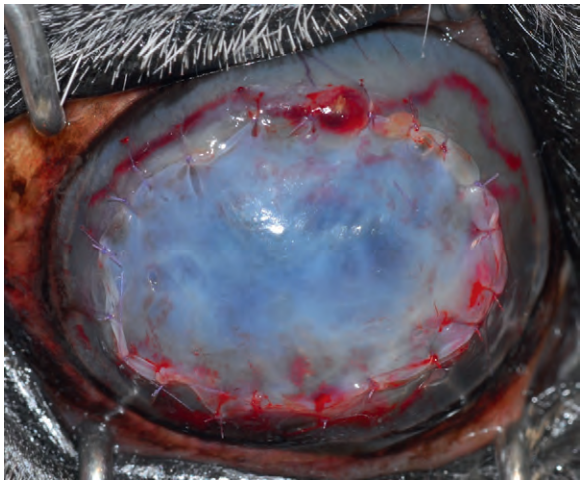


Figure 5-48. Intraoperative photograph of right eye of a 14-year-old Warmblood gelding following placement of an amnion graft for severe ulcerative stromal keratitis.

NONULCERATIVE KERATITIS: NONINFECTIOUS

IMMUNE-MEDIATED KERATITIS

Andy Matthews

PREVALENCE AND CLASSIFICATION

Immune-mediated keratitis (IMMK) is a heterogeneous collection of typically nonulcerative corneal diseases characterized by some or all of the following clinical features: vascularization and edema at various levels within the cornea; varying intensity, distribution and depth of inflammatory cellular response; and absence of overt uveal inflammatory pathology. Although geographic ulceration is not a feature of these diseases, local epithelial involvement in a more generalized pathologic process may result in transient painful erosions. Otherwise, minimal ocular discomfort is associated with the often dramatic corneal pathology.

Among the nonulcerative inflammatory keratopathies are relatively rarely recognized entities, such as pannus and episclerokeratitis, which show significant clinical similarity to the diseases in other species.[292] Both eosinophilic keratitis and the superficial nonulcerating keratitis putatively attributed to persistent viral infection may ultimately be classified as IMMKs, as may the poorly defined group of inflammatory diseases characterized principally by rapid and reversible pigment infiltration of the basal epithelial layer or stroma.[292]

However, the largest constituent group of IMMKs is that representing clinically nonspecific pathologies, classified generically according to clinical presentation and progression, depth of inflammation, and response to antiinflammatory or immunomodulatory therapy.[28,292-294] The specific etiologies are

unknown, but it is likely that most if not all are driven to some degree by derangement of the normally inert immunoresponsiveness of the healthy cornea, as previously described.[25,28]

PATHOGENESIS AND GENERAL THERAPEUTIC CONSIDERATIONS

The specific immunopathogenesis of equine IMMK has not been studied in any detail, and medical therapy to date has been based upon attempts to directly suppress the inflammatory response and modulate the presumptive immune events driving that response. It is highly likely that the molecular events determining the clinical expression of IMMK to be described involve an interdependent multimolecular cascade triggered primarily by antigen-presenting cell (APC)/T cell interaction, with a subsequent autocrine and amplifying proinflammatory response encompassing cytokine-driven angiogenesis and leucocyte chemoattraction. The inherent complexity of these events, where molecular homeostasis is likely to determine the positive or negative expression of individual inflammatory pathways, makes it likely that any response to therapy will vary between individual cases. However, empirical modulation of individual components of the immunoinflammatory response using available chemotherapeutic agents permits some degree of rationally targeted therapy. Several drugs, used alone or in combination, have been aimed at targeting specific components of the immunoinflammatory response, with varying results.

GLUCOCORTICOIDS

Drugs in the glucocorticoid (GC) class have diverse antiinflammatory, immunosuppressive, and antiangiogenic effects and are a primary empirical therapy in equine IMMK. Through activation of the pleiotropic glucocorticoid receptor (GR) and inhibition of the central transcription factors nuclear factor κB (NF-κB) and AP-1, T-cell activation and expression of proinflammatory cytokines are downregulated.[295,296] GCs also reduce local expression of chemotactic proteins and cell adhesion molecules, restricting migration of inflammatory cells to sites of tissue injury.

Dexamethasone induces T-cell suppression and impairs T-cell receptor signaling in a nongenomic fashion,[297] in part by blocking maturation of the immune synapse (IS) at the T cell/APC contact site.[298] Acting via the GR, glucocorticoids interfere with toll-like receptor (TLR) signaling to downregulate the expression of innate immunity on the ocular surface.[299]

Glucocorticoids inhibit corneal angiogenesis via decreased gene expression of VEGF and inhibition of the macrophage precursors of corneal vascular endothelium, and as such potentially are of therapeutic value in ameliorating the local neovascularization that is a fundamental factor in the loss of corneal immune privilege.

CYCLOSPORIN A AND TACROLIMUS

Cyclosporin A (CsA) and tacrolimus are potent immunosuppressive agents in the calcineurin inhibitor class. They act to downregulate immunocyte activity via suppressing transcription of proinflammatory cytokines, principally IL-2. Calcineurin is responsible for the induction of a family of nuclear transcription factors known as *nuclear factors of activated T lymphocytes* (NFATs), which define the expression of proinflammatory peptides (Fig. 5-49). CsA is a cyclic nonribosomal peptide that binds the cytosolic immunophilin cyclophilin in activated T cells, forming a complex that inhibits the cytoplasmic phosphatase, calcineurin (see Fig. 5-49). Tacrolimus (FK506) is a macrolide lactone that forms a calcineurin-inhibiting complex with the cytosolic FK506 binding cyclophilin of T cells (see Fig. 5-58). Additionally, both CsA and tacrolimus selectively prevent T-cell receptor conjugation with APCs at the immune synapse (IS).[298] Calcineurin inhibitors have been used as glucocorticoid-sparing drugs in human medicine. In the horse, the IMMKs appear to be variably responsive to both classes of drug in single use, and their combined topical use at full therapeutic doses is often employed.

SIROLIMUS (RAPAMYCIN)

Sirolimus is a macrolide immunosuppressive agent that binds to the cytosolic FK-binding protein 12 (FKBP12) of T cells, forming a complex that inhibits the mammalian target of rapamycin (mTOR) and blocking the cytoproliferative response to IL-2 (Fig. 5-50). In addition, unlike the calcineurin inhibitors, rapamycin promotes the expansion of regulatory T-cell clones in vivo, suggesting a possible tolerance inducing role for the drug in the management of immunoinflammatory disease.[300] There are as yet no reports of its topical use in the management of corneal disease in the horse.

DOXYCYCLINE

In addition to its antibiotic properties, doxycycline has specific antiinflammatory and immunosuppressive actions based principally on suppression of T-cell co-stimulation via downregulation of IL-1β expression by macrophages and dendritic cells.[89] In addition, inhibition of $TGF\beta_1$–induced expression of MMP-9 may give the drug some antiangiogenic and anticytoproliferative properties.[301] The antiinflammatory effects of doxycycline appear to be dose dependent, suggesting topical rather than systemic administration may be appropriate, in addition to avoiding the potential side effects of systemic use. To date there is anecdotal evidence only to support systemic use of the drug to manage equine IMMKs.

CLINICAL APPEARANCE AND TREATMENT

Chronic Superficial Keratitis

This disease, initially unilateral but potentially becoming bilateral, is characterized by an insidious onset with only slight to moderate discomfort. Matthews[292] reported the lesions to be initially restricted to the area under the upper eyelid and less frequently the third eyelid, although Gilger et al.[294] recorded lesions most commonly in the paracentral region. There is prominent subepithelial arborizing vascularization from the limbus, perivascular epithelial edema, and superficial stromal cell infiltrate (Fig. 5-51). Tear production is normal, and no fluorescein uptake occurs. The apposing palpebral conjunctiva is moderately hyperemic.

Topical treatment with 0.2% CsA ointment twice daily usually results in clearing of the cornea in 7 to 10 days in acute cases.[292] Chronic cases may require constant cyclosporin or may be refractory to treatment. Matthews[292] reported no clinical benefit from topical corticosteroids, although Gilger et al.[294] reported control of a minority of cases using constant corticosteroid medication. Gilger et al.[294] also reported successful resolution of refractory disease after superficial keratectomy and conjunctival grafting.

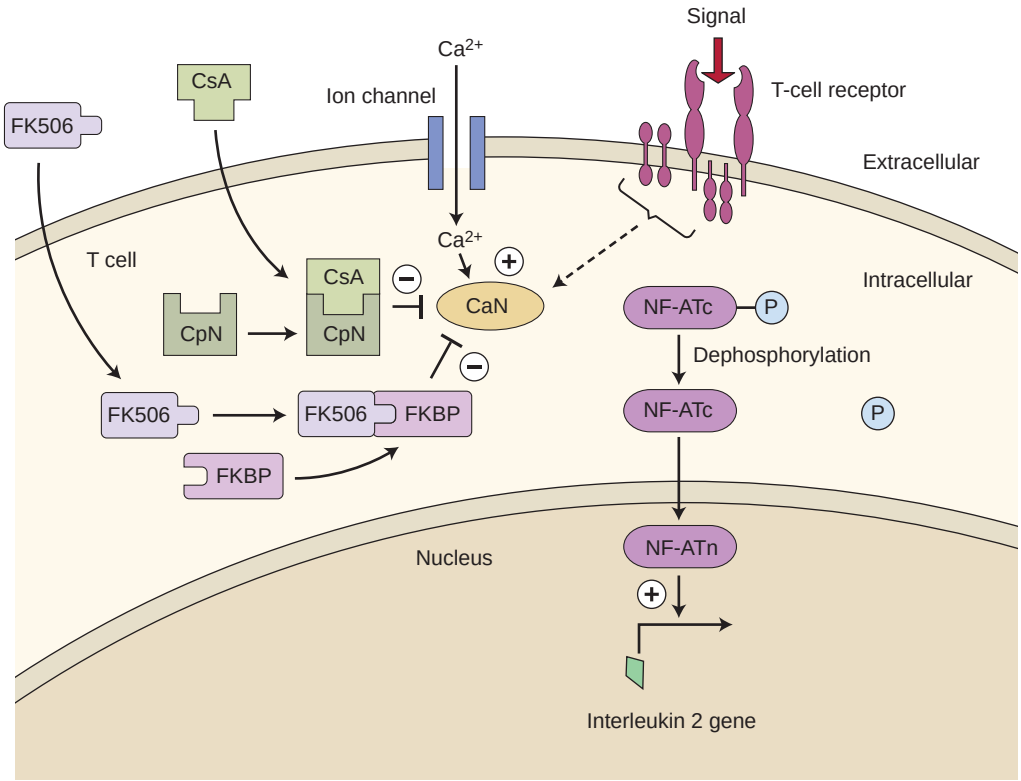


Figure 5-49. Diagram of the mechanism of action of cyclosporin (CsA) and tacrolimus (FK506) on T cells. Both drugs penetrate the cell to bind to and inhibit calcineurin (CaN) via their individual intracellular receptors (cyclophilin [CpN] for cyclosporin, FK506 binding protein [FKBP] for tacrolimus). Inhibition of calcineurin ultimately prevents transcription of the proinflammatory cytokine, interleukin 2 (IL-2), within the nucleus of the T cell.

Chronic Deep Keratitis

This keratitis recurs at irregular intervals of up to several years, frequently subsequent to a history of initiating ocular trauma,[292,293] which may incite a local adaptive response to autoantigen in an immunocompetent cornea, perpetuating immune-mediated recurrence.

In the acute or active phase of the disease, there is an extensive, dense, mid- to deep-stromal edema and fibrovascular response (Fig. 5-52). The intensity of the stromal changes varies among cases and episodes, but despite the dramatic appearance of affected eyes, ocular pain is absent. Subepithelial bullae may form and rupture to create superficial erosions, causing transient ocular discomfort. In some eyes, lacunae of greenish-tinged fluid may collect within the midstromal central and paracentral cornea (Fig. 5-53). Subepithelial calcium deposition may occur in some eyes. In the quiescent or inactive phase of the disease, there is modest diffuse stromal fibrosis and superficial vascularization (Fig. 5-54).

Acute episodes of the disease will eventually subside without treatment in most cases. The therapeutic benefit of topical corticosteroids alone is very limited, although they may accelerate clearing of the cornea in some cases. Topical cyclosporin twice daily results in significant suppression of the acute corneal reaction and clearing of the cornea within 10 to 14 days in most cases. However, treatment may need to be maintained at a reduced frequency for a protracted period to prevent recrudescence of the disease until such time as corneal reactivity subsides spontaneously.

In the series of midstromal IMMK reported by Gilger et al.,[294] periodicity and recurrence of the disease was not a feature. Constant topical CsA and dexamethasone therapy controlled the disease in 3 of 5 cases, and in one case superficial keratectomy and conjunctival grafting resulted in healing of the cornea.

Endotheliitis

This is a disease of acute onset characterized by unilateral central edema and deep stromal vascularization. In all cases, there is no obvious etiology, although aberrant endothelial immunoreaction to local antigen presentation may be involved.

Deep, diffuse fibrocellular opacity and stromal edema in the central cornea may evolve rapidly into corneal hydrops (Fig. 5-55). Isolated arborizing blood vessels encroach upon the affected area at the level of the posterior stroma or endothelium (Fig. 5-56). In some cases, dense clumps of cells may be evident adherent to the endothelium in the region of the terminal vessel. In long-standing cases, stromal mineralization can occur. The anterior chamber is normal.

Matthews[292,293] reported rapid clearing of the cornea and regression of the blood vessels using topical dexamethasone in short-standing cases. Treatment should continue for 5 to 7 days following corneal clearing. However, Matthews[292,293] described recurrence of the disease in a small number of long-standing cases. Gilger et al.[294] reported a poor response to topical medical therapy in their series of cases, but they did record a successful outcome in one case following penetrating keratoplasty.

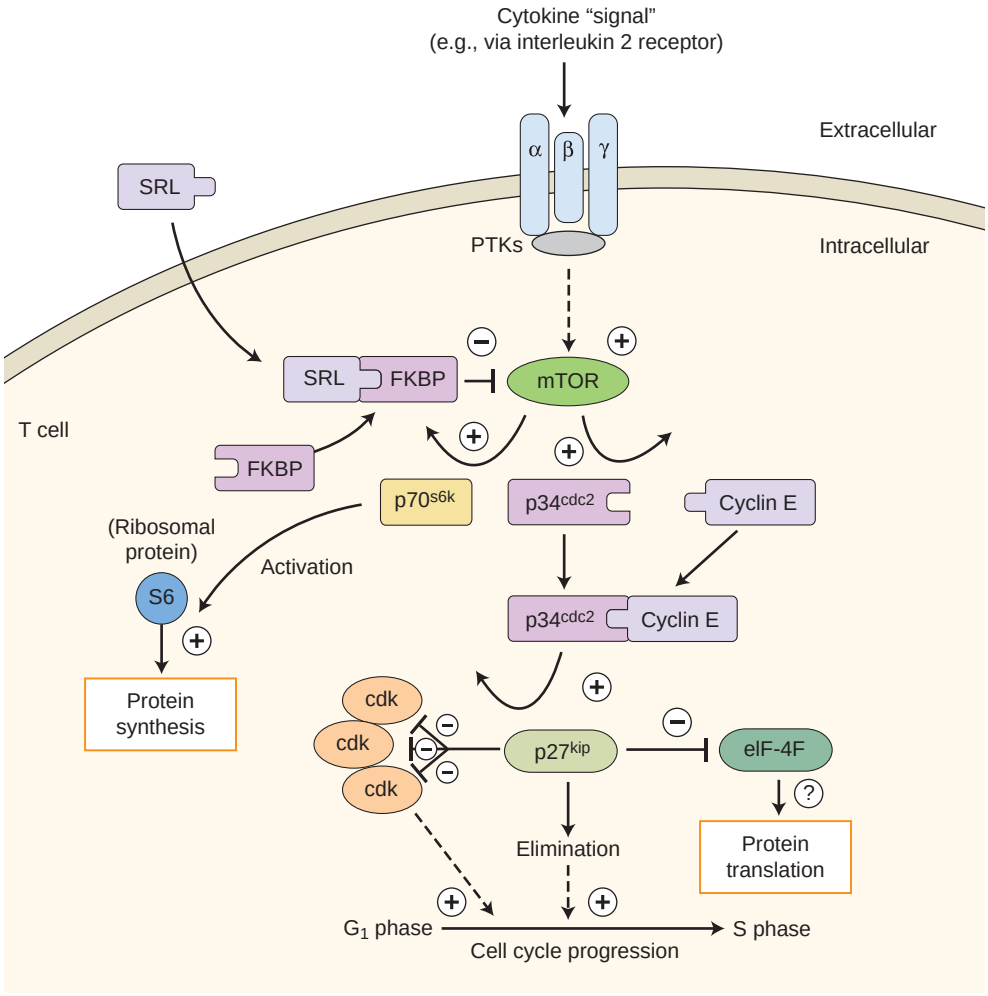


Figure 5-50. Diagram of mechanism of action of sirolimus (rapamycin) on T cells. Sirolimus binds FK12 binding protein (FKBP), and the resulting complex inhibits the mammalian target of rapamycin (mTOR), blocking the cytoproliferative signal induced by the proinflammatory molecule, interleukin 2 (IL-2).

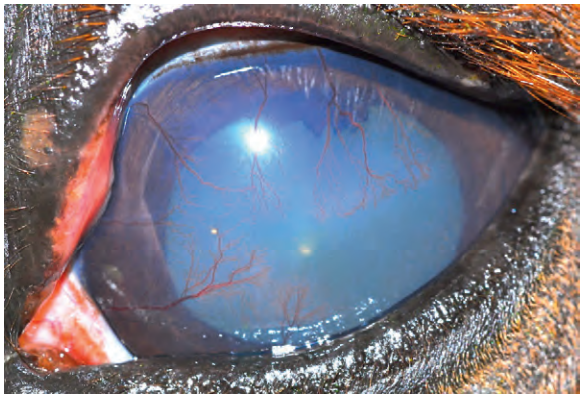


Figure 5-51. Clinical photograph of left eye of a 19-year-old Quarter Horse gelding with chronic superficial keratitis manifested by superficial vascularization with faint multifocal opacification at distal ends of vessels. Note absence of signs of overt uveitis (horse has not received topical atropine).

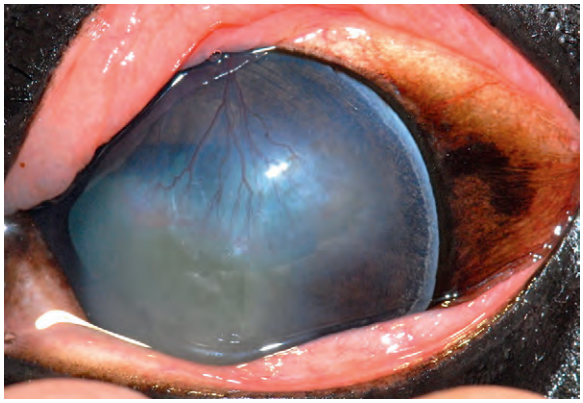


Figure 5-52. Clinical photograph of a horse with chronic active deep keratitis, demonstrating prominent corneal vascularization, edema, and cellular infiltration.

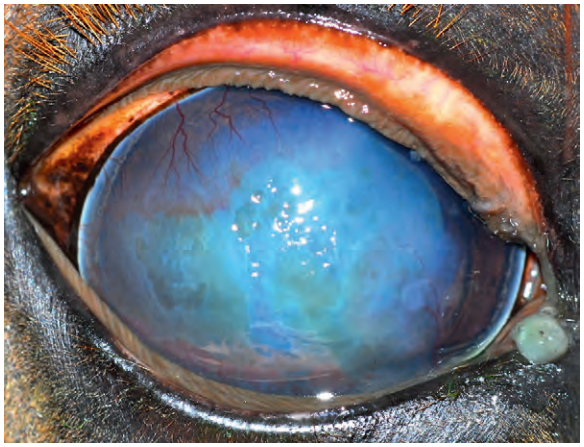


Figure 5-53. Clinical photograph of right eye of an 18-year-old Quarter Horse gelding with chronic deep keratitis, characterized by extensive vascularization, diffuse corneal edema, and multifocal greenish lacunae within the central cornea.

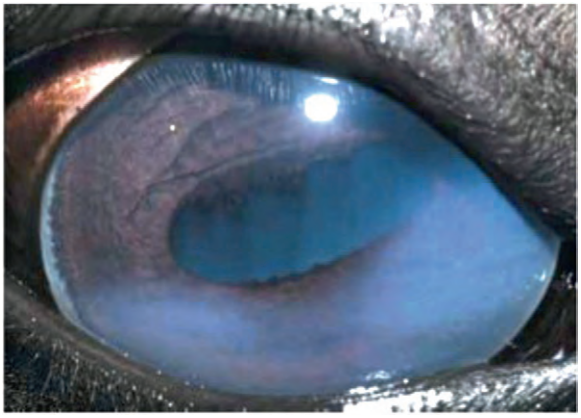


Figure 5-55. Clinical photograph of moderate endothelial edema, indicative of endotheliitis.

Figure 5-54. Clinical photograph of quiescent chronic deep keratitis, characterized by fibrosis and mild superficial vascularization.

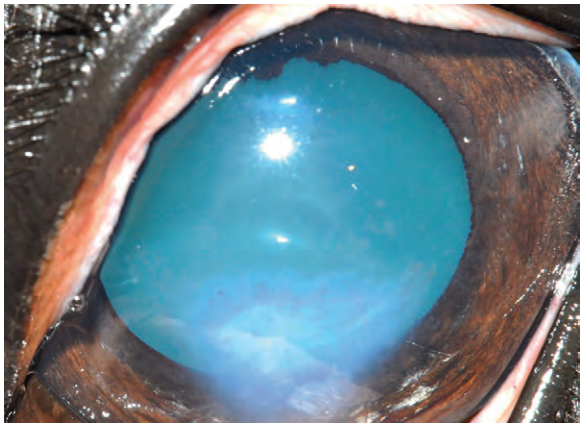


Figure 5-56. Clinical photograph of faint endothelial vessels and mild edema, indicative of endotheliitis.

Epithelial Keratopathy

This is a unilateral disease affecting horses of any age. It differs from the preceding diseases in that vascularization is not a feature of the disease, although in other aspects it meets the clinical criteria of nonulcerative keratitis. There is a diffuse, central, superficial corneal opacity, usually associated with a very slight blepharospasm (Fig. 5-57). There may be some associated conjunctival hyperemia or chemosis. The superficial opacity represents irregular coalescing clumps or islands of thickened epithelium with no underlying stromal edema. The unaffected areas of cornea appear normal. Fluorescein and rose bengal stains are retained in the interstices between the islands of abnormal epithelium. The Schirmer tear test I is normal.

Topical dexamethasone results in rapid corneal clearing in most cases, and the disease has not been observed to recur after successful treatment. However, persisting focal anterior stromal opacities have resulted in a few cases.

Figure 5-57. Photograph of epithelial keratopathy. (Photograph courtesy Dr. Andy Matthews.)

NONULCERATIVE KERATOUVEITIS

PREVALENCE

Nonulcerative keratouveitis (NUKU) is a relatively uncommon disease in horses, with the first report in 1990[302] and only sporadic subsequent reports in the United States and Japan.[293,303,304]

CLINICAL APPEARANCE

The hallmarks of NUKU are fleshy corneal stromal infiltrate located at the limbus, absence of corneal ulceration, and profound anterior uveitis.[302,303] Nonspecific signs of ocular pain (blepharospasm, enophthalmos, epiphora, conjunctival hyperemia) will be present, along with limbal corneal edema, vascularization, cellular infiltration, and miosis, aqueous flare, and hypopyon.

DIFFERENTIAL DIAGNOSES

Differential diagnoses for NUKU include infectious causes of nonulcerative keratitis (e.g., bacterial or fungal stromal abscess, onchocerciasis), and noninfectious causes of keratitis (e.g., neoplasia, immune-mediated keratitis, eosinophilic keratitis, corneal dystrophy or degeneration, calcific keratopathy). The diagnosis is made based on clinical appearance, response to nonspecific antiinflammatory therapy, and histopathology. Histopathologic evaluation identifies invasion of fibroblasts, lymphocytes, and blood vessels, as well as corneal epithelial hyperplasia.[302,304]

PATHOGENESIS

The pathogenesis of NUKU is unknown. The histopathologic findings of vascularization and lymphocyte infiltration are suggestive of an immune-mediated or inflammatory process. One horse was seropositive of *Leptospira interrogans*, and the authors suspected systemic infection initiating the ocular disease.[304] The increased presence of complement in the peripheral cornea relative to central cornea makes the peripheral cornea more susceptible to altered immunologic mechanisms, such as autoimmunity to corneal antigens, as may be involved in NUKU.[302,305]

MEDICAL TREATMENT

Medical treatment with topical and systemic antiinflammatories is the mainstay of therapy for NUKU. Topical corticosteroids and NSAIDs may be administered as frequently as every 4 hours, and topical atropine to treat the anterior uveitis may be administered every 6 to 12 hours as needed. Topical cyclosporin may also be administered, but its efficacy for treating intraocular disease is limited by minimal intraocular penetration.[165] Systemic NSAIDs are indicated for their antiinflammatory and analgesic effects. Treatment is typically necessary for weeks to months, and recurrence is possible with premature discontinuation.[302] It is critical that a stromal abscess, which may frequently be fungal, be ruled out prior to administered antiinflammatory therapy.

SURGICAL TREATMENT

No surgical treatment is indicated for NUKU.

PROGNOSIS

The need for lifelong treatment for NUKU carries a poor prognosis in horses. Chronic topical steroid administration may predispose horses to corneal degeneration or infectious keratitis, while chronic inflammation may result in phthisis.[293] Enucleation may be necessary in some cases.[304]

NONULCERATIVE KERATITIS: INFECTIOUS

STROMAL ABSCESSES

PREVALENCE

Reports of equine corneal stromal abscesses suggest the prevalence is increasing, but whether this is due to increased recognition or a true increase in occurrence is unknown. In a report from Cornell, 5 of 53 eyes affected with keratomycosis between 1978 and 1996 presented as stromal abscesses,[244] and a 2005 report from the United Kingdom documented abscesses in 2 of 6 eyes with keratomycosis.[258] Between 1991 and 1993, 14% (32/228) of horses presenting to the University of Florida ophthalmology service were diagnosed with stromal abscesses, with an increased incidence each successive year[260]; in 1996, two of four horses with keratomycosis presented with stromal abscesses.[251] Abscesses may be bacterial, with one study of 10 eyes yielding 60% positive bacterial cultures for *Streptococcus* spp. or *Staphylococcus* spp.[306] More frequently, however, surgical biopsy specimens suggest abscesses are either sterile or fungal. In one study, histopathologic evaluation of 13 biopsy specimens identified cocci in only one sample versus fungal hyphae in 5/13 (38%) and no etiologic agent in 7/13 (54%).[260] Similar results were obtained in another study of 11 biopsy specimens, with fungal hyphae identified in 36% (4/11), and no infectious agent in 64% (7/11).[267] More recently, fungal hyphae have been identified in 50 and 70% of surgical biopsy specimens, frequently localized near or in Descemet's membrane.[266,290]

CLINICAL APPEARANCE

Stromal abscesses may occur at any location in the cornea (i.e., axial, paraxial, peripheral) and at any depth (i.e., superficial stromal, midstromal, endothelial). They are characterized by whitish to yellow cellular infiltrate, which may be clearly demarcated within the stroma or may have diffuse, hazy edges with feathery extensions into adjacent stroma (Figs. 5-58 and 5-59).[244,251,258,306] Fluorescein staining is generally negative, but focal dye uptake may be present.[244,260,306] A characteristic feature of stromal abscesses is a waxing and waning clinical course, manifested by periods of severe ocular pain, corneal opacification, and anterior uveitis alternating with periods of relatively mild clinical signs.[260] Abscesses located adjacent to the endothelium may rupture into the anterior chamber, producing more consistent signs of pain and intraocular inflammation, commonly with attachment of an inflammatory mass (fibrin, hypopyon) to the posterior aspect of the abscess (Fig. 5-60).

DIFFERENTIAL DIAGNOSES

Any condition causing corneal opacification should be considered as a differential diagnosis for a stromal abscess: inflammatory conditions (e.g., immune-mediated keratitis, eosinophilic keratitis, nonulcerative keratouveitis, corneal foreign body, parasitic keratitis); noninflammatory conditions (e.g., calcific band keratopathy, mineral or lipid deposition, corneal endothelial degeneration, corneal fibrosis, granulation tissue); and neoplastic conditions (e.g., SCC, angiosarcoma, amelanotic

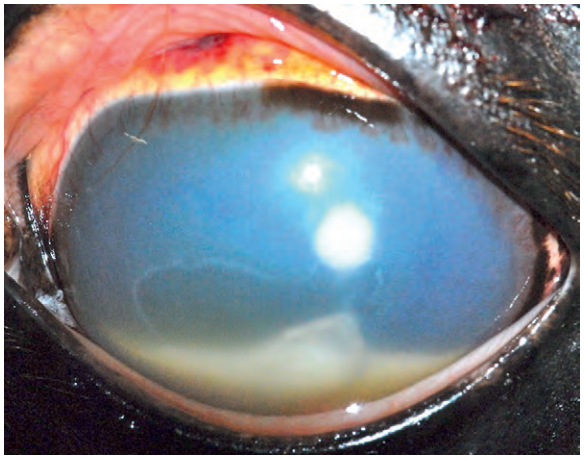


Figure 5-58. Left eye of a 10-year-old Thoroughbred mare with a clearly demarcated deep stromal abscess and mild diffuse corneal edema. Abscess is the 3- to 4-mm diameter yellow opacification dorsolateral of the central cornea. The yellow opacification ventrally is significant hypopyon.

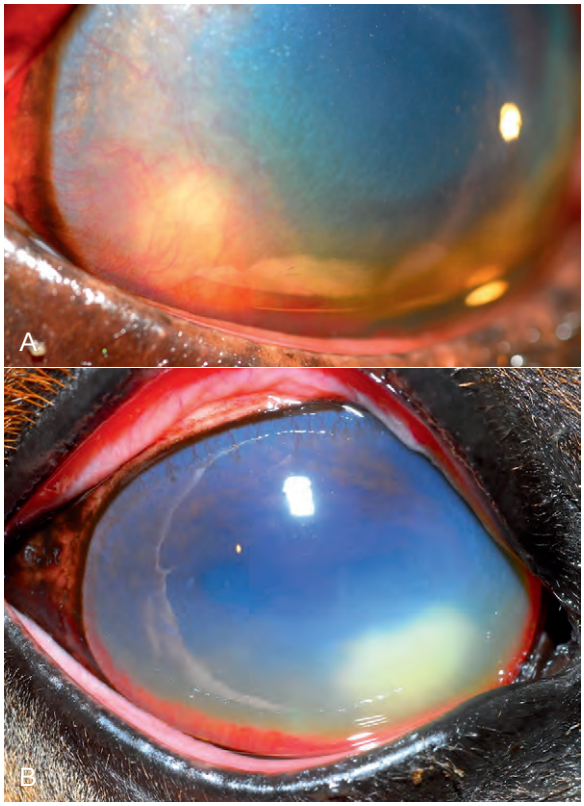


Figure 5-59. **A,** Right eye of a 3-year-old Quarter Horse stallion with a poorly demarcated, mildly vascularized deep stromal abscess. Vessels appear to be encircling but not penetrating the abscess, which is also associated with moderate surrounding edema and infiltration. Pupil is relatively mydriatic due to atropine treatment. **B,** Right eye of a 10-year-old Paint Horse gelding with a large deep stromal abscess. The yellow abscess is associated with moderate corneal edema and perilimbal vascularization, while the miosis and hypopyon are indicative of secondary reflex anterior uveitis.

melanoma) should all be considered. For diagnosis, cytology and culture can be performed prior to surgery, but an intact epithelium may interfere with collection of samples. Evaluation of biopsy specimens and cultures obtained at the time of surgical therapy provide a more certain diagnosis. Routine

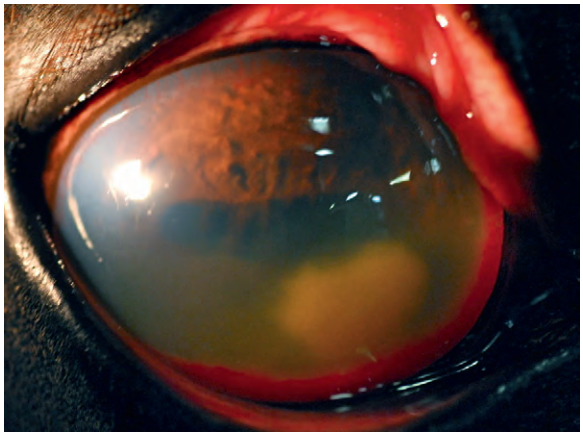


Figure 5-60. Large stromal abscess that has ruptured into the anterior chamber. Note extreme miosis, iritis, and inflammatory cells and protein within the anterior chamber.

hematoxylin-eosin staining may identify fungal hyphae and/or bacteria. Special stains (PAS, Gomori's methenamine silver [GMS]) may be necessary to more definitively identify hyphae (Fig. 5-61).[260,267] Cellular infiltrate is predominantly neutrophilic with variable lymphocyte, plasma cell, and macrophage involvement, and vascularization and fibroblastic cells may be present.[260,267] Molecular techniques to detect DNA from infectious organisms have also been used in the diagnosis of corneal infections.[261,307]

PATHOGENESIS

Corneal stromal abscesses result when a break in the epithelial barrier (i.e., ulceration, penetrating trauma) enables infection by ocular surface or environmental organisms, following which reepithelialization traps organisms within the stroma.[260,306] Regardless of whether bacteria or fungi are involved, neutrophils recruited to the area release enzymes that degrade the stroma and cause intense anterior uveitis. Vascularization, necessary for healing a stromal abscess, may be intense or mild in relation to the degree of infection, possibly due to antiangiogenic properties of fungal organisms. *Fusarium* spp. and *Aspergillus* spp. isolates from equine keratomycosis demonstrated inhibition of vascular growth in an in vitro assay,[255] but further evaluation of this capability has not been performed in horses in vivo. Histopathologic recognition of fungal organisms adjacent to and within Descemet's membrane suggests a possible tropism for fungi to the glycosaminoglycans located in the deeper stroma.[115]

MEDICAL TREATMENT

Medical therapy is an integral component to the successful management of stromal abscesses. As with ulcerative infectious keratitis, placement of a subpalpebral lavage catheter (see Chapter 2) greatly facilitates administration of medications, with administration of antimicrobials often occurring as frequently as every 2 to 4 hours. Because the location of stromal abscesses may preclude identification of a specific etiologic agent, empiric antimicrobial therapy is targeted toward bacteria and, in warm humid climates, fungal organisms. Selection of individual drugs must take into consideration that biphasic drugs, or those with both hydrophobic and hydrophilic properties, are best able to penetrate the intact corneal epithelium and

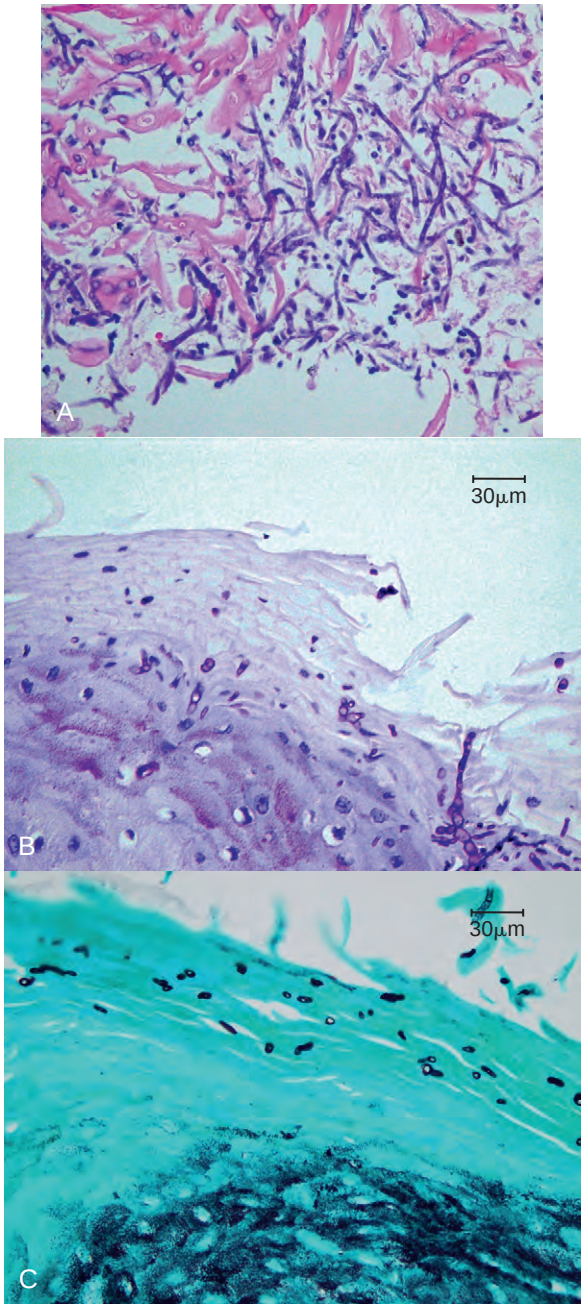


Figure 5-61. Histologic image of corneal sample obtained from a horse with a stromal abscess. **A,** Numerous filamentous hyphae are present, along with scattered inflammatory cells and stromal collagen fragments. Histologic image of corneal sample obtained from a horse with a stromal abscess, stained with H&E (×400). **B,** Fragments of hyphae scattered within the corneal stroma demonstrate positive staining, stained with periodic acid Schiff (×400). **C,** Histologic image of corneal sample obtained from a horse with a stromal abscess, stained with Gomori's methenamine silver (×400). Positive black staining of hyphal fragments is demonstrated scattered within the cornea.

stroma to reach the site of infection. Levels achieved with individual drugs may vary with species differences in corneal anatomy. For antibiotic selection, chloramphenicol and some fluoroquinolones penetrate the cornea in other species, while aminoglycosides generally do not.[308] In normal equine eyes, 0.5% moxifloxacin has been demonstrated to reach greater intraocular concentrations following topical administration than 0.3% ciprofloxacin (Clode AB, in press). Ciprofloxacin was shown to have a long half-life of elimination from the equine tear film, potentially indicating a stromal reservoir following topical application.[309] For antifungal selection, topical 5% natamycin is generally believed to minimally penetrate the corneal epithelium, but topical 1% voriconazole has been demonstrated to have good intraocular penetration in normal equine eyes.[275] It is important to note that increased (and potentially therapeutic) drug levels can be reached with more frequent application, as is possible topically, and with ocular inflammation, as is present with disease. Additionally, therapeutic débridement of the overlying corneal epithelium may be used to increase intraocular penetration of medications.

Oral antibiotics and antifungal agents, as for treatment of bacterial and fungal keratitis (see Tables 5-9 and 5-14), are indicated for stromal abscesses, in consideration of their potential involvement as etiologic agents, as well as the potential devastating effects of incomplete therapy. In addition, topical atropine and systemic NSAID administration is necessary to control inflammation and provide analgesia. With the exception of oral tetracyclines (doxycycline), use of anticollagenase agents is generally not indicated, owing to uncertain penetration and the potential for protection associated with endogenous anticollagenases provided by vascularization.

SURGICAL TREATMENT

Stromal abscesses frequently require surgical intervention to achieve complete resolution. Options include lamellar keratectomy with adjunctive grafting procedures (conjunctiva, amnion, biosynthetic materials),[260,267] corneoconjunctival transposition,[111] PK,[260,267,291,310] PLK,[266,291] and DLEK (Figs. 5-62 and 5-63).[290,291] Following surgical therapy, medical therapy should continue for infectious (bacterial and fungal) keratitis, pending histopathologic evaluation of cornea specimens obtained at the time of surgery. If medical or surgical therapy fails, enucleation may be indicated.[111,244,258,260]

PROGNOSIS

As with ulcerative keratomycosis, the prognosis depends upon aggressive, appropriate therapeutic intervention. Of five horses diagnosed with fungal deep stromal abscesses treated with medical therapy only, vision was retained in three, and the globe was retained in one, with a 3- to 6-week time frame for healing.[244] Of 11 horses with stromal abscesses of fungal or undetermined etiology receiving medical and surgical therapy, the globe was saved in 10.[267] One of two horses with ruptured stromal abscesses and iris prolapse retained its globe, but vision was lost.[111] Ten horses receiving DLEK for deep stromal abscesses (7 of 10 confirmed fungal via histopathology) retained vision following an average of 6.7 weeks of adjunctive medical therapy,[290] while eight of nine horses receiving PLK retained vision, with an average of approximately 24 days of adjunctive medical therapy.[266]

PARASITIC INFECTION: ONCHOCERCIASIS

PREVALENCE

Onchocerca cervicalis is a parasite that infects equine ocular tissues, particularly the cornea, conjunctiva, and dermal tissues. Correlation of dermal and ocular infections is inconsistent, with

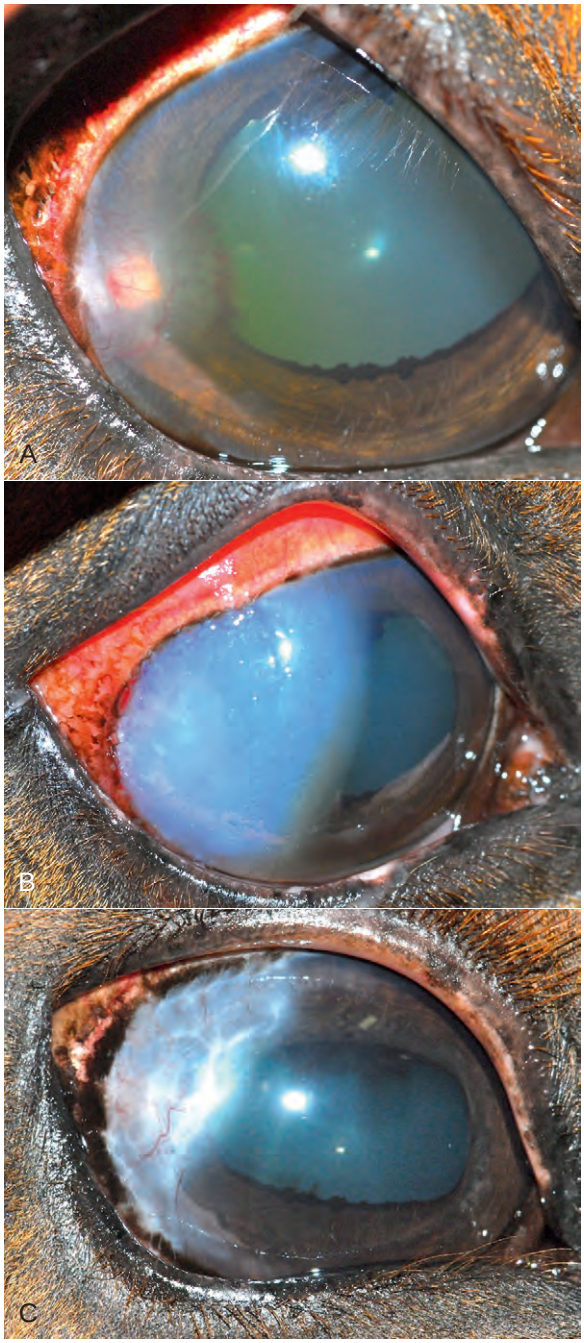


Figure 5-62. Series of photographs of a 7-year-old Quarter Horse gelding with a deep stromal abscess, which was treated with a deep lamellar endothelial keratoplasty (DLEK). **A,** Minimally vascularized deep stromal abscess adjacent to lateral limbus. Note marked yellow infiltrate and hazy edges indicating surrounding infection and inflammation. **B,** Immediately postoperative image demonstrating marked edema of lateral cornea associated with undermining anterior corneal flap (see discussion of surgical procedures). Donor corneal button is not clearly visible beneath patient's edematous anterior corneal flap, which is sutured along the limbus using a double saw-toothed pattern. **C,** Five weeks postoperative image showing moderate scarring and vascularization of lateral cornea, with minimal edema and no recurrence of cellular infiltrate. Anterior chamber is clear and quiet.

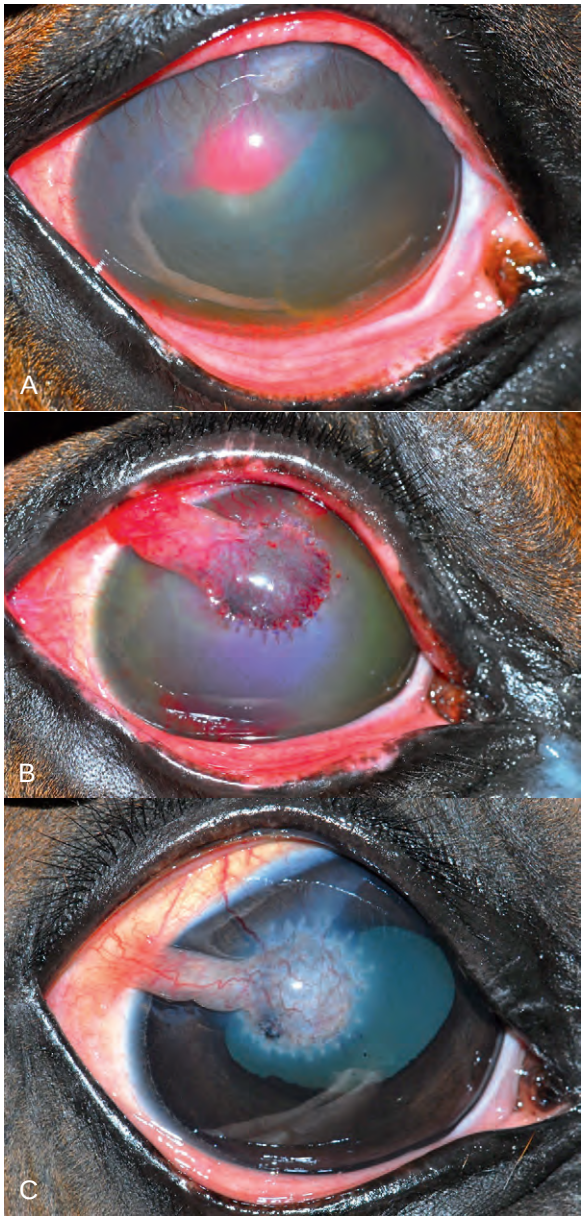


Figure 5-63. A, Clinical photograph of vascularized deep stromal abscess with persistent corneal edema and anterior uveitis unresponsive to aggressive medical management. **B,** Same horse 2 days following surgical removal of stromal abscess and repair via penetrating keratoplasty and overlying conjunctival graft placement. Note vascularization of graft, moderate diffuse corneal edema, and inability to clearly observe the anterior chamber. **C,** Same horse 6 weeks postoperatively, showing marked improvement in overall corneal and intraocular clarity, with focal opacification associated with surgical site. The pedicle of the graft was trimmed at this time.

reports documenting both the presence and absence of dermal and/or ocular microfilariae, with or without consistent ocular lesions.[118,311] A more recent report from the southeastern United States identified dermal microfilariae in nearly 53% (153/292) of horses examined at a slaughterhouse; of these, 40% (60/153) had ocular changes consistent with onchocerciasis, while over 40% without dermal microfilariae (58/138) had similar ocular lesions.[312] A positive correlation exists between increased age of horses with increased likelihood of ocular microfilariae, with or without clinical lesions.[118] Prevalence rates may vary by geographic locale. Microfilariae were detected in only 1.1% (4/368) of horses in France, none of which had ocular lesions.[313] The prevalence may be decreasing, attributed to increasing use of ivermectin as a deworming agent, which is effective against the microfilariae but not adult worms residing in the nuchal ligament.[314]

CLINICAL APPEARANCE

Acute and chronic presentations of ocular onchocerciasis have been defined,[311] but they actually represent a continuum of clinical disease. The most consistent finding in all cases is conjunctivitis, manifesting most distinctly as lateral limbal nodules and focal vitiligo (Fig. 5-64).[118,311,312] Additional ocular surface lesions in acute cases may include multifocal feathery, whitish superficial stromal opacities located in close proximity to the lateral limbus, diffuse corneal edema,[311] and multifocal scleral opacities[312]; corneal ulceration appears to be an infrequent finding. With chronicity, corneal fibrosis and vascularization may develop.[311,312] Anterior uveitis may also be present, and affected individuals appear most likely to present with signs of ocular pain (blepharospasm, epiphora, photophobia), with or without keratitis.[311] Active (subretinal infiltrates, retinal detachment) and inactive (depigmentation, hyperreflectivity) posterior uveitis has also been documented.[311,312]

DIFFERENTIAL DIAGNOSIS

Differential diagnoses for ocular onchocerciasis include other causes of nonulcerative keratoconjunctivitis (stromal abscess, immune-mediated keratitis, eosinophilic keratoconjunctivitis, NUKU, habronemiasis), neoplasia (particularly SCC), and other causes of uveitis (e.g., trauma, ERU). Definitive diagnosis is made by identifying microfilariae via conjunctival snip biopsies and ruling out other possible diagnoses as appropriate (i.e., ocular surface cytology, cultures).

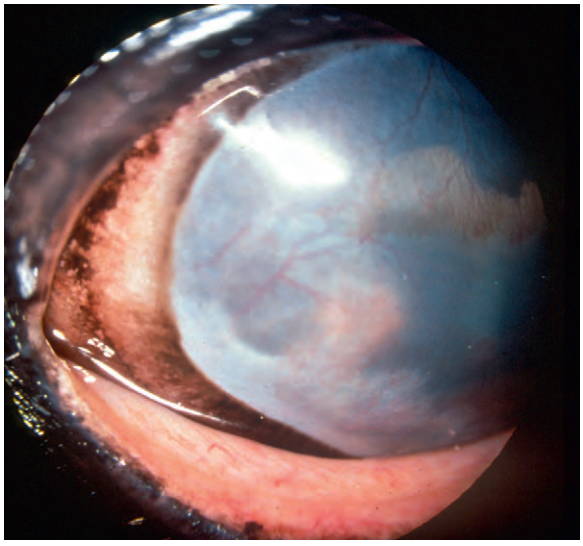


Figure 5-64. Clinical photograph of interstitial *Onchocerca* keratitis with vascularization.

PATHOGENESIS

Adult *Onchocerca* nematodes live in the nuchal ligament of horses and produce microfilaria which migrate through adjacent subcutaneous tissues and are then ingested by a *Culicoides variipennis* fly. Following development into their infective stage within the fly, microfilariae are transmitted to another horse through a fly bite, where they subsequently develop into an adult. Aberrant migration of noninfective microfilariae to the ocular region results in clinical signs and lesions of ocular onchocerciasis, which are thought to be more severe in conjunction with microfilarial death.[311]

TREATMENT

Ivermectin (0.2 mg/kg IM or PO) and moxidectin (0.4 mg/kg PO) are effective at reducing microfilarial numbers but have no effect on the adult worms. Minimizing the development of an adult worm burden is best achieved by following a regular deworming protocol, which will ideally decrease development of clinical disease. Individuals who have current or previous signs consistent with ocular onchocerciasis can be pretreated with a systemic NSAID prior to administration of a parasiticide. Therapy for ocular lesions is symptomatic: keratitis without ulceration and anterior uveitis are treated with topical corticosteroids, topical atropine, and oral NSAIDs.

PROGNOSIS

Considering the prevalence of the vector *(Culicoides)* in the environment, as well as the inability to treat the adult worms, routine deworming is the most important and effective method for prevention of onchocerciasis. Resolution of clinical ocular signs may occur following treatment of microfilaria, but conjunctival depigmentation generally remains.

CORNEAL DYSTROPHIES AND DEGENERATIONS

ENDOTHELIAL DYSTROPHY/DEGENERATION

PREVALENCE

Endothelial cell dysfunction associated with either dystrophy or degeneration of endothelial cells is a relatively rare condition in the horse and may be either unilateral or bilateral, without an apparent breed predilection.[293,315,316]

CLINICAL APPEARANCE

Regardless of the underlying cause, endothelial cell dysfunction manifests clinically as corneal edema. In early stages, it is not diffuse but is clearly delineated by a band opacity at the junction of normal and edematous cornea (Fig 5-65; see Fig. 5-9).[315] It is nonpainful; however, it may progress and ultimately become associated with development of epithelial bullae, which may rupture and form painful corneal ulcers.[315,316] Perilimbal vascularization may also develop with chronicity (Fig. 5-66).[117] If endothelial cell dysfunction is truly a primary process, no other ocular abnormalities are present.

Figure 5-65. Clinical photograph of clearly demarcated endothelial edema in the cornea of a 12-year-old Westphalian gelding.

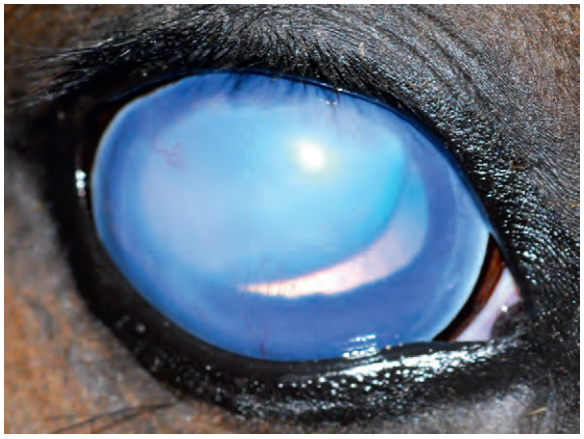


Figure 5-66. Clinical photograph of a 6-year-old Thoroughbred gelding with corneal edema and superficial corneal vascularization. The lens is cataractous and subluxated, demonstrated by the aphakic crescent.

DIFFERENTIAL DIAGNOSES

Edema resulting from primary endothelial cell dysfunction must be differentiated from that occurring secondary to other ocular disease processes, such as corneal ulceration, trauma (including blunt, penetrating, or surgical), glaucoma, anterior uveitis, endothelial IMMK, or anterior lens luxation. A thorough history should be obtained and a complete ophthalmic examination performed to rule out these possible causes for corneal edema.

PATHOGENESIS

Sodium-potassium adenosine triphosphate pumps lining the lateral endothelial cell margins actively remove water from the corneal stroma, as does carbonic anhydrase located along the apical margins. Intercellular apical tight junctions between adjacent endothelial cells provide a barrier function. All these act together to maintain corneal clarity.[8] Dystrophies, or primary endothelial cell abnormalities, may lead to sufficient endothelial cell dysfunction to result in corneal edema, but the heritable dystrophies, such as those documented in humans and suspected in dogs, have not been definitively identified in horses. Degeneration of normal endothelial cells may occur as a primary process in association with aging or genetics or may be subsequent to subclinical (or prior) ocular disease such as immune-mediated conditions or infections.[315] Degeneration of endothelial cells leads to an increase in cell size (polymegathism) and abnormal cell shape (pleomorphism) as adjacent cells expand to fill gaps, ultimately decreasing their functional capacity and resulting in edema when endothelial cell density declines from a normal of greater than 3000 cells/mm^2 to 400 to 700 cells/mm^2.[7,8] Disease attributable to decreased cell density may be diagnosed clinically by specular or confocal microscopy (see Chapter 1), but not all cases with diffuse corneal edema will manifest microscopically visible endothelial cell abnormalities.[316] Bullous keratopathy, in which edema is accompanied by multifocal bullae formation with or without associated ulceration, is likely induced endothelial cell dystrophy or degeneration.

MEDICAL TREATMENT

In the presence of corneal ulceration, topical prophylactic antibiotic and systemic analgesic therapies are indicated (see Table 5-5). Edema-specific therapy may consist of topical administration of hypertonic saline (5%) to draw fluid out of the cornea, but frequent administration is generally necessary (i.e., 6 times per day). While corneal ulcer healing is enhanced by topical chondroitin sulfate–containing solutions through numerous actions such as enhancing cell adhesion and migration; inhibiting proteolysis, inflammation, and leukocyte function; and mechanically stabilizing healing epithelium, a study comparing two solutions in dogs showed no beneficial effect on healing when endothelial dysfunction was the underlying cause of the ulceration.[317] Even in the absence of improved epithelial healing, the subjective improvement in comfort level obtained with ocular surface lubricants may justify their administration in horses with bullous keratopathy.

SURGICAL TREATMENT

Definitive treatment for endothelial disease involves full-thickness transplantation of fresh, healthy donor cornea with an intact endothelial layer. Due to the current impracticality of that procedure in veterinary medicine,[291,318,319] surgical treatment is primarily directed toward minimizing the effect of painful bullae. When corneal bullae develop, thermal keratoplasty, as reported in dogs with endothelial degeneration[320] and in dogs and horses with nonhealing ulcers,[91] may be performed to induce a fibrotic reaction between epithelium surrounding an ulcer and the anterior stroma, ideally minimizing ulcer recurrence. This procedure has not been reported in horses with endothelial disease but has been successful for ulcer resolution in dogs with the same condition[320]; anecdotally, it has met with success in horses.

PROGNOSIS

The prognosis for horses with endothelial dystrophy/degeneration is guarded. Corneal edema is generally progressive and may result in bullous keratopathy, and the underlying abnormality cannot be sufficiently addressed.

CALCIFIC BAND KERATOPATHY

PREVALENCE

Calcific band keratopathy, a degenerative condition in which calcium hydroxyapatite is deposited in and adjacent to the base-

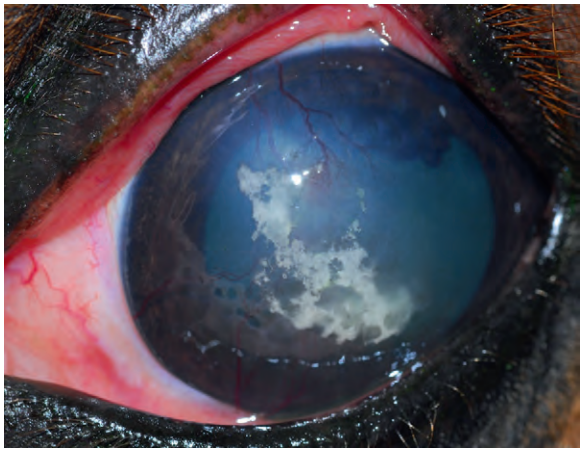


Figure 5-67. Clinical photograph of calcific band keratopathy in the interpalpebral space of a horse with possible immune-mediated keratitis. Note associated corneal vascularization and mydriatic pupil (pharmacologically dilated).

ment membrane of corneal epithelium, has been reported in over 20 horses with concurrent uveitis.[115]

CLINICAL APPEARANCE

Subepithelial deposition of calcium hydroxyapatite crystals is generally distributed within the interpalpebral fissure[315] and appears as variably dense, whitish, chalky plaques (Fig. 5-67). Variable degrees of vascularization may be present, and the plaques may cause significant enough corneal disruption to cause ulceration. Inasmuch as most cases in horses are associated with uveitis, clinical signs suggestive of active or chronic uveitis will likely be present.

DIFFERENTIAL DIAGNOSIS

Differential diagnoses include ulcerative or nonulcerative infectious keratitis (i.e., bacterial or fungal), eosinophilic keratitis, lipid degeneration, and dystrophic calcification. Initial cytology and cultures rule out infectious and eosinophilic keratitis. Histopathologic evaluation reveals amorphous basophilic granular deposits at the level of the lamina propria of the corneal epithelium and the underlying superficial stroma, with positive von Kossa or alizarin red staining indicative of mineral deposition. Dystrophic calcification lesions may appear histologically similar but occur in the region of ocular injury rather than within the palpebral fissure.[315]

PATHOGENESIS

Although the exact pathogenesis is unknown, calcific band keratopathy is thought to occur when corneal pH is increased, predisposing the ocular surface environment to precipitation of calcium and phosphorous.[321] This may occur in association with evaporation of tears, as well as loss of carbon dioxide from the corneal epithelium, which is unable to be effectively buffered by the superficial avascular cornea. Production of lactic acid by anaerobic glycolysis likely maintains a low enough pH to avoid calcium and phosphorous precipitation in the deeper layers, while proximity to vessels minimizes deposition in the perilimbal cornea.[322] The association with uveitis is unknown, but use of steroid- and phosphate-containing topical solutions (as may be used in treatment of uveitis) may be a contributing factor.[323]

MEDICAL TREATMENT

Prophylactic topical antibiotics, mydriatic-cycloplegics, and systemic NSAIDs are indicated to manage ulcerations resulting from the compromised epithelium (see Table 5-5). Topical calcium chelators, such as 1% sodium EDTA, may be administered in an attempt to resolve the mineral deposits. Their efficacy is unknown.

SURGICAL TREATMENT

Superficial keratectomy is indicated in horses with ulcerations and pain resulting from the presence of subepithelial mineral deposits. Postoperative infection rates are reportedly high,[315] possibly due to previous use of topical corticosteroids to control underlying uveitis, or due to the compromised corneal integrity.

PROGNOSIS

The prognosis for horses with calcific band keratopathy is variable and largely depends upon the size of the lesion, the underlying cause (uveitis), and the ability to control the underlying cause.

CORNEAL NEOPLASIA

SQUAMOUS CELL CARCINOMA

PREVALENCE

Squamous cell carcinoma (SCC) is the most common tumor of the equine cornea.[324] Horses with minimal ocular and periocular pigmentation, as may be found frequently in breeds with two or more coat colors such as Appaloosas, Quarter Horses, and Paints, are at increased risk for developing SCC.[132,324-329] Thoroughbreds,[327,330] Haflingers,[331] and draft horses (Belgians, Shires, Clydesdales) also demonstrate an increased prevalence, even with adequate ocular pigmentation.[325,327,329,330,332] Prevalence increases with age, with the mean age of affected individuals between 9 and 13 years.[132,324-328,330,332,333] No clear sex predilection has been identified, although some studies show a higher occurrence in geldings.[325,326] Bilateral involvement can be as high as 20%.[324,325,327,328,332] Other factors associated with increased prevalence include heredity, high levels of solar radiation and UV light exposure, increasing longitude and altitude, and decreasing latitude.[325]

CLINICAL APPEARANCE

Corneal SCC originates from the cornea, conjunctiva, or limbus. The lateral limbus is the most frequent location, with lesions commonly appearing nodular, elevated, white-pink, and fleshy (Figs. 5-68 to 5-70).[132,334-336] Secondary infection or necrosis may be present, making some individual tumors more friable. Corneal SCC may also present as non-raised lesions infiltrating the corneal stroma (Fig. 5-71).[326,334] Affected horses generally have no to only mild signs of discomfort (i.e., blepharospasm, epiphora) and minimal to no accompanying anterior uveitis.[331,334,336]

DIFFERENTIAL DIAGNOSES

Other neoplastic (i.e., mastocytosis, lymphosarcoma, amelanotic melanoma, angiosarcoma) and infiltrative (stromal abscess, immune-mediated, eosinophilic keratitis, corneal

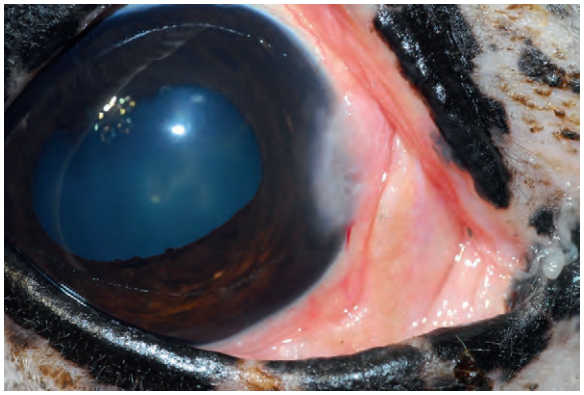


Figure 5-68. Clinical photograph of right eye of a 14-year-old Appaloosa gelding with corneolimbal squamous cell carcinoma. Note the pink, fleshy appearance of the conjunctiva, with the vascularized proliferative lesion extending past the limbus to the cornea.

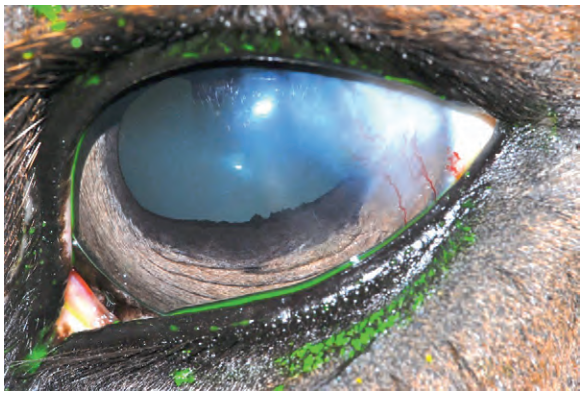


Figure 5-69. Clinical photograph of left eye of a 12-year-old Clydesdale mare with lateral limbal squamous cell carcinoma. Note the vascularized, almost fibrotic appearance, with minimal proliferation.

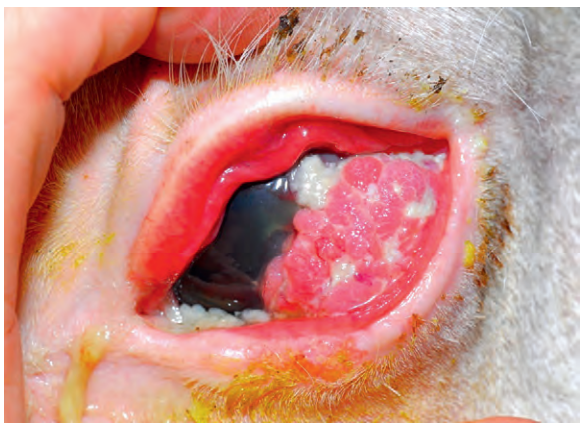


Figure 5-70. Clinical photograph of left eye of an 8-year-old Paint gelding with extensive corneoconjunctival squamous cell carcinoma, with significant vascularization and irregular surface of the proliferative mass, which was firm to the touch. Significant ocular and periocular mucoid discharge is present. Note the absence of periocular pigmentation.

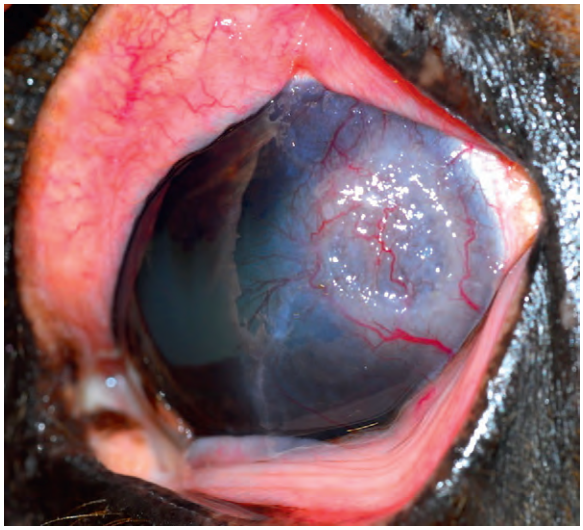


Figure 5-71. Clinical photograph of a 22-year-old Quarter Horse gelding with invasive corneal squamous cell carcinoma. Note the granular, vascularized, proliferative appearance. Slit-lamp biomicroscopy examination identified extension of lesion into corneal stroma.

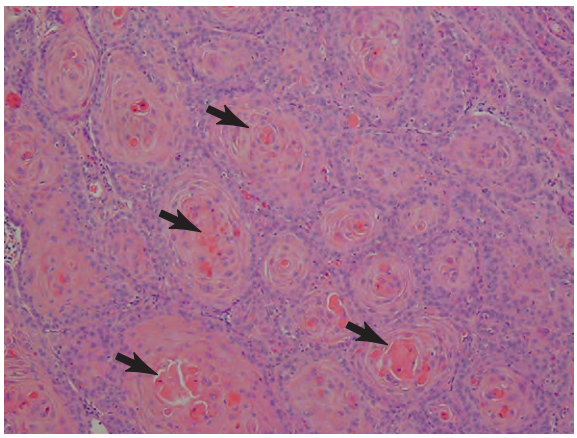


Figure 5-72. Histologic image of corneal sample obtained from a horse with extensive invasive corneal squamous cell carcinoma (SCC). Neoplastic cells are arranged in whorls surrounding brightly eosinophilic keratin pearls *(arrows)*, a hallmark of SCC. Neoplastic cells exhibit moderate anisocytosis and anisokaryosis, with few mitotic figures (H&E ×100).

degeneration, granulation tissue) diseases should be considered as differential diagnoses for SCC. Histopathologic evaluation of biopsy specimens provides a definitive diagnosis. Characteristic features include sheets, cords, and whorls of malignantly transformed epithelial cells exhibiting pleomorphism, nuclear hyperchromasia, prominent nucleoli, mitotic figures, and keratin pearl formation (Fig. 5-72).[84] If invasion of the basement membrane and extension of tumor into the corneal stroma has occurred, the tumor is considered to be invasive.[132] Invasion through Descemet's membrane has not been reported, but extensive tumors may invade the anterior chamber by growing around Descemet's and penetrating the iridocorneal angle.[337] An additional variant of corneal SCC, termed *corneal stromal invasive SCC* has been identified, in which tumor cells are present only in the corneal stroma, with the overlying epithelium being either normal or dysplastic.[326]

PATHOGENESIS

SCC can be considered a continuum of epithelial transformation, beginning with nonneoplastic dysplasia and progressing to neoplastic changes. The underlying pathogenesis of ocular SCC in all species is incompletely understood; however, UV light,[338] p53 mutations[339,340] viral infection,[341] genetics,[342] hormonal,[343] and immune factors[342] may contribute.[329,338] One study detected expression of a p53 mutant in all of six samples of equine SCC from unspecified ocular locations, which may result from UV radiation–induced damage.[339] An additional pathophysiologic mechanism may involve cyclooxygenase 2 (COX-2) enzyme overexpression, which has been detected in precancerous and cancerous skin lesions in humans, dogs, and cats.[344-347] COX-2 activity results in production of prostaglandins, which increase cell proliferation, inhibit apoptosis, promote angiogenesis, alter cellular adhesion, inhibit immune surveillance, and activate xenobiotics into reactive carcinogenic substances.[348] Results vary with study methodology, but immunohistochemistry (IHC) evaluation has identified increased COX-2 expression in equine corneas with SCC versus normal equine corneas.[330,342,349]

MEDICAL TREATMENT

Medical therapy alone is ineffective as sole treatment for corneal SCC but may constitute an effective adjunctive therapeutic measure. Use of mitomycin, a DNA-crosslinking chemotherapeutic agent, has been described for treatment of corneolimbal SCC in horses, using protocols of either a 1- or 5-minute application of 0.4 mg/mL mitomycin solution at the time of surgical removal.[333] Although it has not been evaluated as therapy for corneal SCC, topical 5-fluorouracil has shown efficacy in treatment of cutaneous SCC in horses.[350] Based on identification of increased COX-2 expression in equine ocular SCC and pending further clinical evaluation, systemic administration of COX-2–specific inhibitors may be useful.[351]

SURGICAL TREATMENT

Surgical removal with various adjunctive therapies is most effective for treating SCC. Consideration must be given to the extent of tumor growth, including depth, surface area, and involvement of adjacent eyelid or third eyelid.[334,335] In some cases, tumor invasion may be significant enough to necessitate enucleation or exenteration, rather than simple tumor resection.[327,328,332,334,335] Resection of tumor from the corneolimbal area is achieved with superficial keratectomy/sclerectomy/conjunctivectomy, with or without placement of a bulbar conjunctival or amniotic membrane graft (Fig. 5-73).[132,331,352] Invasive tumors may necessitate removal of deeper corneal tissue.[352] Adjunctive therapies include cryosurgery,[327,331,335] chemotherapy,[333] radiofrequency hyperthermia,[327,353] carbon dioxide laser ablation (see Fig. 5-85),[336] and beta irradiation (^{90}Sr).* General anesthesia is recommended when performing most surgical procedures and adjunctive therapies; however, early or small lesions may be effectively removed under standing sedation and local anesthesia (i.e., retrobulbar, auriculopalpebral, frontal nerve blocks).

*References 132, 327, 329, 334, 352, and 355.

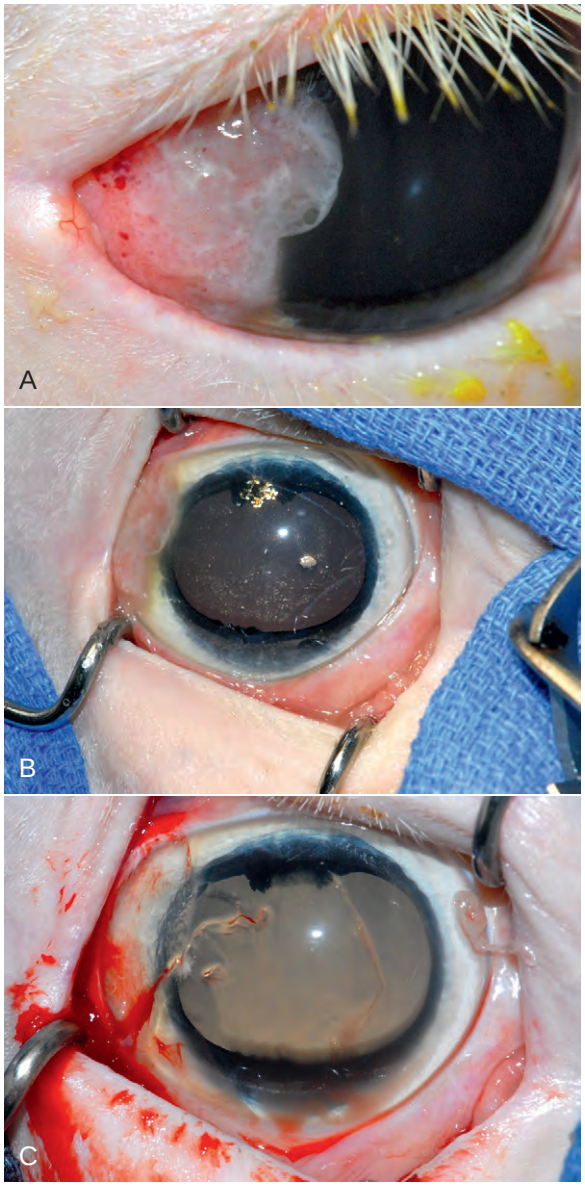


Figure 5-73. Photographs of right eye of a 6-year-old Paint gelding. **A,** Clinical appearance of lateral limbus of right eye, demonstrating vascularized proliferation typical of squamous cell carcinoma (SCC). **B,** Intraoperative view of lateral limbal SCC, showing full extent of corneal margins. **C,** Immediately postoperative image following removal of corneoconjunctival SCC via superficial keratectomy. A conjunctivectomy was performed as well, which is not visible beneath the lateral canthus in this image.

Following surgical removal of the tumor or for tumors less than 2 cm^2,[331] cryosurgery may be performed using compressed nitrous oxide or liquid nitrogen cryosurgical units.[335] The ideal cryonecrosis temperature range is −20°C to −40°C, achieved with two fast-freeze/slow-thaw cycles to achieve optimal cell death,[335] which is most safely ensured by insertion of a thermocoupler into the tissue being treated. In the cornea, use of a thermocoupler carries significant risk, therefore appropriate temperatures can only be assumed when the frozen area extends 2 to 3 mm beyond the visible tumor margins.[331] The inability to finely control the temperature and degree of accompanying damage potentially makes cryosurgery a less ideal form of

adjunctive therapy. If performed, close-tipped probes rather than open-spray units should be used to assure greatest control of the area to be frozen.[335]

Beta irradiation using ^{90}Sr, with a tissue penetration of 1 to 2 mm, is a good option for treating corneal lesions while minimizing potential lens or retinal damage.[334,353] Following tumor removal, a handheld probe is used to deliver 80 to 120[328,329] or 200 Gy[132,354] of radiation per site, generally for one to six sites total. Topical prophylactic antibiotics and a therapeutic mydriatic-cycloplegic, as well as an oral NSAID for analgesia, are administered until the surgically induced ulcer heals.[334,352] Reepithelialization may be delayed,[334] and transient corneal clouding[329] may occur postoperatively. Beta irradiation has been implicated in the development of progressive corneal edema, bullous keratopathy,[129] and more severe corneal damage in humans.[355] Most strontium units are portable and easy to use and maintain. Their primary disadvantage is availability and the need for a radiation-handling license.

Radiofrequency hyperthermia utilizes the greater sensitivity of malignant cells (compared to normal cells) to temperatures between 41°C and 45°C to enable selective destruction of tumor cells, with or without initial surgical removal.[327,353] Using a portable unit, small (<4 cm diameter) superficial ocular surface tumors are heated to 50°C for 30 seconds.[353] Postoperatively, topical prophylactic antibiotics, a therapeutic mydriatic-cycloplegic agent, and oral NSAIDs are administered as needed.[353] Healing is evidenced by visible color changes and sloughing of the lesion, generally within 3 days following treatment, with formation of granulation tissue that resolves to a leukoma.[353] Advantages of radiofrequency hyperthermia include availability of portable units and comparatively easier technical application.[353]

The carbon dioxide (CO_2) laser emits radiation in the infrared spectrum (10,600 nm), which is absorbed by water molecules.[336] Flash boiling and vaporization of cells result, leading to tissue ablation when applied at a lower energy with a defocused beam.[336] Tumor removal can be performed with the CO_2 laser itself (Fig. 5-74), or laser energy can be applied to the tumor bed following resection by superficial keratectomy.[336] Excision followed by laser therapy is preferred, as this provides a tissue sample of the lesion for histopathologic evaluation. Postoperative care includes topical prophylactic antibiotic and therapeutic mydriatic-cycloplegic application, as well as systemic NSAID administration.[336] Minimal chemosis, corneal edema, or signs of ocular pain are evident postoperatively, and most surgical wounds reepithelialize within 14 days, resolving to a corneal leukoma over subsequent weeks to months.[336] Advantages of the CO_2 laser include rapid tumor removal with a zone of cellular destruction in adjacent remaining tissue, effective hemostasis, and maintenance of a dry surgical field for maximal visualization. Sealing of nerve endings and vessels by the laser reduces postoperative edema, exudation, patient discomfort, and the potential for metastatic spread and infection.[336] Disadvantages include delayed reepithelialization, as well as availability, cost, and use of equipment.[336]

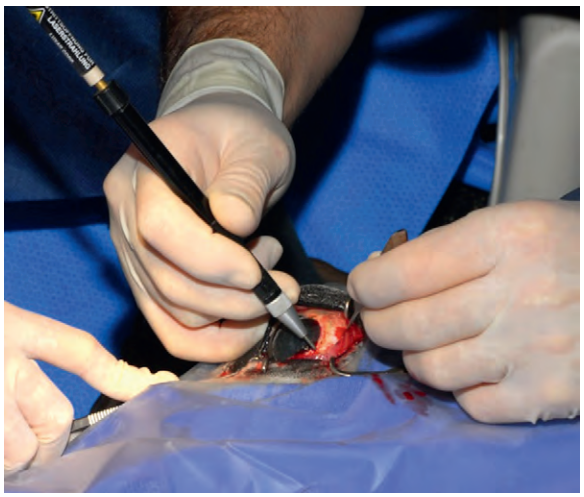


Figure 5-74. Intraoperative photograph demonstrating application of CO_2 laser energy to the surgical site following superficial keratectomy/conjunctivectomy of a squamous cell carcinoma.

PROGNOSIS

The prognosis for globe retention in horses with corneal/limbal/conjunctival SCC is dependent largely upon tumor size and selection of adjunctive treatment (Table 5-15). The risk of metastasis with ocular SCC is reportedly low (0.3 to 18.6%),[324,327,332,355a,357] but the tumor is frequently locally invasive with a potentially high risk of recurrence.[327,328] A study of 10 eyes treated with topical 0.4 mg/mL mitomycin C following surgical resection and CO_2 laser ablation of the tumor showed 11-month 60% and 80% nonrecurrence rates following application duration of 1 and 5 minutes, respectively.[333] Superficial keratectomy combined with cryosurgery for limbal neoplasia resulted in a 71% success rate over a mean follow-up period of 4.5 years (range 12 months to 18 years), with a significantly greater chance of recurrence when lesions had a surface area greater than 2 cm^2.[331] Of five corneal lesions treated with beta irradiation following surgical cytoreduction, none recurred over the 2-year duration of follow-up, with transient corneal clouding being the most common side effect.[329] A more recent study found 35.2% (12/34) of corneal lesions treated with surgery alone recurred, versus 0% (0/9) of those treated with adjunctive beta irradiation.[328] The same study found 51.5% (17/33) of limbal or bulbar conjunctival lesions recurred when treated with surgery alone, versus 30.8% (4/13) of those also treated with beta irradiation.[328] Twelve eyes treated with superficial keratectomy (with or without ^{90}Sr-irradiation or cryotherapy) followed by placement of amnion or bulbar conjunctival grafts had no tumor recurrence for the 21 to 1163 (mean 226) days of follow-up.[354] Due to the small number of horses receiving bulbar conjunctival grafts (n = 3), no comparison could be made regarding relative nonrecurrence between the two graft types. A larger study of 38 eyes treated with superficial keratectomy, ^{90}Sr-irradation, and bulbar conjunctival grafts identified 63% (24/38 eyes) were tumor free for the length of follow-up, which increased to 83% (24/29 eyes) when evaluating only horses followed longer than 2 weeks.[132] The mean duration until recurrence was 1754 days, with 40% recurring within 3 months, and mean days to recurrence of 709 for the remaining 60%. Two horses in that study experienced significant corneal damage (melting ulcer and iris prolapse), although no speculation was made regarding whether the damage resulted from any portion of the therapeutic intervention. Penetrating keratoplasty for treatment of corneal SCC which recurred following surgical excision, beta irradiation, and radiofrequency hyperthermia maintained a visual eye in the affected horse.[352]

Table 5-15 | **Success Rates for Adjunctive Therapies Following Surgical Resection of Corneolimbal Squamous Cell Carcinoma in Horses**

TREATMENT MODALITY	REFERENCES	NUMBER OF EYES	PROTOCOL	NON-RECURRENCE	SIDE EFFECTS
Topical mitomycin C	Rayner and Van Zyl, 2006[333]	10 eyes	CO_2 laser ablation of lesion; 1 (n = 5) or 5 (n = 5) min intraoperative topical	60% nonrecurrence (1 min) and 80% nonrecurrence (5 min) for	Epiphora Localized corneal edema
Cryotherapy	Bosch and Klein, 2005[331]	14 eyes	Solid, closed-tip probe; liquid nitrogen; 2-3 mm overlap between successive	71% nonrecurrence with mean follow-up 4.5 years; all with	Postoperative discomfort Transient focal corneal edema
	Mosunic et al., 2004[328]	34 eyes	As above	45% nonrecurrence (11/34 lost to follow-up)	Temporary bullous keratopathy
	Schoster, 1992[335]	3 eyes	As above	No recurrence over length of follow-up (21 to 36 months)	Granulation tissue
Cryotherapy + bulbar conjunctival graft	Ollivier et al., 2006[354]	1 eye	Double freeze/thaw	No recurrence over length of follow-up (1 year)	Postoperative discomfort Mild persistent corneal opacification
Radiofrequency hyperthermia	Grier et al., 1980[353]	45 tumors, location not specified, cattle and horses	Minimal surgical debulking; contact electrodes in place for 30 sec after tissue temperature of 50°C reached	75% (6/8) horses tumor free at 2 to 10 months	Postoperative discomfort Visible tumor sloughing over 1 week Subsequent leukoma Uveitis
CO_2 laser	English et al., 1990[336]	4 eyes	Continuous mode, power setting 3 to 6 on low scale (3-W to 8-W output); defocused beam Superficial keratectomy performed in 2 eyes prior to laser application Tumor removed via laser ablation in 2 eyes	No recurrence for length of follow-up (7 to 20 months) Recurrence in one eye at 4 months	Minimal postoperative discomfort Ocular discharge Reepithelialization in 7 to 14 days Single linear laser burn
Beta irradiation	Walker et al., 1986[329]	5 eyes	100 Gy ^{90}Sr irradiation	No recurrence of length of	Swelling Cloudiness
	Rebhun, 1990[334]	24 eyes	8000 to 10,000 rad ^{90}Sr per tumor immediately following keratectomy	No recurrence in 25 eyes over length of follow-up (1-9 years)	Reepithelialization in 3-4 weeks
	Mosunic et al., 2004[328]	23 eyes surgery only; 22 eyes surgery and ^{90}Sr	Single dose of 80 to 120 Gy ^{90}Sr (22 eyes)	Surgery only: 15% nonrecurrence (3/23 lost to follow-up) Surgery and ^{90}Sr: 65% nonrecurrence (11/23 lost to follow-up)	
Beta irradiation + bulbar conjunctival graft	Plummer et al., 2007[132]	38 eyes	^{90}Sr probe; 1 to 6 sites; 20 Gy (20,000 β-rad) per site	9 lost to follow-up Mean duration nonrecurrence for 24/29 was 1754 ± 1319 days Mean duration to recurrence for 5/29 449 ± 339 days	Melting ulcer Iris prolapse
	Ollivier et al., 2006[354]	2 eyes	^{90}Sr probe; 1 to 4 sites; 20 Gy (20,000 β-rad) per site; conjunctival (versus	No recurrence over length of follow-up (225 and 1163 days)	Postoperative discomfort Mild persistent corneal opacification
Beta irradiation + equine amnion graft	Ollivier et al., 2006[354]	7 eyes	^{90}Sr probe; 1 to 4 sites; 20 Gy (20,000 β-rad) per site; amnion placed over large or multiple keratectomy sites	No recurrence over length of follow-up (range 21-223 days)	Postoperative discomfort Mild persistent corneal opacification
Equine amnion graft	Ollivier et al., 2006[354]	2 eyes	Amnion graft placed over superficial keratectomy site	No recurrence over length of follow-up (230 and 778 days)	Postoperative discomfort Mild persistent corneal opacification

VASCULAR TUMORS

PREVALENCE

Benign and malignant blood vascular tumors (hemangioma and hemangiosarcoma, respectively) and lymph vascular tumors (lymphangioma and lymphangiosarcoma, respectively), as well as benign and malignant vascular tumors of undetermined origin (angioma and angiosarcoma, respectively), are rarely reported to involve the equine cornea. Limbal hemangiomas, hemangiosarcomas, and angiosarcomas have been described in the eyes of middle-aged horses. All three described cases in one series were Thoroughbreds,[356] and other reported breeds include Appaloosa, Quarter Horse, and Arabian.[358-361]

CLINICAL APPEARANCE

The clinical appearance of ocular surface vascular tumors is highly variable. They may appear as enlarged limbal blood vessels, focal corneal vascularization and edema, red cystic limbal masses, or solid pink corneoconjunctival masses, with or without invasion into deeper corneal layers (Figs. 5-75 and 5-76).[356,358-361] They may also be accompanied by significant serosanguineous ocular discharge, with variable clinical signs of pain or intraocular inflammation.[356,358,359]

DIFFERENTIAL DIAGNOSES

Other corneoscleral neoplastic diseases (SCC, lymphosarcoma, amelanotic melanoma, mastocytoma), as well as inflammatory lesions (granuloma, stromal abscess), are differential diagnoses for vascular tumors. Definitive diagnosis is by histopathology. Hemangiomas are typically well circumscribed and composed of variably sized vascular spaces lined with a single layer of uniform endothelial cells with rare mitotic figures.[358] Hemangiosarcomas have a combination of well-defined rudimentary vascular channels, with or without red blood cells, lined by pleomorphic endothelial cells with bulging nuclei and frequent mitotic figures; they may be locally invasive as well as metastatic.[359,360] Considering the variable presence of red blood cells in blood vascular tumors, distinction between blood and lymph vascular tumors can be difficult. Immunohistochemical evaluation with factor VIII–related antigen (FVIII-RAg), a marker strongly expressed by blood vascular endothelial cells,[360] may aid in the distinction; however, tumors of both tissue types may be immunohistochemically positive.[362]

PATHOGENESIS

The pathogenesis of vascular tumors is currently unknown. Ultraviolet light and decreased periocular pigmentation may play a role.[356,359-360]

TREATMENT

Ocular hemangiomas have been successfully treated with surgical removal with adjunctive beta irradiation or cryotherapy.[356,361] Enucleation was performed in one horse with a large lesion that had no evidence of metastatic disease.[360] Malignant tumors are more aggressive clinically, invading the orbit and periorbital sinuses and metastasizing through mandibular and cervical lymph nodes.[356,359,360] In contrast to ocular hemangiomas, angiosarcomas do not appear to be radiosensitive.[356,359]

PROGNOSIS

The prognosis for benign vascular tumors of the cornea appears favorable, provided detection is early.[361] The prognosis for malignant vascular tumors is guarded, with early and aggressive recognition and treatment necessary. Of four horses with histologically confirmed angiosarcoma, all died within 18 months, due either to confirmed metastasis or extensive local recurrence.[358] Early and aggressive surgical debulking, including orbital exenteration, was performed on several horses, only one of which was alive 18 months postoperatively.[356,360]

MELANOMA

PREVALENCE

Melanomas of the cornea and sclera, termed *limbal* or *epibulbar melanomas*, are rare in horses. A benign epibulbar melanoma was reported in a 7-year-old miniature Argentine horse,[363] and a low-grade malignant epibulbar melanoma was reported

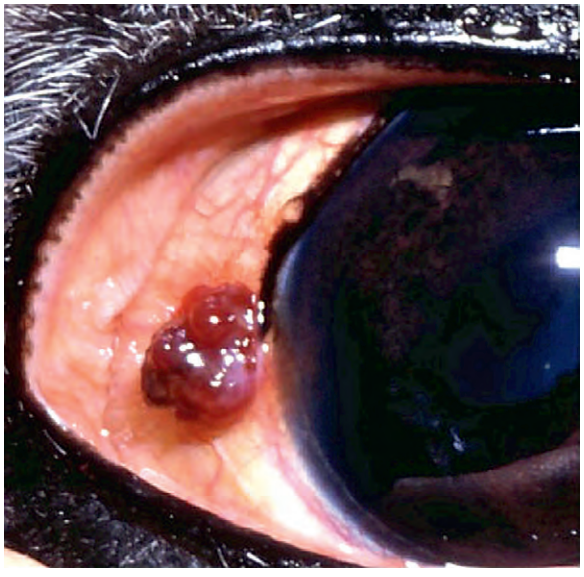


Figure 5-75. Clinical photograph of a limbal hemangioma, characterized by focal distension of conjunctival blood vessels and vascular extension into the limbal cornea.

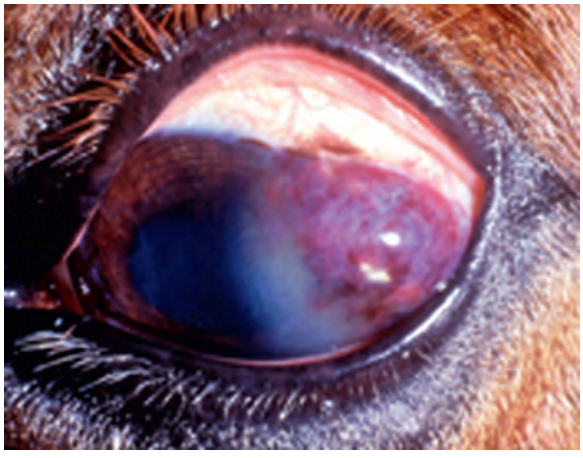


Figure 5-76. Clinical photograph of limbal hemangiosarcoma, with invasive extension into the cornea.

in a 6-month-old Hanoverian.[364] A nonpigmented corneal melanoma occurring in conjunction with a pigmented conjunctival melanoma was reported in a 20-year-old Tennessee Walking horse.[365] While equine dermal melanomas and melanomatosis occur in grey horses,[366] no predisposing factors for the occurrence of corneal or scleral melanomas have been identified.

CLINICAL APPEARANCE

Signs of ocular pain or irritation may be absent or very mild in affected horses.[363-365] The mass may be present at any location on the limbus and is frequently raised, firm, and fixed to the underlying limbus,[365] visibly infiltrating the adjacent corneal stroma (Figs. 5-77 and 5-78).[364] The mass itself may be heavily pigmented[364] or unpigmented,[365] and the overlying conjunctiva may be heavily pigmented[363] or unpigmented.[364] One horse had an unpigmented corneal lesion adjacent to a pigmented conjunctival lesion.[365]

DIFFERENTIAL DIAGNOSES

Differential diagnoses for epibulbar or limbal melanomas include nonneoplastic proliferative diseases (eosinophilic keratoconjunctivitis, parasitic keratoconjunctivitis, bacterial or fungal keratitis, granulation tissue), and neoplastic diseases (SCC, angiosarcoma, mastocytoma). Additionally, nonproliferative diseases such as subconjunctival fat prolapse, staphyloma, orbital cyst, or dermoid should be considered. Procedures that may be helpful for complete clinical evaluation include gonioscopy and ocular ultrasound, but definitive diagnosis requires a biopsy. Histopathologic evaluation of samples from previous cases identified packets and bundles of spindyloid to polygonal cells with indistinct borders and eosinophilic cytoplasm separated by a fine fibrovascular stroma (Fig. 5-79).[363,364] Pigmentation was variable, and mitotic figures were absent[363,364] or infrequent.[365] Depending upon the degree of pigmentation, bleaching may be necessary.[364] If the neoplastic cell type is difficult to identify, such as may occur in amelanotic or poorly pigmented masses, special stains (Fontana-Masson) or immunohistochemical markers (S-100, melanin A, tyrosinase, HMSA 45) may be utilized.[84]

PATHOGENESIS

The inciting cause for proliferation of melanocytes at the corneoscleral limbus is unknown, but UV radiation, chemical exposure, trauma, chronic irritation, coexistence of cutaneous

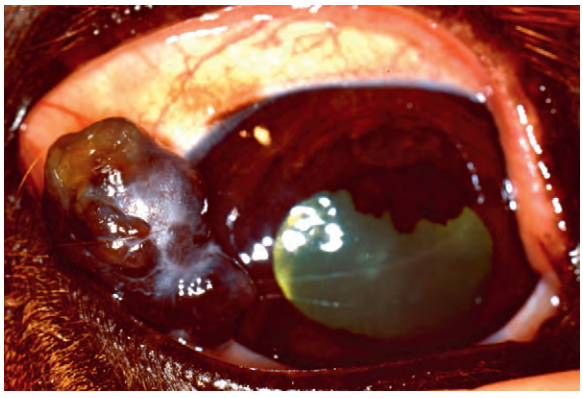


Figure 5-77. Clinical photograph of a lateral limbal melanoma.

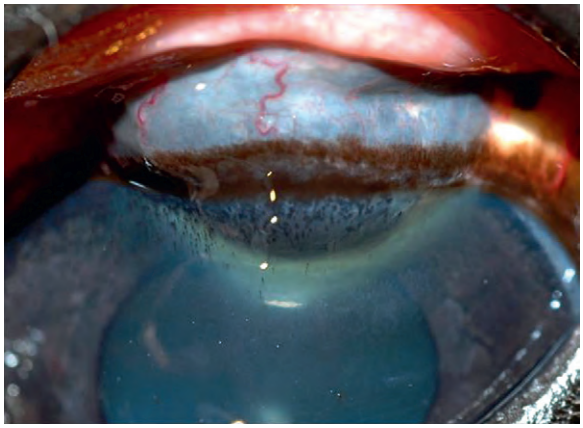


Figure 5-78. Darkly pigmented mass approximately 15 mm wide at the dorsal limbus, extending 6 mm into the cornea within the stroma, causing this area of the cornea to be elevated 5 to 7 mm higher than the adjacent corneal tissue. Diffuse pigmentation can be seen extending into the cornea from along the leading edge of the mass. A distinct crescent-shaped arc of corneal edema delineates the edge of the mass within the cornea. (From McMullen RM, et al: Epibulbar melanoma in a foal, Vet Ophthalmol 11:44–50, 2008.)

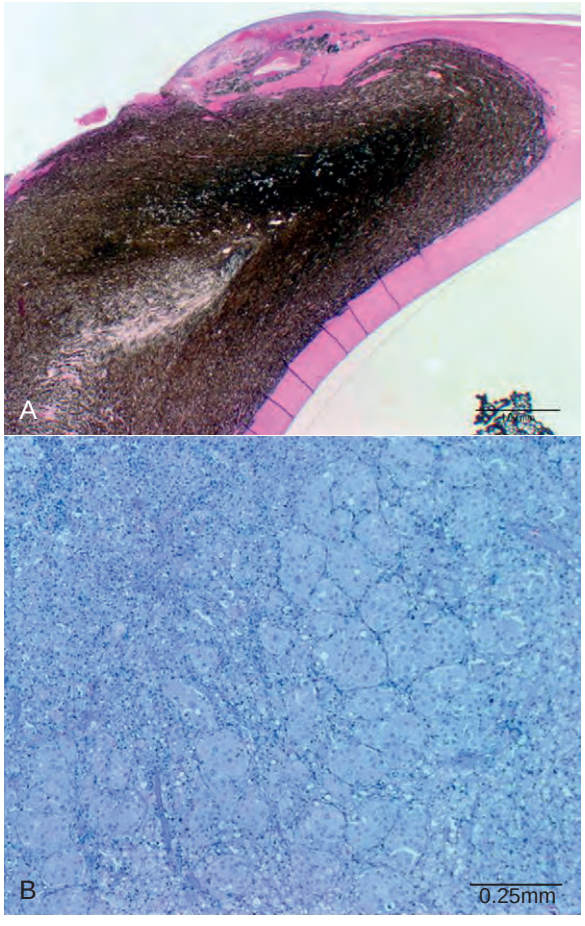


Figure 5-79. **A,** Photomicrograph of the unbleached H&E section. Heavily pigmented limbal melanoma is infiltrating into the cornea, well beyond the limbus (bar = 500 μm). **B,** Photomicrograph of the limbal biopsy. Paraffin section is heavily bleached (potassium permanganate to remove pigment) and stained with H&E. Neoplastic cells are arranged in large aggregates within a fine fibrovascular stroma. In this section, the neoplastic cells are polygonal with abundant cytoplasm and vesiculated nuclei. The neoplastic cells exhibit mild anisocytosis and moderate anisokaryosis (bar = 0.25 mm). (From McMullen RM, et al: Epibulbar melanoma in a foal, Vet Ophthalmol 11:44–50, 2008.)

melanomas, and genetic variables have been considered as potential factors in animals and humans.[81,363,367,368]

MEDICAL TREATMENT

Systemic administration of the histamine H_2 antagonist, cimetidine, has been reported in horses with cutaneous melanoma, with variable ability to effect tumor regression.[369-371] Additional nonsurgical treatments reported for cutaneous melanoma include autogenous vaccination with select tumor antigens that aid tumor recognition and elimination,[371] and intratumoral vaccination with a viral-derived suicide gene that sensitizes tumor cells to antiviral medication.[372] Each of these treatments may be combined with surgical excision if indicated, but none has been evaluated specifically as treatment for corneal melanoma.

SURGICAL TREATMENT

As reported in horses or other species, surgical resection of epibulbar melanomas may be performed via lamellar corneosclerectomy or full-thickness resection with reconstruction by homologous corneoscleral, third eyelid, or synthetic grafting procedures.[363,365,373-378] Adjunctive procedures may include cryotherapy, beta irradiation, or laser photocoagulation.[379-381] In cases with significant extension or local invasion, enucleation may be indicated.[364]

PROGNOSIS

In consideration of the few reported cases in veterinary literature, the prognosis for limbal melanoma in horses is difficult to determine. Of the reported cases, one was histopathologically diagnosed as low-grade malignant melanoma and was particularly locally aggressive, with marked proliferation within days of partial resection necessitating enucleation 8 days later.[364] No evidence of systemic metastasis was present, and no local recurrence was noted 14 months later. The two other cases were diagnosed as benign, and affected horses were free of recurrence for 10 months and 2 years, respectively, following mass removal.[363,365]

MAST CELL TUMOR

PREVALENCE

Proliferative mast cell lesions involving the eye have been rarely reported in the horse. The terms *mast cell tumor* and *mastocytoma* are used to describe growths with neoplastic tendencies, while *mastocytosis* describes mast cell lesions without neoplastic characteristics.[382] Mastocytomas have been reported in a 12-year-old Quarter Horse,[383] a 12-year-old Dutch Warmblood, and a 23-year-old New Forest horse,[384] and mastocytosis has been reported in a 9-month-old Arabian colt[385] and a 5-year-old pony.[386]

CLINICAL APPEARANCE

With the exception of ocular discharge, minimal signs of pain are present in affected animals.[383-386] Reported lesions have all arisen at the limbus and have varied in color from grayish-white to tan to pinkish-white (Fig. 5-80).[383,385,386] They may be flat or irregular, and the surface may be roughened or smooth.[383,385,386] Given the small number of horses affected, no conclusions can be drawn regarding clinically differentiating mastocytosis from mastocytoma.

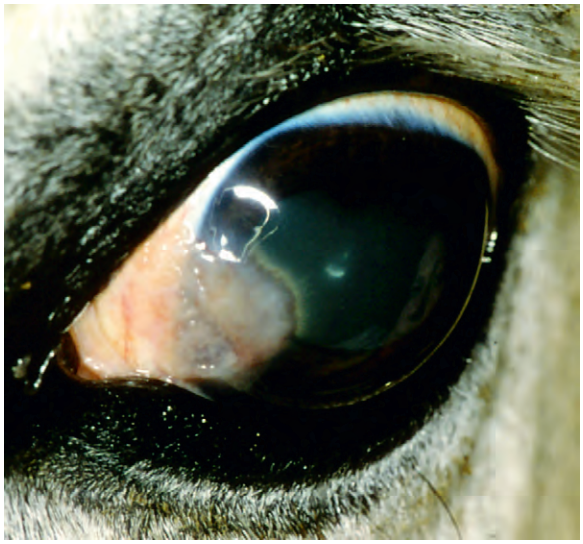


Figure 5-80. Clinical photograph of a proliferative lateral limbal lesion. Cytologic evaluation identified a predominance of mast cells, which was confirmed histopathologically as a mastocytoma.

DIFFERENTIAL DIAGNOSES

Other neoplastic lesions (SCC, lymphosarcoma, melanoma), as well as non-neoplastic lesions (eosinophilic keratitis, granulation tissue, parasitic granuloma, orbital fat prolapse, corneal abscess, subconjunctival cyst) should be considered as differential diagnoses for mast cell lesions. Cytology and histopathology provide definitive diagnosis. Histologic evaluation of biopsy specimens identifies sheets of large, well-differentiated round cells with hyperchromatic nuclei and granular eosinophilic cytoplasm. The granules stain metachromatically with toluidine blue, confirming them to be mast cells. Eosinophilic inflammation is common, and mitotic figures are rare. Although one case was described as mastocytoma, each reported case of corneoscleral mast cell lesions fit the histologic diagnosis of mastocytosis.[385]

PATHOGENESIS

The underlying cause of mastocytosis/mastocytoma is unknown, and it is unknown whether the accumulation of mast cells is a reactive or a neoplastic change.[386] One report of generalized mastocytosis in a foal detailed 1 year of the appearance of multiple skin nodules followed by spontaneous regression, but the underlying stimulus was not identified.[387]

TREATMENT

Surgical excision via lamellar sclerectomy or corneosclerectomy was performed in five cases,[383-386] with one of those cases receiving adjunctive strontium-90 therapy[383] and two others receiving cryotherapy[384] at the time of surgery.

PROGNOSIS

Cutaneous mastocytosis may undergo spontaneous remission,[387] which may also occur with ocular lesions. If the tumor is large and interfering with appropriate eyelid function, surgical excision is recommended to avoid secondary complications such as exposure keratopathy. Although few cases have been reported, the prognosis was favorable. Surgical excision of the

masses was curative for the duration of follow-up of 3[383] to 45[385] months. No recurrence was identified in one case,[383] while proliferative tissue was noted at the surgical site in another horse 3 months postoperatively.[386] The two cases receiving adjunctive cryotherapy had no reported recurrence, although follow-up information was not available.[384]

LYMPHOSARCOMA

PREVALENCE

Corneoscleral lymphosarcoma (LSA) is rare in the horse, with 2 of 21 cases presenting with corneal masses, one bilaterally affected and one unilaterally.[388]

CLINICAL APPEARANCE

Corneoscleral LSA was located in the temporal or ventrotemporal quadrants, crossing the limbus to include both cornea and sclera.[388] The masses were raised, smooth, firm, nonulcerated, pink to pink-white, and well vascularized. The presence of ocular pain or secondary uveitis was not reported.

DIFFERENTIAL DIAGNOSES

Other neoplastic lesions (SCC, hemangioma, angiosarcoma, melanoma, MCT), immune-mediated keratitis, eosinophilic keratitis, granulation tissue, and corneoscleral foreign bodies should be considered as possible differential diagnoses for corneoscleral LSA.

PATHOGENESIS

The pathogenesis of LSA is unknown,[389] but corneoscleral LSA is considered to be an ocular manifestation of the multicentric form of systemic LSA, which frequently involves peripheral lymph nodes and skin.[388,389]

TREATMENT

As it is a manifestation of systemic LSA, treatment for ocular LSA involves staging the overall disease state in the patient and treating accordingly.

PROGNOSIS

The prognosis for LSA is grave, potentially because of delayed detection associated with difficult detection of peripheral lymph node or visceral organ involvement. Twenty of 21 horses with ocular LSA (eyelid, orbital, third eyelid, intraocular, and corneal) died or were euthanized within 6 months due to systemic disease associated with LSA lesions.[388] Recognition of ocular lesions may precede identification of systemic signs, potentially enabling more rapid diagnosis and aggressive treatment.

CORNEAL SURGERY

EQUIPMENT

Appropriate equipment is vital to the ability to successfully perform corneal surgery. A focal light source and magnification, provided by either surgical loupes or an operating microscope, are essential. The specific instruments utilized for each procedure will vary, but a standard intraocular pack is generally sufficient (see Table 5-15).

Appropriate suture selection is equally important. Absorbable suture types are most common in veterinary ophthalmology, since removal is not necessary, whereas removal of nonabsorbable sutures may require a repeat general anesthetic episode. Absorbable sutures incite a greater local inflammatory response, however, which may be detrimental to maintenance of corneal clarity. All sutures indicated for use in the cornea are attached to a spatula needle (Fig. 5-81) which splits the corneal lamellae and enables placement of sutures at the appropriate depth.

PATIENT PREPARATION

Depending upon the surgical procedure, facility, patient condition and temperament, and comfort level of the surgeon, corneal

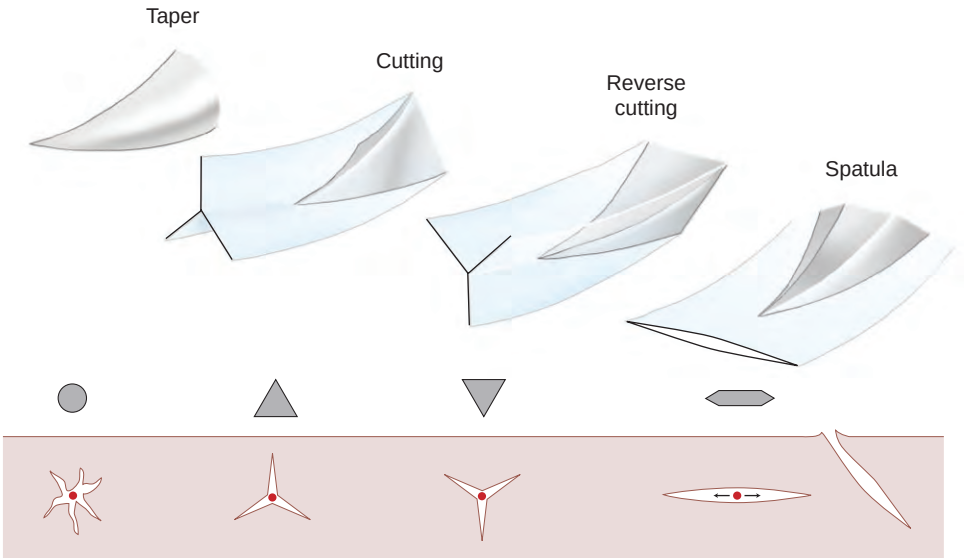


Figure 5-81. Diagram of spatula needle versus cutting and reverse cutting and taper needles.

Table 5-16 | **Surgical Supplies and Microsurgical Instruments Appropriate for Corneal and Conjunctival Procedures**

General supplies	Balanced Salt Solution (or other wetting solution)
	Cellulose sponges
	Viscoelastic material (for intraocular procedures)
	Sterile surgical towels
	Sterile eye drape
	Jones towel clamps
	Irrigating canulas (27-gauge, 30-gauge, anterior chamber irrigating canula)
	Castroviejo eyelid speculum
Blades	#64, #65, #67, or #69 microsurgical (Beaver) blades
	Microsurgical (Beaver) blade handle
	Diamond knife
	Corneal knife
	Martinez lamellar corneal dissector
Forceps	Colibri (or similar) tissue forceps (0.12 mm, 0.3 mm tips)
	Suture tying forceps (i.e., Harms, Castroviejo, McPherson, Tennant)
Scissors	Left- and right-handed corneal section scissors
	Westcott tenotomy scissors (blunt)
	Stevens tenotomy scissors
	Stitch scissors
Needle drivers	Barraquer (or similar) curved needle holder (delicate and very delicate)
Sutures	Braided absorbable suture (i.e., polyglactin 910), sizes 7-0, 8-0, or 9-0
	Monofilament nonabsorbable suture (i.e., nylon), sizes 7-0, 8-0, or 9-0

procedures may be performed either under standing sedation with local anesthesia or under general anesthesia (Table 5-16).[93] When performing procedures under standing sedation, local anesthetic blocks should be utilized to minimize eyelid movement (auriculopalpebral block), provide ocular surface anesthesia (frontal block, topical anesthetic administration), and minimize globe movement (retrobulbar block [see Chapter 1]). These same blocks are appropriately used when the patient is under general anesthesia as well. Neuromuscular blocking agents may be used instead, provided mechanical ventilation is available.

Preparation of the surgical site begins with careful trimming of eyelashes and periocular hair. Dilute Betadine (1:50), baby shampoo, and sterile eyewash should be used to clean the ocular and periocular area. Chlorhexidine, alcohol, and other surgical prep solutions should not be used around the eye. Careful cleaning of the conjunctival fornices with cotton swabs soaked in dilute Betadine should be performed, with care taken to avoid damaging potentially compromised cornea. Topical local anesthetic should be administered following the surgical preparation. Ointments should not be administered prior to corneal or intraocular surgery, as they are potentially damaging to tissues and may interfere with proper surgical technique.[391]

SURGICAL PROCEDURES

GENERAL CONSIDERATIONS

EPITHELIAL DÉBRIDEMENT

Even if healthy, the epithelium surrounding corneal wounds should be débrided with sterile cotton-tipped applicators, cellulose swabs, or a Beaver #64 microsurgical blade (Fig. 5-82). This helps to prevent downgrowth of the epithelium into the wound margins, which can lead to wound leakage and graft dehiscence and stimulates vascular ingrowth. Frequent irrigation (i.e., every 20 to 30 seconds) of the epithelium with an ocular-specific irrigating solution, such as balanced saline solution (BSS), throughout the procedure is essential to prevent drying and corneal ulceration.

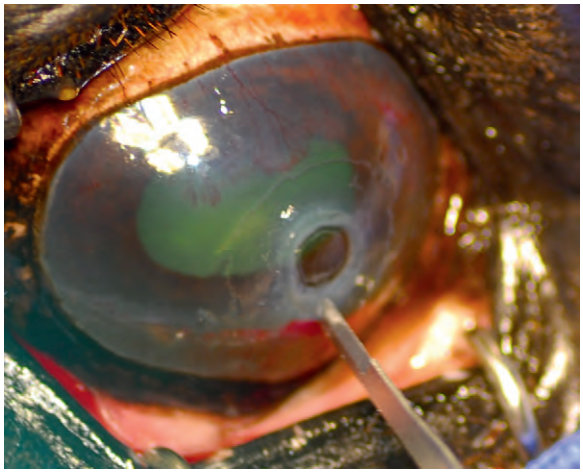


Figure 5-82. Photograph of débriding of the epithelium around a corneal ulcer with microsurgical blade during surgery,

SUTURE PLACEMENT

When placing sutures in a full-thickness wound, sutures should be placed to a depth of 75% to 90% of the corneal stroma (Fig. 5-83).[286,289] If sutures are placed too superficially, the internal aspect of the wound will not be apposed, and healing will be inhibited. If placed too deep with penetration of the endothelium, wound leakage and intraocular infection may occur. When suturing a graft over a corneal wound, the first bite should be through the grafting material, and the second bite into the cornea, either at the edge of a keratectomy wound or more superficially (i.e., half to two-thirds thickness of the stroma), 1- to 2-mm distance into the surrounding cornea (see Fig. 5-96).[289] Initial sutures should be placed through the distal end of the graft.

ANTERIOR CHAMBER MAINTENANCE

When full-thickness corneal wounds are present preoperatively or will be made intraoperatively, maintenance of the anterior chamber is critical for the health of the eye and for accurate surgical correction of the corneal defect. Sterile viscoelastic materials are used, because they balance viscosity, cohesiveness, coatability, pseudoplasticity, and elasticity to maintain the shape of the globe and protect the endothelium.[146] Ideally, such substances are removed from the anterior chamber at the conclusion of surgery to minimize the risk of postoperative ocular hypertension, but that may not be possible in certain procedures in which salvaging the globe is the goal.[146]

HEMOSTASIS

Topical administration of dilute (1:10,000) epinephrine is helpful for maintaining hemostasis, leading to vasoconstriction

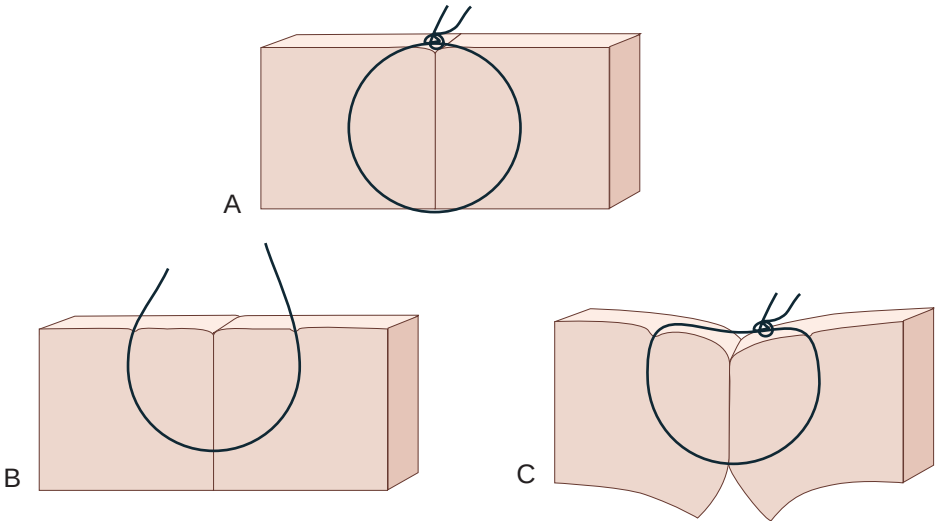


Figure 5-83. Illustration of proper suture depth placement during corneal surgery. **A,** Full-thickness suture placement may result in leakage, seeding of bacteria into anterior chamber, or epithelial downgrowth. **B,** Appropriate deep stromal placement of corneal sutures. **C,** Too shallow placement of corneal sutures results in posterior wound gaping and increased possibility of wound dehiscence and scar formation.

of conjunctival and corneal vessels. Wet-field cautery may also be used.

DIRECT CORNEAL SUTURING

INDICATIONS

Direct corneal suturing may be performed to repair wounds without loss of tissue that can be accurately apposed with minimal tension, such as partial- or full-thickness lacerations or very small (<1 mm) corneal perforations.[110,111] If tissue at the margins of the wound is necrotic or appears infected, the tissue should be removed and grafting procedures considered.

PROCEDURE

Epithelium surrounding the wound should be débrided. Wound edges may be apposed with absorbable 7-0 to 9-0 suture in a simple interrupted, simple continuous, or double saw-toothed pattern, with sutures placed 75% to 90% depth in full-thickness wounds.[286] A conjunctival graft can be placed over the primary repair if greater assurance of vascular supply is desired, but this is not always necessary. To ensure that watertight wound closure has been achieved, a Seidel test may be performed by applying concentrated fluorescein stain, which will appear yellow-orange, to the corneal surface. Aqueous humor leakage will dilute the fluorescein, causing a focal change in color from yellow-orange to green.

POSTOPERATIVE CARE

Medical therapy with topical antibiotics, a therapeutic mydriatic-cycloplegic agent, and a systemic NSAID are indicated. If the wound is partial-thickness, fresh, and has no signs of infection, a prophylactic antibiotic may be appropriate. Full-thickness wounds or perforations should be treated with a therapeutic topical antibiotic with good intraocular penetration to provide greater protection against endophthalmitis. Systemic antibiotic administration may be indicated as well.

COMPLICATIONS

Complications that may follow direct suturing of a partial-thickness corneal wound include infection, dehiscence, excessive scar formation, and altered corneal curvature (astigmatism). Additional complications that may be encountered following repair of a full-thickness corneal wound include reperforation with subsequent aqueous humor leakage, iris prolapse, or globe collapse, as well as complications secondary to likely severe anterior uveitis (synechiae, cataract).[110,111]

SUPERFICIAL KERATECTOMY

INDICATIONS

Superficial keratectomy (SK)—removal of the corneal epithelium, basement membrane, and anterior stroma—is indicated to remove neoplastic,[132] dysplastic (dermoid),[83] or infected corneal tissue,[185,267] or to promote healing of immune-mediated keratitis[294] or nonhealing ulceration.[93] The resulting wound bed may be left to heal by second intention, but a graft may be performed over the keratectomy site if the depth of the keratectomy is greater than half the corneal thickness, if the diseased tissue cannot be entirely removed, or if other concerns regarding ability of the wound to heal are present (e.g., deficient tear production).[286]

PROCEDURE: COMPLETE INCISIONAL KERATECTOMY

The entire involved portion of cornea to be removed is outlined to the appropriate surface area and depth with a dermal biopsy punch, corneal trephine, diamond knife, or microsurgical blade in a round, square, or triangular shape. The edge of the cornea to be removed is grasped with microsurgical (e.g., Colibri) forceps, and lamellar dissection of the entire incised area is performed with either a Martinez lamellar corneal dissector or a Beaver #64 microsurgical blade angled parallel to the stromal lamellae (Fig. 5-84). The excised tissue should be submitted

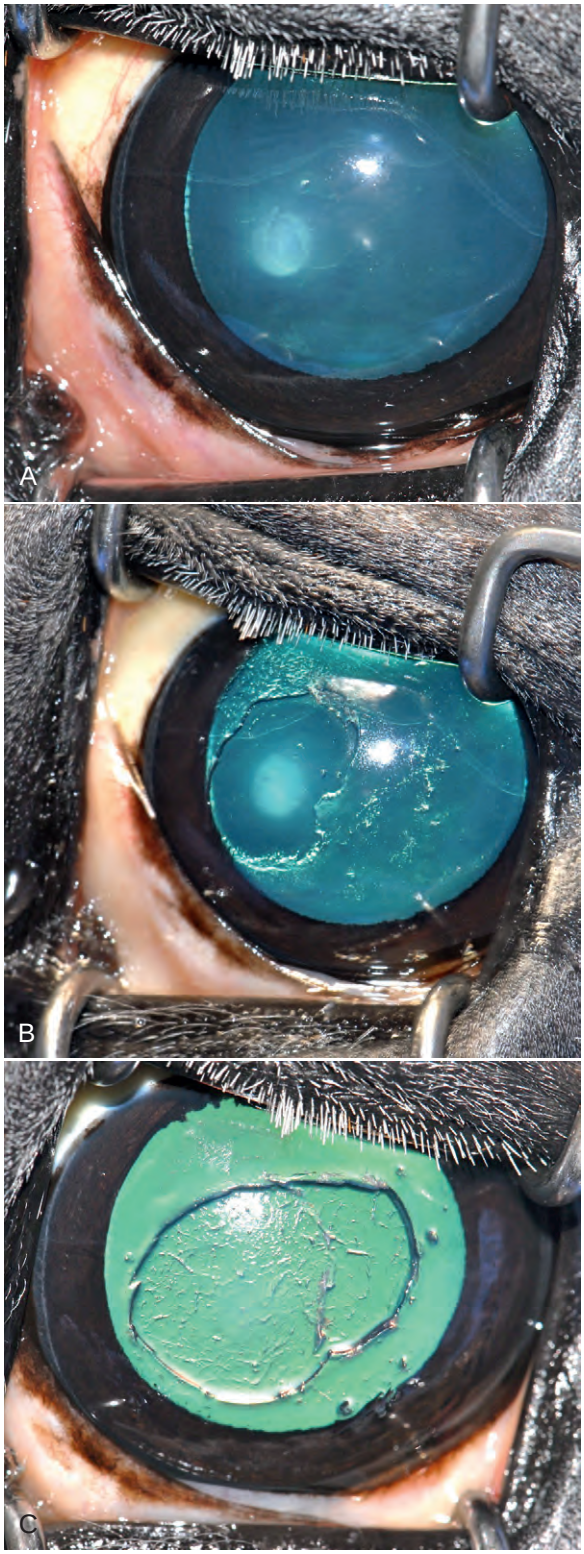


Figure 5-84. Images from a 6-year-old Thoroughbred gelding with a nonhealing ulcer, for whom corneal cytology and cultures were negative for infectious agents or inflammatory cells. **A,** Clinical photograph showing superficial ulcer with mild corneal edema. **B,** Clinical photograph following débridement of surrounding nonadherent epithelium with a cellulose surgical sponge. **C,** Clinical photograph of corneal surface following partial-incision superficial keratectomy encompassing entire region of débrided epithelium.

for histopathology and, if appropriate, bacterial and fungal cultures.

PROCEDURE: PARTIAL INCISION KERATECTOMY

A small corneal incision is made to the appropriate depth, adjacent to the involved portion of cornea that is to be removed. The width of the incision should allow a microsurgical blade or lamellar corneal dissector to be inserted between the underlying corneal lamellae, following which complete lamellar dissection of the involved corneal tissue is performed. Corneal section scissors are then inserted through the initial incision to complete the keratectomy. The excised tissue should be submitted for histopathology and, if appropriate, bacterial and fungal cultures.

General anesthesia is frequently preferred for surgical procedures of the equine cornea, but superficial keratectomies can be performed with the horse standing under heavy sedation (e.g., detomidine 0.01 mg/kg). Because the partial incision keratectomy requires only a single perpendicular corneal incision, it is the procedure of choice in the standing horse. Use of regional anesthetic (topical ocular anesthetic; auriculopalpebral, frontal, and retrobulbar nerve blocks; see Chapter 1) and other methods of restraint (e.g., humane twitch) greatly facilitate the procedure.

POSTOPERATIVE CARE

Topical antibiotics should be administered as for a corneal ulceration, with selection depending upon disease process (i.e., prophylactic versus therapeutic antibiotics, with or without antifungal medications). Topical mydriatic-cycloplegic and systemic NSAID administration is also necessary. If treating corneal neoplasia, adjunctive therapies may be indicated, such as beta irradiation, CO_2 laser, or topical chemotherapy.

COMPLICATIONS

Depending upon the underlying disease process for which a superficial keratectomy is performed, complications are generally minimal. Such complications include delayed healing, infection and deep stromal involvement, perforation, recurrence of the original lesion, and increased corneal opacification in the formation of excessive scarring, pigmentation, or granulation tissue formation.

CONJUNCTIVAL GRAFTS

INDICATIONS

Conjunctival grafts, indicated for corneal diseases that require immediate vascularization, provide fibroblasts, growth factors, antiproteases, and anticollagenases, epithelial cell coverage, and tectonic support.[392] Such conditions include deep ulcers, melting ulcers, and descemetoceles,* as well as immune-mediated[294] and nonhealing ulcers[93] in which the underlying pathogenesis may not be definitively known prior to surgery. Variations of conjunctival grafts include pedicle, bipedicle, bridge, hood, 360-degree, island, and tarsopalpebral grafts, with the type selected depending upon the extent and location of the disease process. Pedicle grafts, with one end of the graft supplying blood vessels (Fig. 5-85), are the most commonly

*References 168, 245, 251, 258, 260, 267, 284, and 287.

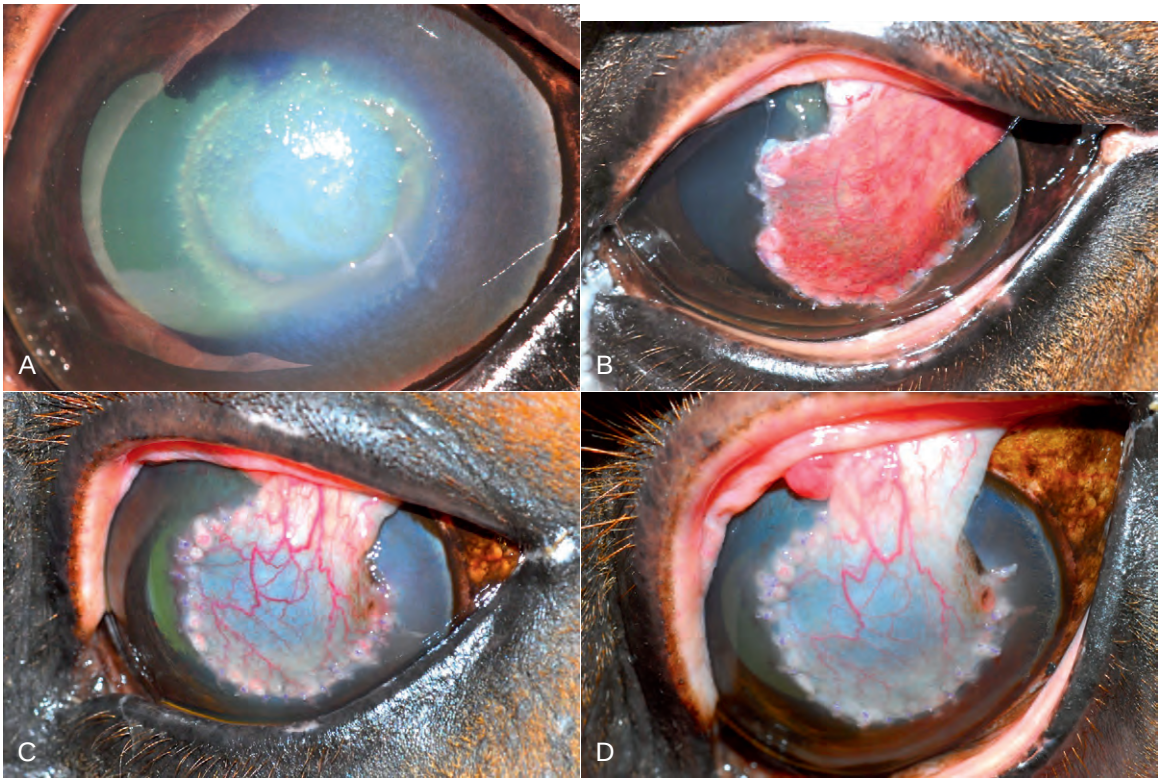


Figure 5-85. The following photographs are from a 10-year-old Hanoverian gelding with fungal keratitis. **A,** Clinical photograph showing cellular infiltration and ulceration of the axial superficial stroma. **B,** Immediately postoperative photograph of conjunctival graft sutured over area of diseased cornea, which was removed via superficial keratectomy at the time of surgery (not shown). **C,** Two weeks postoperative image of the conjunctival graft, which is well vascularized and becoming incorporated into the corneal stroma. Pupil is nicely dilated, indicating good control of the corneal disease subsequent to surgical therapy and treatment with topical atropine. **D,** Three weeks postoperative image of conjunctival graft, showing mild granulation tissue at limbal margin in area where conjunctival graft was harvested. Remaining portion of the conjunctival graft is adherent and well vascularized, and the pupil remains well dilated.

performed. Minimal healthy cornea is covered, which allows evaluation of uninvolved cornea and intraocular structures, and both centrally and peripherally located lesions may be effectively treated. Bipedicle and bridge grafts provide dual blood supply for larger central or linear lesions and require less corneal suturing, but a greater proportion of uninvolved cornea may be covered. Hood grafts effectively cover smaller peripheral lesions and minimally affect the ability to visualize the remainder of the cornea or intraocular structures. In contrast, 360-degree grafts, utilized for extensive corneal disease, cover the entire corneal surface, blinding the patient and eliminating the ability to evaluate intraocular structures. Free island grafts lack blood supply entirely and are therefore rarely indicated in the management of equine corneal disease. Tarsopalpebral grafts are harvested from the palpebral conjunctiva, making them more susceptible to tension from eyelid movement and compromised blood supply from the frequently extensive length of the graft. In the absence of sufficient viable bulbar conjunctiva, however, they may be useful. Overall graft selection is based upon the location and size of the lesion, ease of access to prepare the graft site, proximity to the limbus, and presence of conjunctival pigmentation.[289] The ideal orientation for grafts is in a dorsal-ventral direction so as to decrease drag associated with eyelid movement, with the pedicle(s) as short as possible.

PROCEDURE

The epithelium surrounding the wound edges is débrided, and necrotic or infected tissue is removed with corneal scissors. Once the appropriate graft type and harvesting location are selected, the bulbar conjunctiva is grasped 1 mm posterior to the limbus with 0.12-mm Colibri forceps, and a snip incision is made with curved, blunt-tipped Westcott tenotomy scissors (Fig. 5-86, *A*). The tip of the scissors is inserted through the incision between the conjunctiva and the deeper, closely adherent fibrous connective tissue, Tenon's capsule. Tenon's capsule is separated from the conjunctiva by blunt dissection, because retention of this tissue creates graft tension and inhibits effective epithelial adherence, increasing the risk of dehiscence. Once blunt dissection of the entire graft is complete, and without regrasping with the Colibri forceps, Westcott tenotomy scissors are used to make a cut parallel and 1 mm posterior to the limbus (see Fig. 5-86, *B*). For a pedicle graft, a cut 1- to 2-mm wider than the wound to be covered is made at the tip of the incision, directed toward the fornix. A third cut parallel to the initial limbal cut and directed from the tip toward the

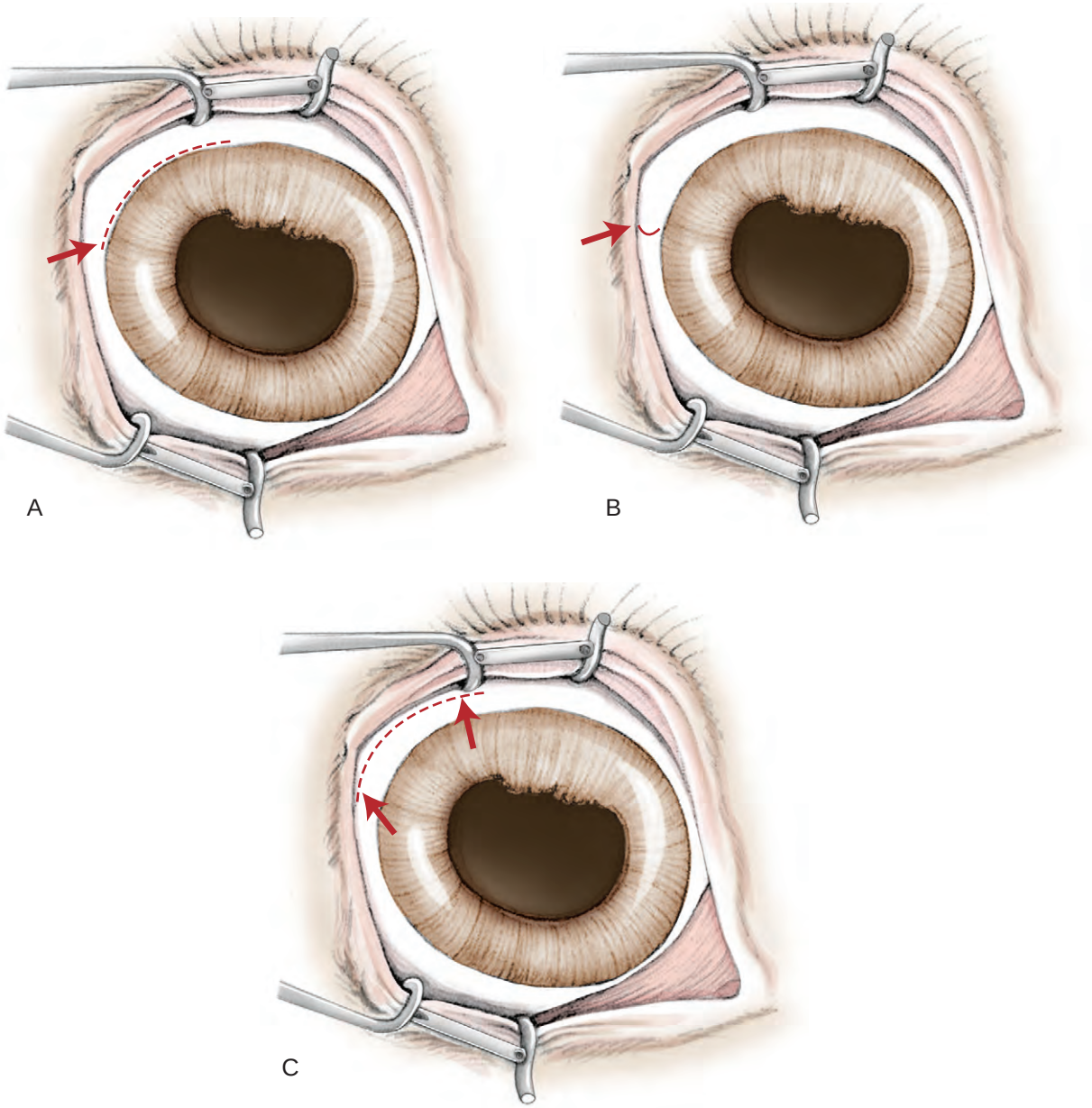


Figure 5-86. Steps for performing a conjunctival pedicle graft. **A,** Location of starting incision for conjunctival graft. The bulbar conjunctiva is grasped 1 mm posterior to the limbus with Colibri forceps, and a snip incision is made with scissors. **B,** Once blunt dissection of the entire graft is complete, tenotomy scissors are used to make a cut parallel and 1 mm posterior to the limbus. **C,** For a pedicle graft, a cut 1 to 2 mm wider than the wound to be covered is made at the tip of the incision, directed toward the fornix. A third cut parallel to the initial limbal cut and directed from the tip toward the base of the graft is made, completing the rotational pedicle graft.

Continued

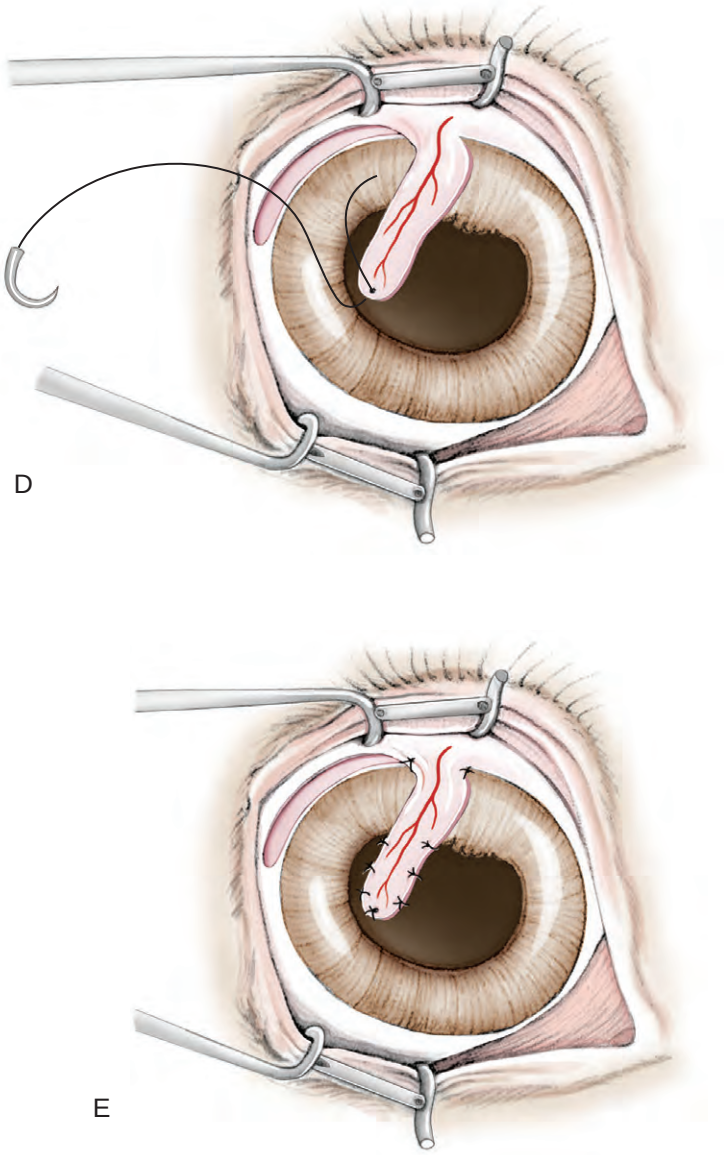


Figure 5-86, cont'd. D, Suturing tip of conjunctival graft to ulcer. **E,** Sutured pedicle graft.

base of the graft is made, completing the rotational pedicle graft (see Fig. 5-86, *C*). Given the single source of blood supply, the base of a pedicle graft should be wider than the tip, and the graft should not be rotated greater than 45 degrees (see Fig. 5-86, *D* and *E*).[289] A bipedicle graft is created by harvesting a graft in a similar manner so the base of the second graft is located 180 degrees to the base of the first, and the tips of the graft meet over the lesion (Fig. 5-87). A bridge graft is created by an initial cut parallel to the limbus extending 180 degrees around the limbus, with a second parallel cut near the fornix creating a graft that is 1 to 2 mm wider than the lesion (Fig. 5-88). To trim a hood or advancement graft, an incision parallel to the limbus on either side of a peripheral lesion is made, and a perpendicular incision extending posteriorly is made on either side to enable the graft to be slid over the defect (Fig. 5-89). Island grafts are harvested from any available conjunctiva (Fig. 5-90), whereas tarsopalpebral grafts are harvested in a manner similar to pedicle grafts, with the base anchored near the eyelid margin and the tip of the graft originating from the conjunctival fornix (Fig. 5-91). Regardless of graft configuration, 7-0 to 9-0 absorbable (polyglactin 910, polyglycolic acid) or nonabsorbable (monofilament nylon) suture material in a simple interrupted, simple continuous, or double saw-toothed continuous pattern is used to anchor the graft to the cornea. If desired, the conjunctiva surrounding the donor site may be sutured in a simple continuous pattern. A partial temporary tarsorrhaphy may be placed to protect the ocular surface from injury during recovery from general anesthesia.

POSTOPERATIVE CARE

Topical antibiotics, antifungals, and a therapeutic mydriatic-cycloplegic, as well as systemic antibiotics, antifungals, and NSAIDs should be administered as appropriate for the disease condition being treated. Topical antiprotease medications may

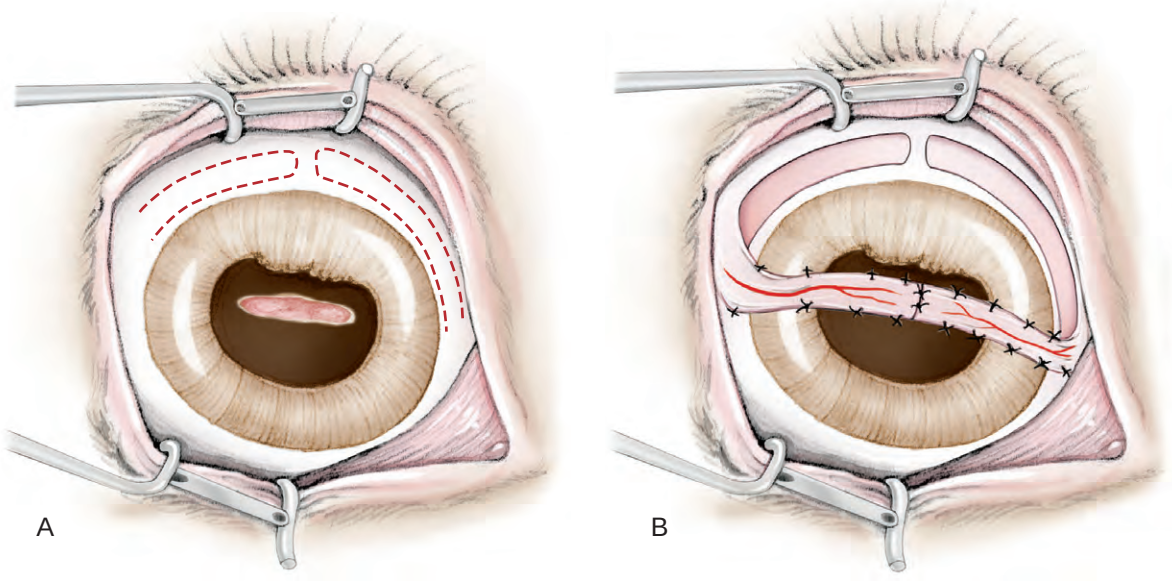


Figure 5-87. A bipedicle graft is created by harvesting a graft in a similar manner so the base of the second graft is located 180 degrees to the base of the first, and the tips of the graft meet over the lesion.

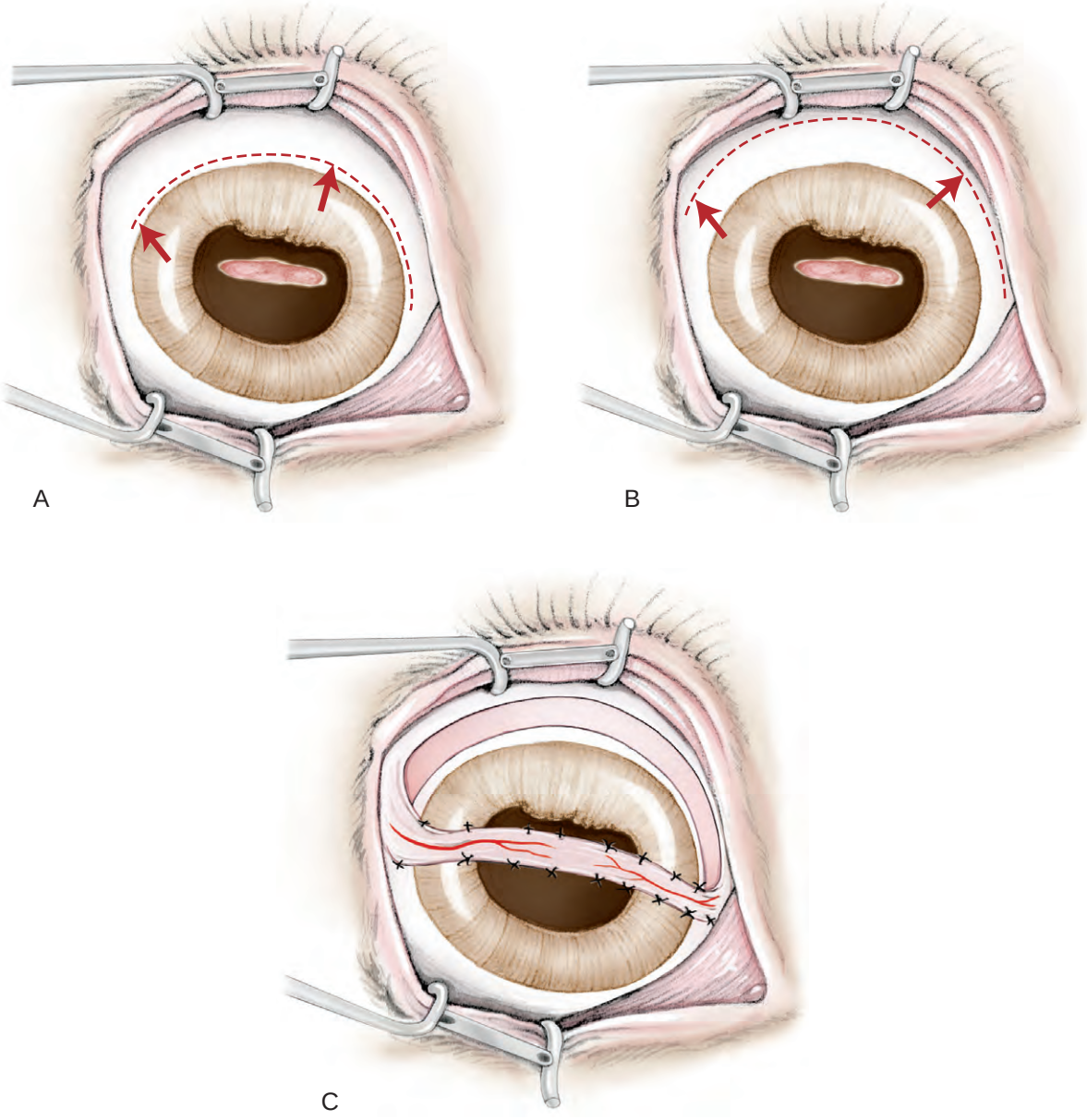


Figure 5-88. A bridge graft is created by an initial cut parallel to the limbus, extending 180 degrees around the limbus, with a second parallel cut near the fornix, creating a graft that is 1 to 2 mm wider than the lesion, then extending the entire "bridge" to cover the lesion.

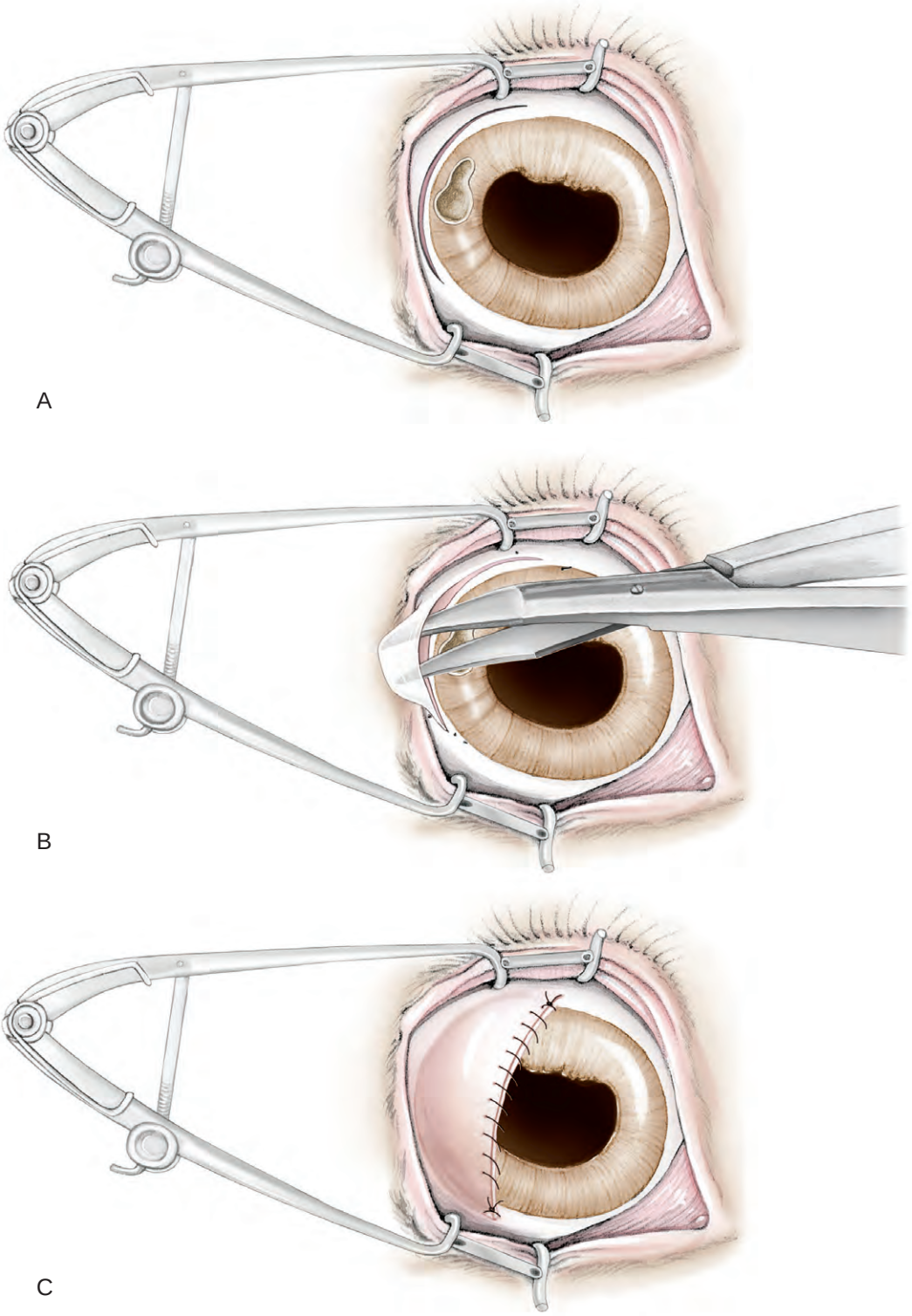


Figure 5-89. A hood or advancement graft is created by making an incision parallel to the limbus on either side of a peripheral lesion; then a perpendicular incision extending posteriorly is made on either side to enable the graft to be slid over the defect.

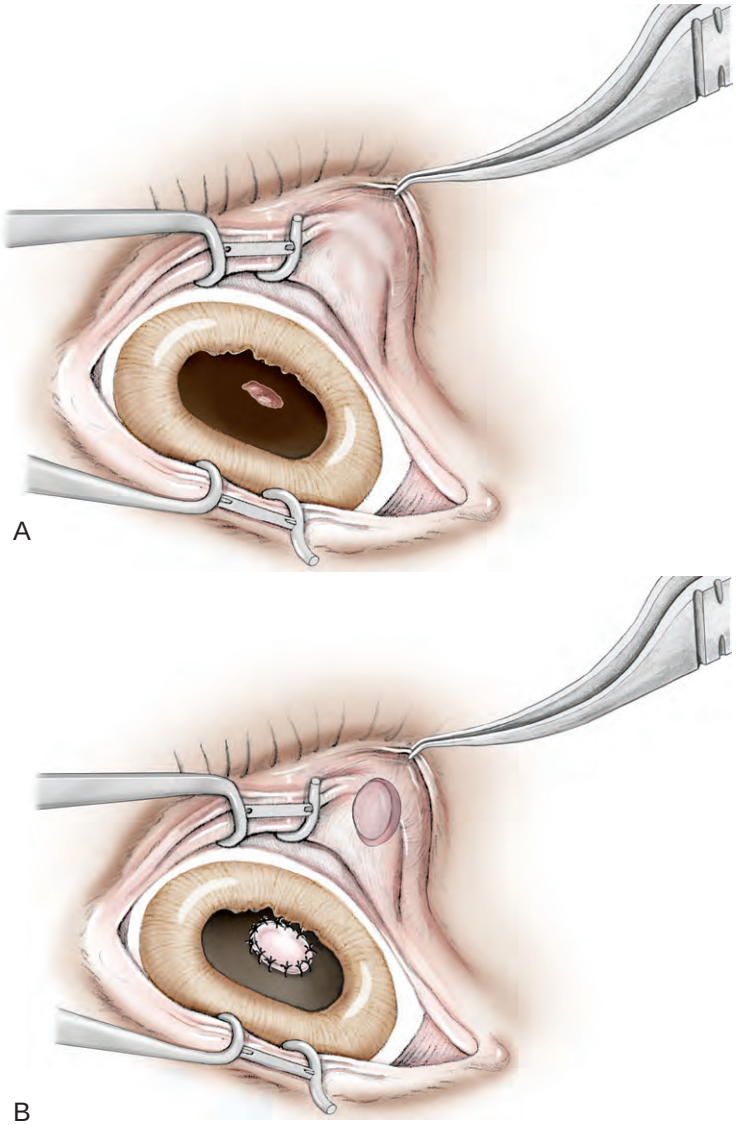


Figure 5-90. Free island conjunctival grafts are not attached to conjunctival vasculature; instead, island grafts are harvested from any available conjunctiva and sutured into the corneal ulcer.

not be necessary, since direct blood supply will now provide serum and its associated antiproteases. In the first days postoperatively, the graft should be well vascularized and apposed, because the risk of dehiscence is greatest within the first week following surgery. As the disease process resolves, most consistently indicated by increased comfort and decreased anterior uveitis and often accompanied by decreased vascularization of the graft, medications may be reduced. A minimum of 4 to 6 weeks postoperatively, the pedicle portion of the graft is trimmed, allowing incorporation of the graft into the cornea and minimizing scar formation.[115] Trimming of the graft is accomplished with or without sedation, utilizing topical ocular anesthetic and topical phenylephrine or dilute (1:10,000) epinephrine for vasoconstriction.

COMPLICATIONS

Depending upon the underlying disease process being treated, conjunctival grafts have a high rate of success for stabilizing the cornea. Factors that increase the risk for failure include improper débridement of the surrounding cornea, which may allow epithelium to grow under the graft in inhibit attachment; inadequate débridement of Tenon's capsule, which may inhibit epithelial healing and place excess tension on the graft; inadequate size of the graft, which may increase tension and dehiscence; improper suture placement; and failure to control infection.[289]

CORNEOCONJUNCTIVAL/CORNEOSCLERAL TRANSPOSITION

INDICATIONS

Corneoconjunctival (and corneoscleral) transpositions are autologous partial-thickness (lamellar) corneal grafts in which the peripheral cornea is grafted into the axial cornea, maintaining its conjunctival (or conjunctival and scleral) vascular attachments. Transposition of adjacent sclera increases the tectonic strength of the peripheral cornea, but the tectonic strength of the remaining scleral bed is decreased, and scarring of the

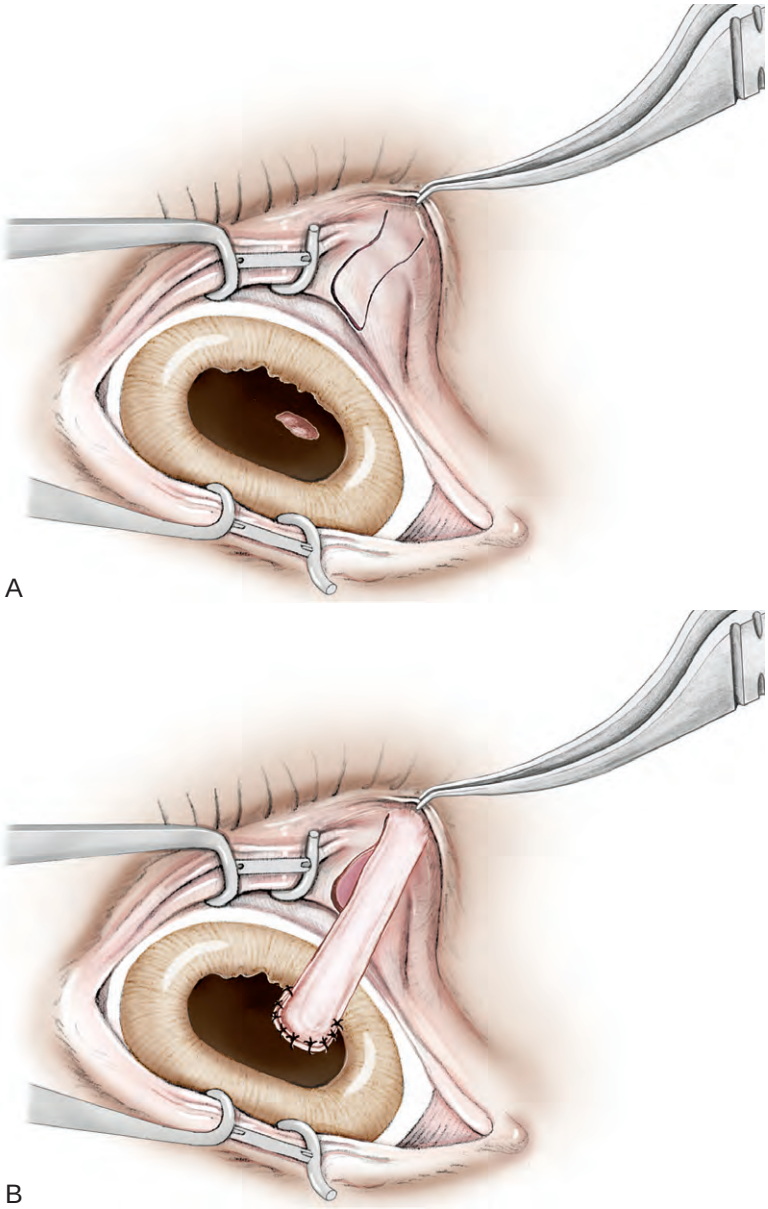


Figure 5-91. Tarsopalpebral grafts are harvested in a manner similar to pedicle grafts, but with the base anchored near the eyelid margin and the tip of the graft originating from the conjunctival fornix instead of the bulbar conjunctiva.

peripheral cornea is increased, making corneoconjunctival transpositions the more commonly performed procedure. A corneoconjunctival transposition is indicated for axial stromal defects less than 30% of the corneal diameter,[289] with the goal of producing less scarring than occurs with a homologous corneal graft. While maintenance of a healthy vascular supply is one of the advantages of this type of sliding graft, the inability to sever the vascular pedicle, as is done with conjunctival grafts, can in fact lead to increased scarring. Relative to a full-thickness homologous corneal graft, corneoconjunctival grafts provide less structural support, since they can only be partial thickness. Furthermore, corneoconjunctival transposition procedures damage normal peripheral cornea, which can be an additional disadvantage.

PROCEDURE

The recipient site is prepared by débridement of the epithelium and necrotic or infected tissue. Ideally, the graft will be anchored dorsally and is created by using a #64 Beaver blade to score two diverging, half-thickness incisions from the medial and lateral edges of the wound toward the limbus (Fig. 5-92). The incisions are extended at least 1 mm into the conjunctiva (or sclera if performing a corneoscleral transposition). Colibri forceps are used to grasp the axial edge of the defect (tip of the graft), and a Beaver #64 microsurgical blade or a Martinez lamellar corneal dissector is used to separate the corneal lamellae toward the limbus, at half thickness of the cornea (see Fig. 5-92). Westcott tenotomy scissors are used to bluntly dissect underlying Tenon's capsule from the conjunctiva and to separate the conjunctiva

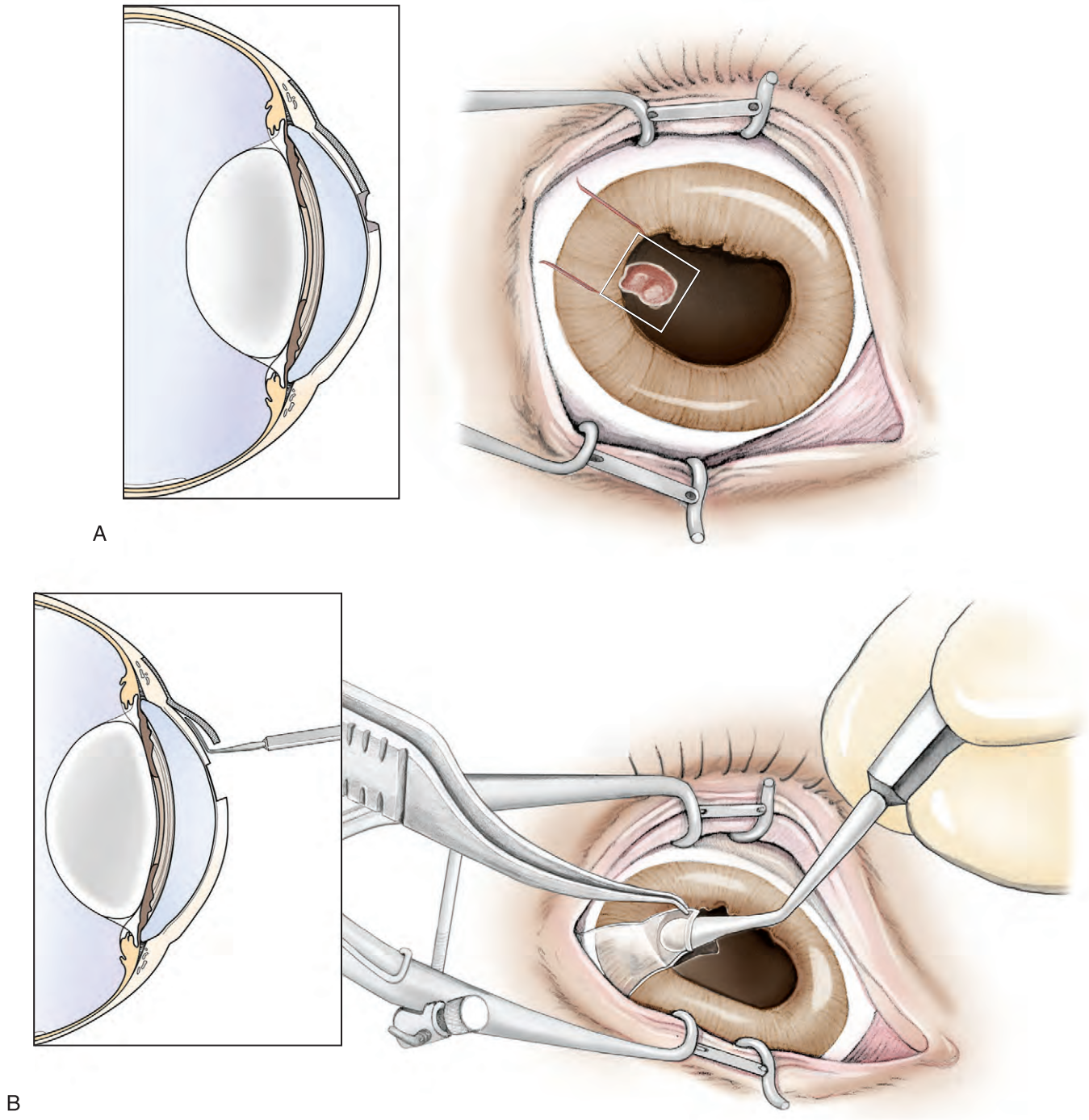
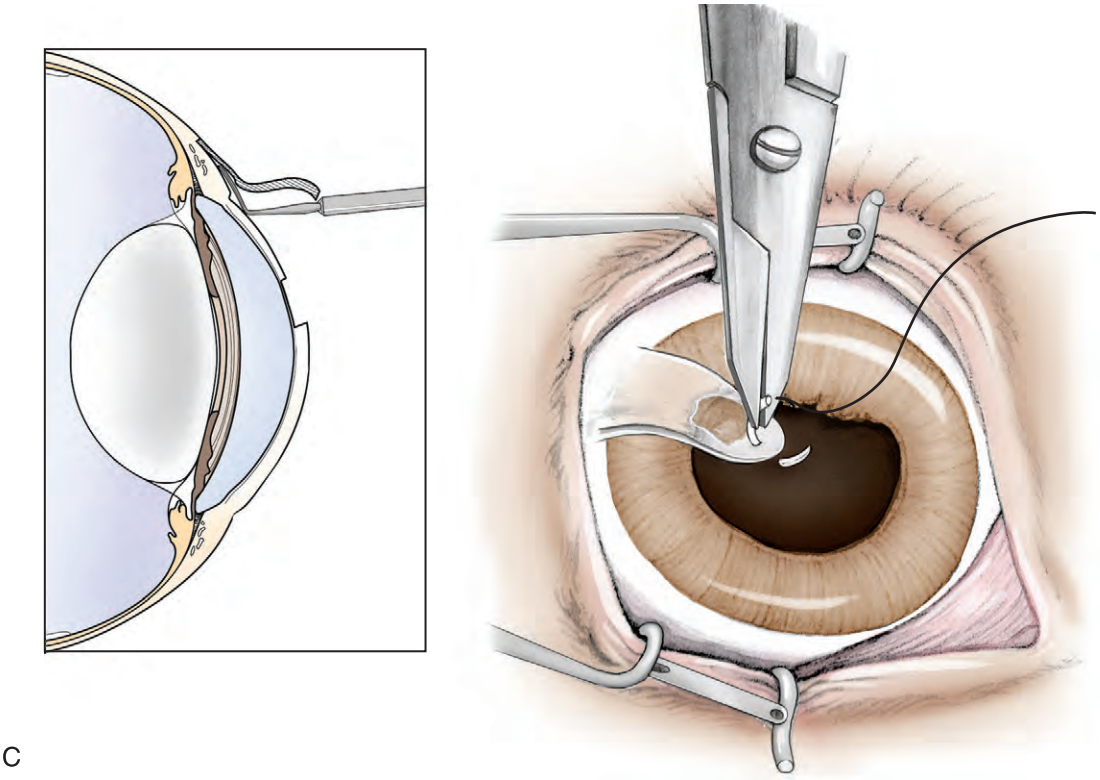
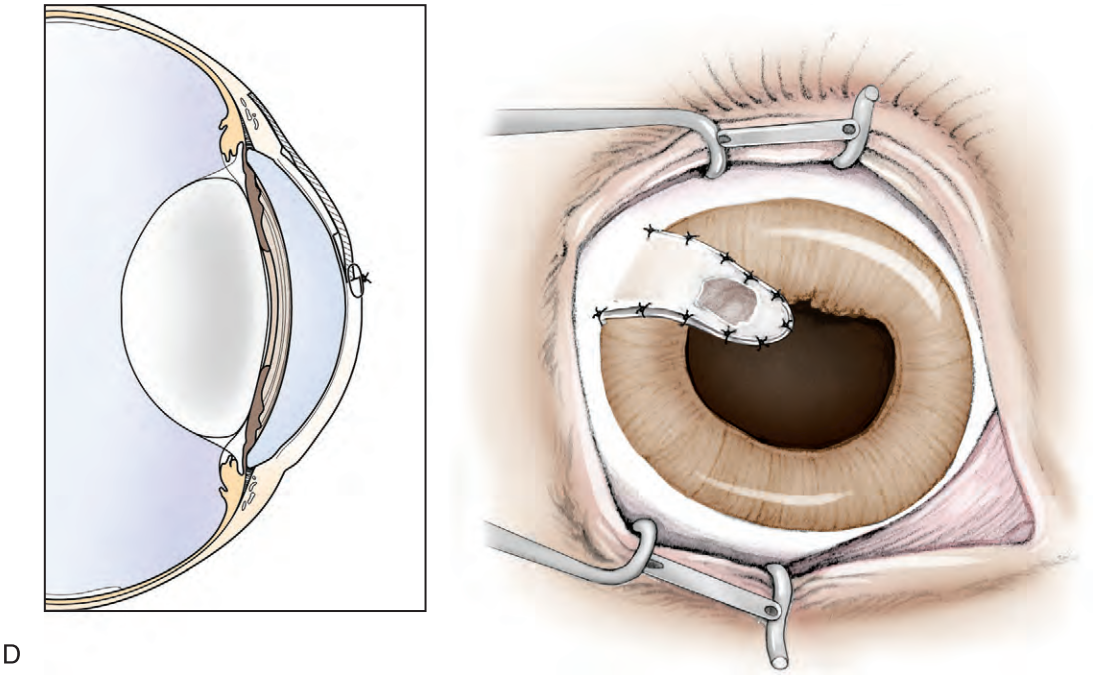


Figure 5-92. **A,** A #64 microsurgical blade to create two diverging, half-thickness incisions from the medial and lateral edges of the wound toward the limbus. **B,** A #64 microsurgical blade or a Martinez lamellar corneal dissector is used to separate the corneal lamellae toward the limbus, at ½ thickness of the cornea.

Continued



C



D

Figure 5-92, cont'd. **C,** Underlying Tenon's capsule is dissected from the conjunctiva and the conjunctival is separated from the superficial sclera from deeper sclera at the limbus, which allows sliding of a flap of cornea and conjunctiva (+/– sclera) axially to cover the defect. **D,** Drawing of sutured corneoconjunctival transposition.

from the limbus (or superficial sclera from deeper sclera at the limbus), allowing sliding of a flap of cornea and conjunctiva (with or without sclera) axially to cover the defect (see Fig. 5-92). Simple interrupted sutures of 8-0 or 9-0 polyglactin 910 (or 9-0 to 10-0 nyl on) are placed from the donor cornea to the recipient wound bed, starting at the distal tip of the graft, and either simple interrupted, simple continuous, or double saw-toothed suture patterns are placed between the conjunctiva and cornea, extending toward the limbus.

POSTOPERATIVE CARE

Postoperative care is similar to that for conjunctival grafts, consisting of topical therapeutic antibiotics, topical antifungals in the presence of keratomycosis, and a topical therapeutic mydriatic-cycloplegic. Systemic antibiotics and antifungals may be indicated, as well as systemic NSAIDs. Topical antiproteases are generally not necessary; antiproteases contained in serum are reaching the graft through direct vascular supply. As the disease process resolves, most consistently indicated by increased comfort and decreased anterior uveitis, medications can be reduced, and corneal clarity will gradually be restored. In contrast to conjunctival grafts, trimming of the vascular supply to the graft is not possible, because it is incorporated into the peripheral cornea.

COMPLICATIONS

Complications associated with corneoconjunctival (corneoscleral) transposition include dehiscence, scar formation, and uncontrolled infection. Few reports on use of these grafts in horses exist, and of two horses receiving this surgery for ulcerative iris prolapse, one became phthisical and one was blind.[111]

PENETRATING KERATOPLASTY

INDICATIONS

Penetrating keratoplasty (PK) is corneal transplantation performed to restore full-thickness corneal integrity. Indications include removal of deep stromal lesions (i.e., abscesses, endothelial inflammation, neoplasia)* and wound repair (i.e., corneal perforations).[111] While grafts as large as 25 mm diameter have been reported, the most common sizes, and those with the best chance of surgical success, are between 6 and 8 mm.[291,294,310] Fresh homologous tissue can be used to perform PK, providing structural support to the globe and improved corneal clarity due to transplantation of viable endothelium, but the logistical difficulty of acquiring fresh tissue at the time it is needed make fresh corneal grafts rare in veterinary ophthalmology. Frozen homologous grafts are frequently used to provide tectonic support; rejection, manifesting clinically as graft vascularization, is expected and desired to promote healing and minimize dehiscence. Placement of a conjunctival graft over a PK may be indicated to provide more immediate vascular supply, with the disadvantage being increased corneal scarring.

PROCEDURE

The donor corneal button should measure 0.5 to 1 mm larger in diameter than the recipient bed. The appropriate size is more readily measured with Jameson calipers in nonperforated corneal wounds (e.g., stromal abscesses), whereas measurement of perforated corneal wounds should be performed following reestablishment of the anterior chamber with viscoelastic material. Donor tissue is most easily harvested on a manufactured Teflon block with a corneal trephine pack, but dermal punch biopsies may be used. The donor tissue is placed epithelial side down, and a perpendicular cut is made from the endothelial side. If it has not separated in the freezing process, the donor epithelium should be removed. Epithelium surrounding the recipient site should be removed as well, following the same principles for other grafting procedures.

If performing a corneal graft for a deep stromal lesion in which perforation has not occurred, the lesion to be excised is measured, and an appropriately sized corneal trephine (or sterile dermal punch biopsy) is used to create a perpendicular corneal incision to approximately 75% depth (Fig. 5-93, *A*). A #65 Beaver blade or other sharp blade is used to enter the anterior chamber at one aspect of the trephine incision, taking care to avoid puncturing the iris or lens (see Fig. 5-93, *B*). Viscoelastic is injected into the anterior chamber, and right and left curved corneal section scissors are used to complete the trephinated wound and remove the lesion (see Fig. 5-93, *C*). The removed cornea is submitted for histopathology and/or cultures as appropriate. The donor button is placed in the surgical site, endothelium side down, with care taken to grasp the button at the epithelial/stromal junction, avoiding contact with the endothelium. Four cardinal simple interrupted sutures are placed from the donor button to the recipient cornea at the 12-, 3-, 6-, and 9-o'clock positions (see Fig. 5-93, *D*), and the remainder of the graft is sutured with simple interrupted, simple continuous, or double-continuous sutures of preferably 9-0 absorbable suture (see Fig. 5-93, *E*). Nonabsorbable suture may also be used but must be removed once healing is complete. To ensure a watertight seal, sterile balanced saline solution is injected into the anterior chamber using a 27- or 30-gauge needle inserted at the limbus. A conjunctival graft may be placed over the corneal graft for immediate vascularization (Fig. 5-94). If performing a PK for a perforated lesion, the procedure is similar, but reestablishing the anterior chamber and débriding infected or necrotic cornea are performed prior to measuring and harvesting the donor button.

POSTOPERATIVE CARE

Postoperative care is similar to that for other grafting procedures, consisting of topical therapeutic antibiotics, topical antifungals in the presence of keratomycosis, and a topical therapeutic mydriatic-cycloplegic. Systemic antibiotics and antifungals may be indicated, as well as systemic NSAIDs. Topical antiproteases are generally not necessary if a conjunctival graft is also placed. Marked swelling of the corneal graft may be present over the first few days but should resolve, provided dehiscence does not occur. As the disease process resolves, most consistently indicated by increased comfort and decreased anterior uveitis, medications can be reduced. Trimming of the vascular supply to the overlying conjunctival graft may be performed a minimum of 4 to 6 weeks postoperatively.

COMPLICATIONS

In human ophthalmology, graft vascularization and scarring are considered a significant complication. However, this occurs in

*References 245, 251, 260, 267, 310, and 390.

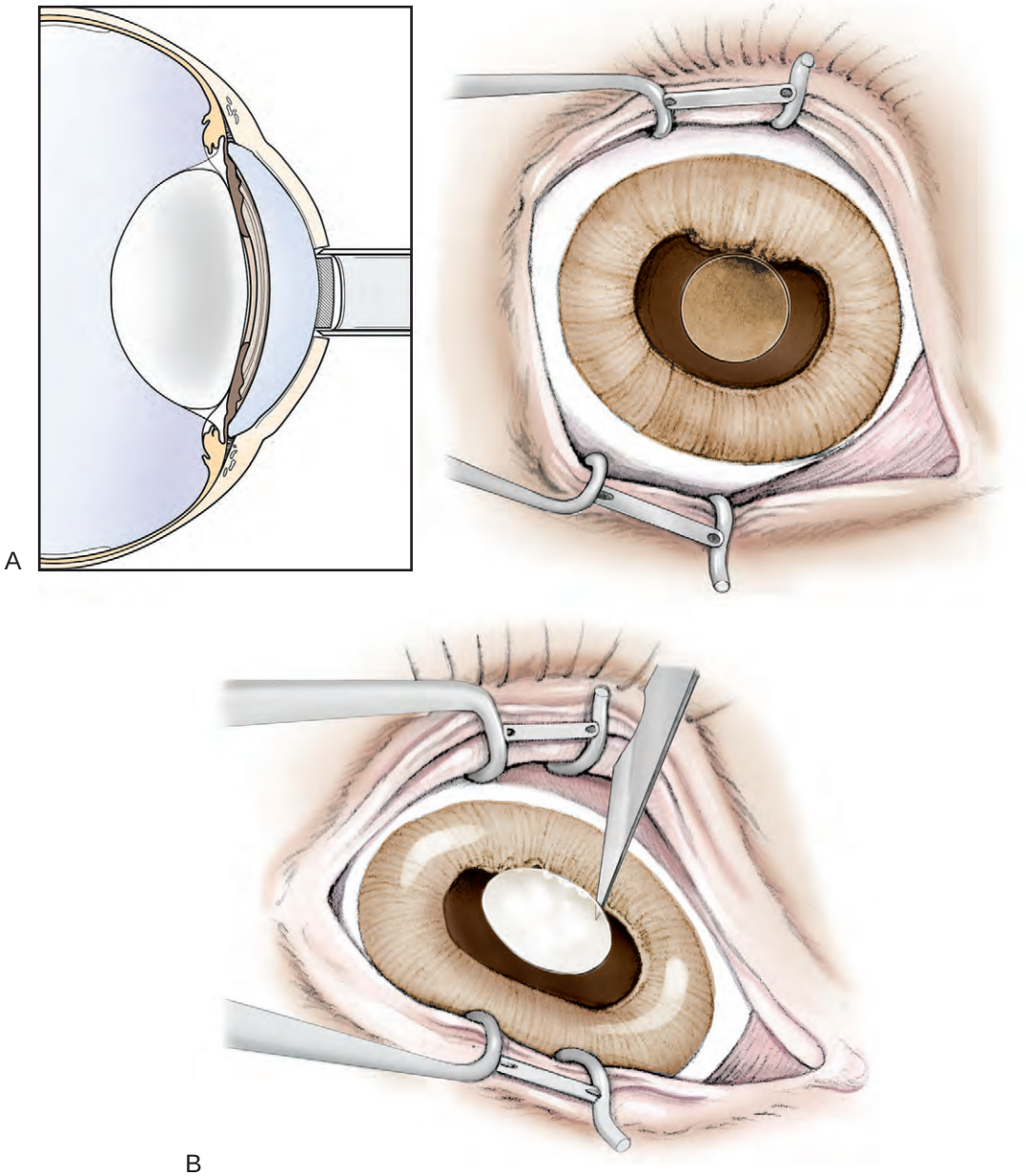
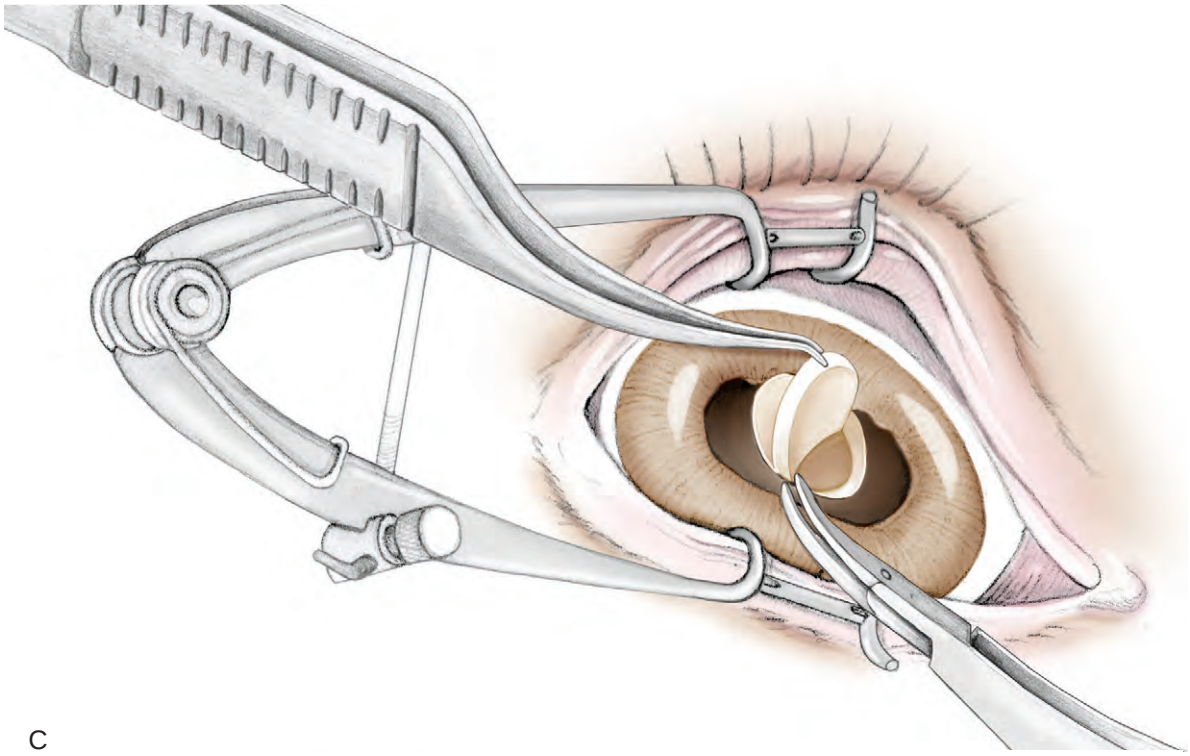
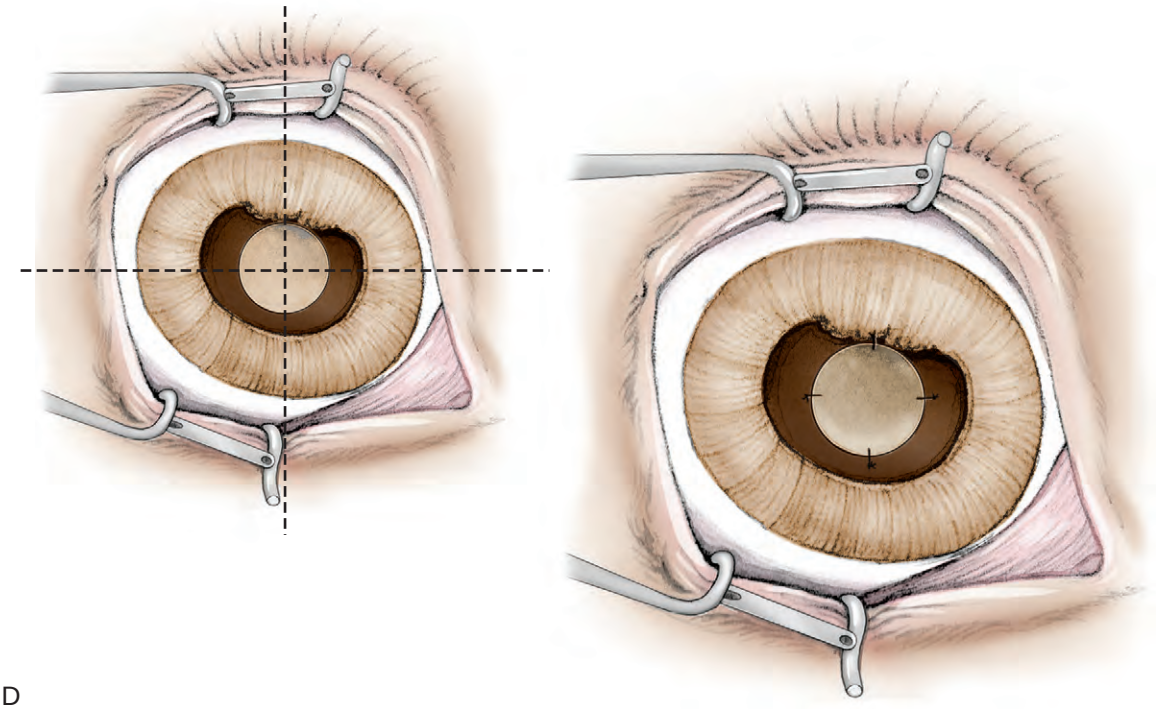


Figure 5-93. **A,** Penetrating keratoplasty. A corneal trephine is used to create a perpendicular corneal incision to approximately 75% depth. **B,** A #65 Beaver blade or other sharp blade is used to enter the anterior chamber at one aspect of the trephine incision, taking care to avoid puncturing the iris or lens.



C



D

Figure 5-93, cont'd. **C,** A #65 Beaver blade or other sharp blade is used to enter the anterior chamber at one aspect of the trephine incision, taking care to avoid puncturing the iris or lens. **D,** The donor button is placed in the surgical site, endothelium side down, with care taken to grasp the button at the epithelial-stromal junction, avoiding contact with the endothelium. Four cardinal simple interrupted sutures are placed from the donor button to the recipient cornea at the 12-, 3-, 6-, and 9-o'clock positions. *Continued*

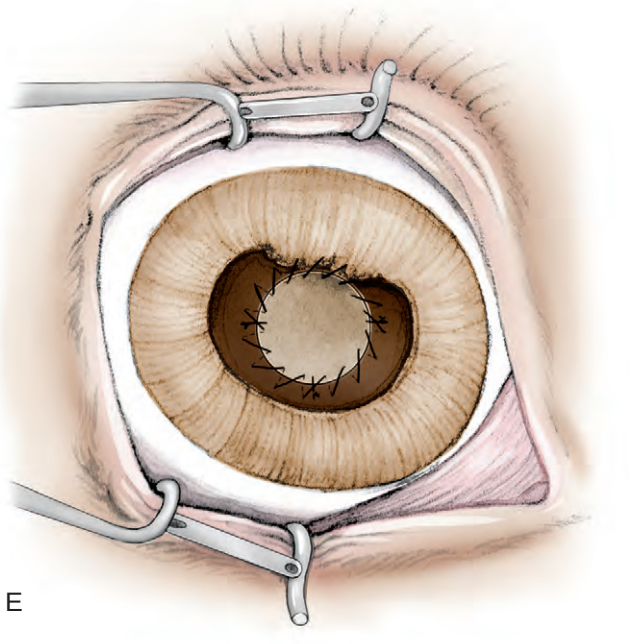


Figure 5-93, cont'd. E, The remainder of the graft is sutured with either simple interrupted, simple continuous, or double-continuous sutures of preferably 9-0 absorbable suture.

all equine corneal transplants and as such should not be considered a complication.[286] The most common complication associated with PK is graft dehiscence, which is more likely to occur with any type of lesion adjacent to the limbus or when grafts are larger than 8 mm.[111,310] Corneal grafts have the greatest chance of success if infection is controlled prior to surgery. Scarring may be marked with frozen corneal grafts, but retention of a globe with comfort and at least partial vision should be considered a success. A survey of 86 eyes receiving PK for a variety of reasons indicated positive visual outcome in 67 (77.9%), with an average healing time of 46.7 ± 23.1 days.[291]

DEEP LAMELLAR ENDOTHELIAL KERATOPLASTY

INDICATIONS

Deep lamellar endothelial keratoplasty (DLEK) is indicated for peripheral or paraxial, deep stromal corneal disease, such as abscesses or endotheliitis, in which the stroma anterior to the lesion appears clinically healthy.[290,291] The advantages of this procedure include the need for fewer, more peripherally located corneal sutures, which serves to minimize surgical and anesthesia time, as well as density of postoperative scarring.[290] Disadvantages include larger surface area of fibrosis and the potential for infection to be spread along corneal lamellae.[290]

PROCEDURE

The diseased cornea is measured with Jameson calipers, including 1 mm of clear surrounding cornea for removal. Prior to entering the eye, donor cornea is harvested, generally from a frozen allograft. Donor tissue is split between the anterior two-thirds and posterior third, as only the posterior portion, including Descemet's membrane, is utilized. Using a corneal trephine or dermal biopsy punch 1 mm larger than the diameter of cornea to be removed, a donor corneal button is created from the posterior section.

Preparation of the recipient bed is achieved by using a #64 Beaver blade to score a one-half to two-thirds depth clear corneal incision along the limbus adjacent to the lesion (Fig. 5-95, *A*). A Martinez lamellar corneal dissector or Beaver #64 microsurgical blade is used to dissect the lamellae surrounding and overlying the lesion, taking care to dissect the peripheral portions of the cornea prior to that directly over the lesion so as to avoid seeding possible infection around the lesion (see Fig. 5-95, *B*). The cornea is gently retracted, and a corneal trephine or dermal biopsy punch is used to score an incision around the lesion (see Fig. 5-95, *C*). A Beaver #65 microsurgical blade is used to enter the anterior chamber, which is maintained by injection of a viscoelastic. Corneal section scissors are used to complete the incision, and the recipient cornea is removed and submitted for histopathology and/or cultures as appropriate. The recipient anterior corneal flap is replaced and partially sutured closed with simple interrupted sutures of 8-0 or 9-0 absorbable or nonabsorbable suture (see Fig. 5-95, *D*). Prior to complete closure of the incision, the donor cornea button is inserted into the hole where recipient cornea was removed, endothelial side down (see Fig. 5-95, *E*). If desired, four cardinal simple interrupted sutures of 8-0 or 9-0 absorbable sutures may be used to anchor the donor button in place. The remainder of the corneal flap is sutured closed, and a conjunctival advancement flap (hood graft) may be sutured over the corneal incision to hasten vascular ingrowth, if desired (see Fig. 5-95, *F;* Fig. 5-96).

POSTOPERATIVE CARE

Postoperative care is similar to that for other grafting procedures, consisting of topical therapeutic antibiotics, topical antifungals in the presence of keratomycosis, and a topical therapeutic mydriatic-cycloplegic. Systemic antibiotics and antifungals may be indicated, as well as systemic NSAIDs. Topical antiproteases are generally not necessary, because DLEK is not indicated for melting corneal disease. However, serum or tetracyclines may be administered immediately postoperatively to minimize collagenolytic activity induced by surgical manipulation.[290] In a series of 10 horses receiving DLEK for stromal abscesses, seven of which had evidence of fungal hyphae on histopathology, some horses also received topical 0.2% cyclosporin to control graft rejection.[290]

COMPLICATIONS

Complications that may be associated with DLEK include transient diffuse corneal edema, subjectively worse when the donor graft is not sutured in place,[290] mild superficial fibrosis, extension of infection, inability to control infection, wound dehiscence, and slippage of the graft.[291] In one reported series of horses receiving DLEK, 7 of 10 (70%) were assessed as having excellent postoperative cosmesis, while the remaining three had good postoperative cosmesis.[290] Medical therapy for the associated cause (generally infection) was necessary for an additional 4 to 10 weeks (average 6.7 weeks), but all globes

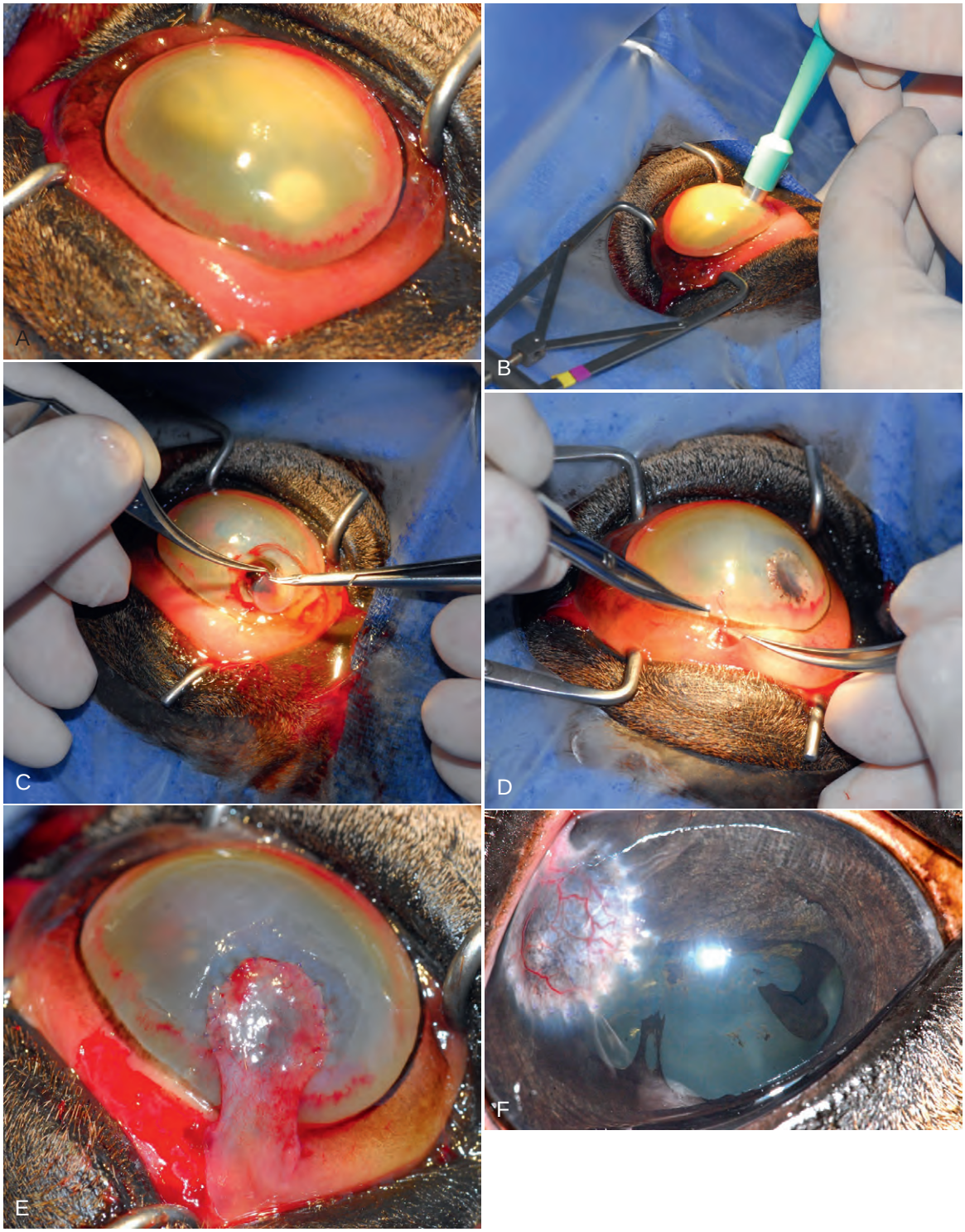


Figure 5-94. **A,** Penetrating keratoplasty in a horse with a deep corneal stromal abscess and secondary uveitis. There is a stromal abscess with significant perilimbal vascularization, diffuse corneal edema, and hypopyon. The conjunctiva is hyperemic and chemotic, associated with the retrobulbar block. **B,** An appropriately-sized (1 mm diameter larger than the abscess) sterile dermal biopsy punch is used to create an incision which is completed with corneal section scissors, removing the full-thickness diseased corneal button. **C,** The initial cardinal suture is placed in the donor corneal button *(arrow)*, to be passed to the recipient corneal wound bed. **D,** The suture is tied and the donor corneal button rests within the recipient corneal wound bed. **E,** The conjunctival graft is sutured in place with simple interrupted sutures, spaced approximately 1 mm apart, over the corneal graft, obscuring the corneal graft from vision. **F,** The appearance of the eye 5 weeks postoperatively. Note the remaining suture remnants, as well as vascularization and scarring of the cornea. The dark pigmentation underlying the graft site is consistent with persistent anterior synechia.

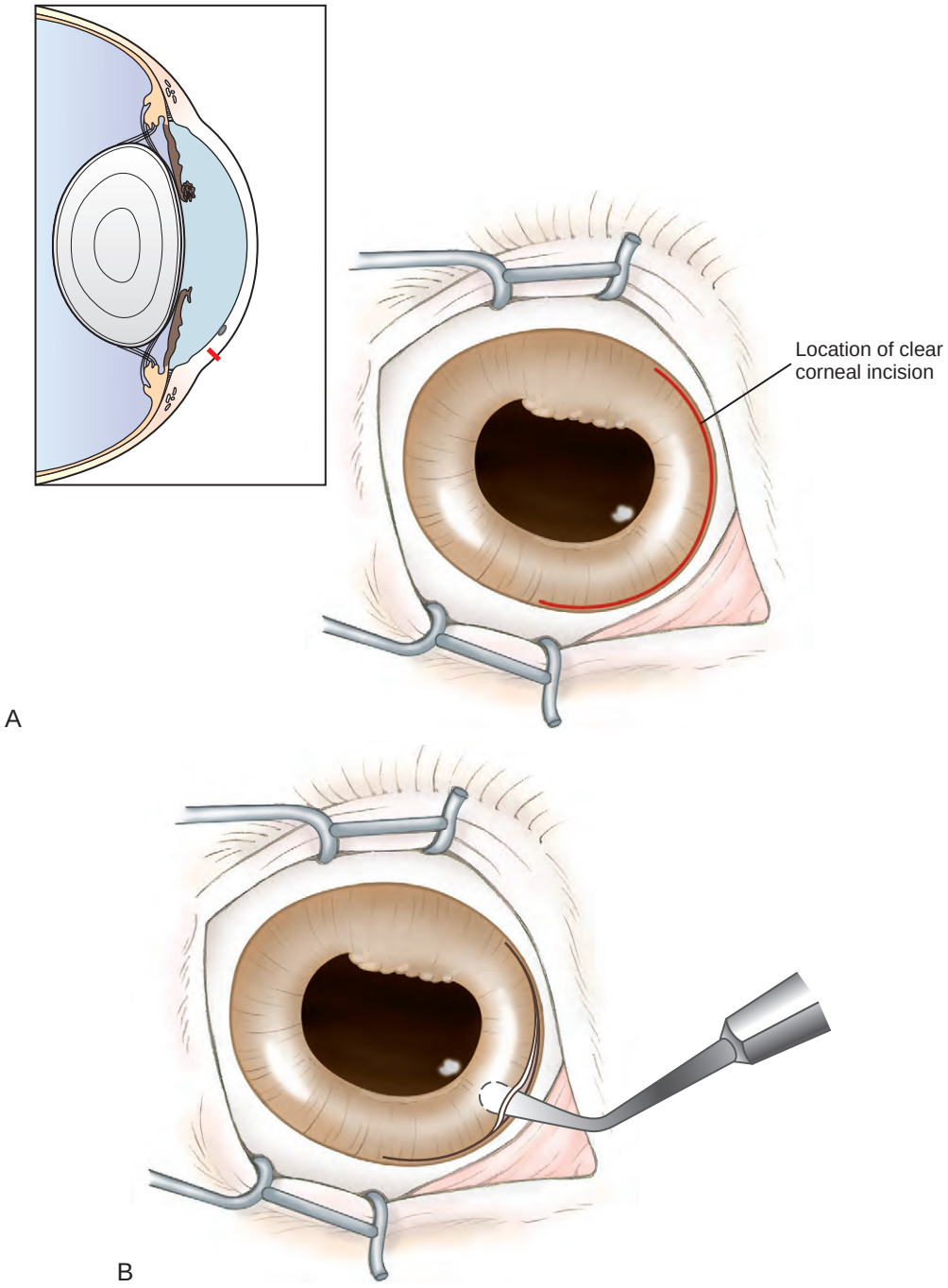
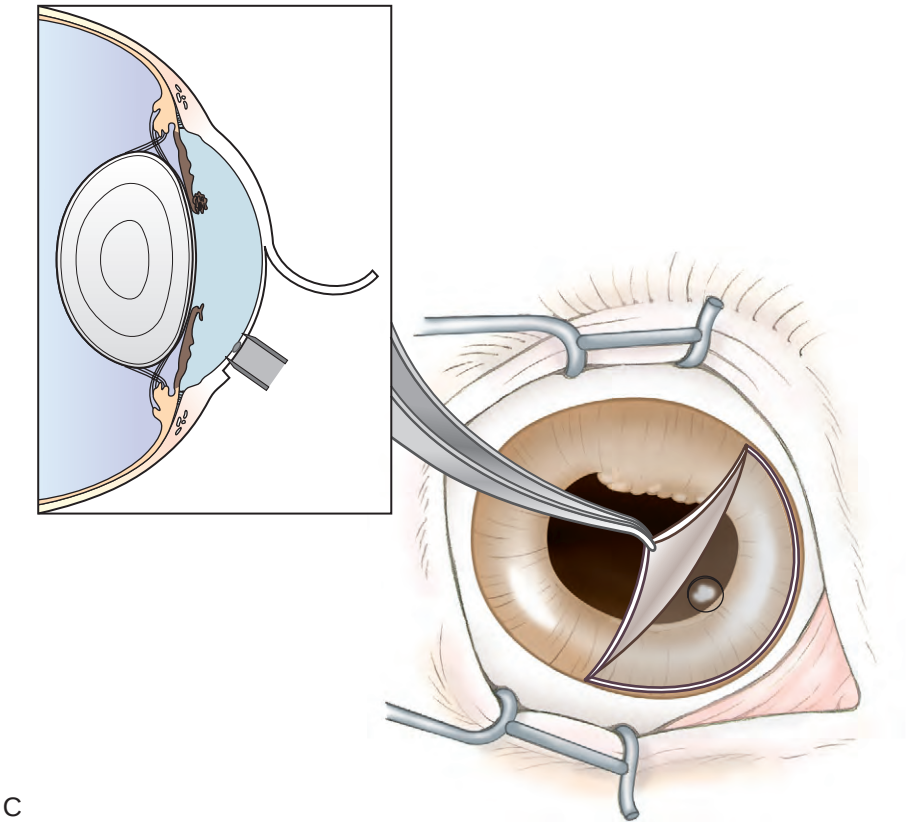
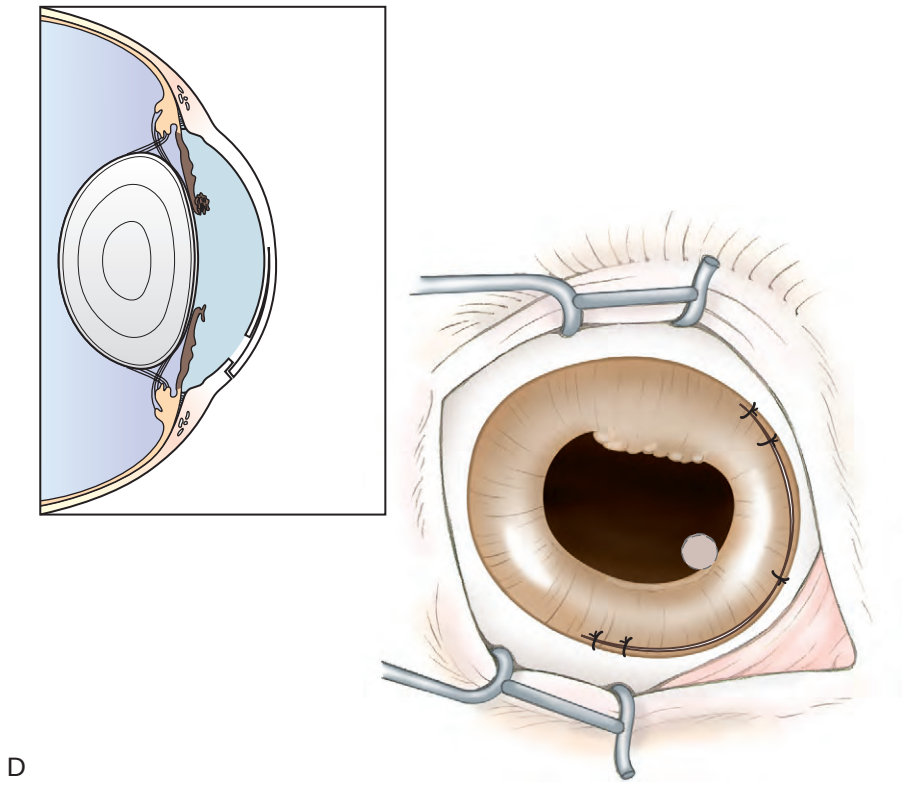


Figure 5-95. Deep lamellar endothelial keratoplasty. **A,** Appropriate location of partial-thickness, clear corneal incision, created with a #64 microsurgical blade, for a medial paraxial deep stromal abscess. **B,** Lamellar corneal dissection, initiated from corneal incision, toward stromal abscess. The plane of dissection is superficial to the lesion to be excised.



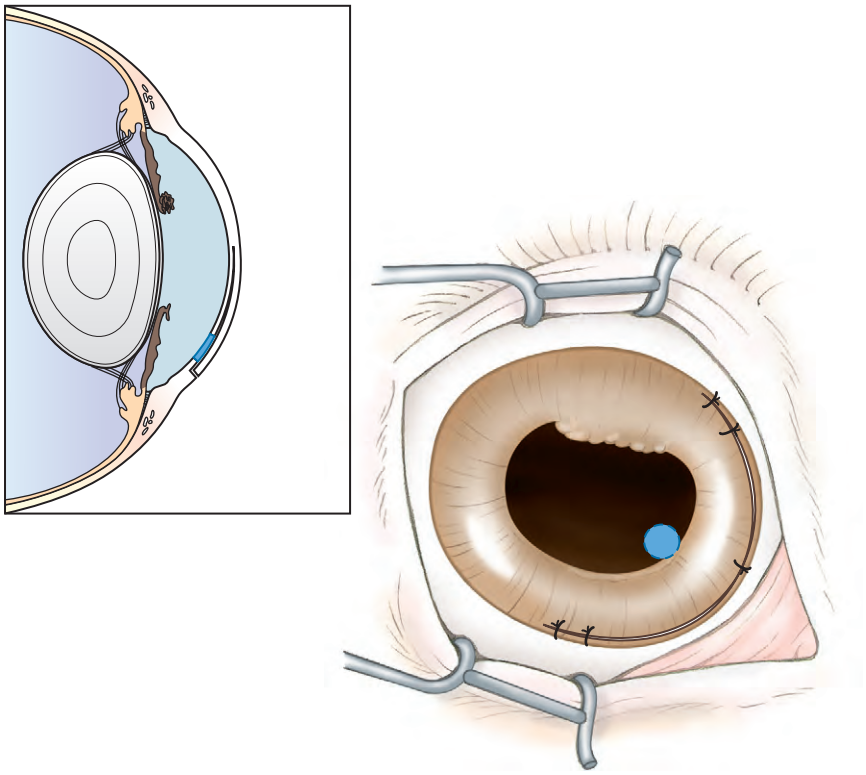
C



D

Figure 5-95, cont'd. **C,** Reflection of anterior stromal flap to expose deeper lesion. An appropriately-sized corneal trephine or sterile dermal biopsy punch is used to excise the lesion *(inset)*. **D,** The flap is replaced and initial cardinal sutures are placed to stabilize the flap.

Continued



E

Figure 5-95, cont'd. **E,** A donor corneal button is inserted under the flap into the hole left following excision of the abscess. The remainder of the corneal flap is sutured with a simple interrupted suture pattern.

were comfortable and visual following surgery. Of 66 eyes summarized in another study, 59 (89.4%) had a positive visual outcome, with an average healing time of 35.8 ± 14.7 days.[291]

POSTERIOR LAMELLAR KERATOPLASTY

INDICATIONS

Posterior lamellar keratoplasty (PLK) is indicated for removal of deep stromal lesions (e.g., abscess, endotheliitis) less than 10 mm diameter, with healthy overlying stroma and ideally no corneal ulceration.[266] Axial, paraxial, and peripheral lesions may all be effectively treated with PLK.[266] The advantages of the procedure include decreased surgical and healing times relative to full-thickness keratoplasty (PK): in one study of PLK in nine horses, the average surgical time was 71 minutes,[266] versus 91 minutes previously reported for PK,[393] and average healing time was 24 days for PLK,[266] versus a previously reported 57 days for PK.[393]

PROCEDURE

The diseased cornea is measured with Jameson calipers. Prior to entering the eye, donor cornea is harvested, generally from a frozen allograft. Donor tissue is split between the anterior half and posterior half, as only the posterior portion, including Descemet's membrane, is utilized. Using a corneal trephine or dermal biopsy punch the same diameter as the lesion to be removed, the donor corneal button is created from the posterior section.

A #64 Beaver blade is used to create a three-sided (rectangular), one-half to three-quarters thickness incision over the deep lesion, with each incision extending 1 mm beyond the edge of the lesion (Fig. 5-97, *A*). The fourth side of the rectangle remains attached to adjacent cornea for creation of an anterior stromal flap. This attached area ("hinge") is directed toward the central cornea. A Martinez lamellar corneal dissector or Beaver #64 microsurgical blade is used for lamellar dissection of the flap, allowing reflection of the flap and exposure of the underlying deep lesion (see Fig. 5-97, *B*). A corneal trephine or dermal biopsy punch is used to score an incision in the posterior stroma surrounding the deep lesion, and a Beaver #65 microsurgical blade is used to enter the anterior chamber (see Fig. 5-97, *C*). Viscoelastic is injected into the anterior chamber, and the incision is completed with corneal section scissors. The removed cornea is submitted for histopathology and/or cultures as appropriate. The donor corneal button is placed in the recipient site, and four cardinal simple interrupted sutures, at 12-, 3-, 6-, and 9-o'clock are placed from the graft

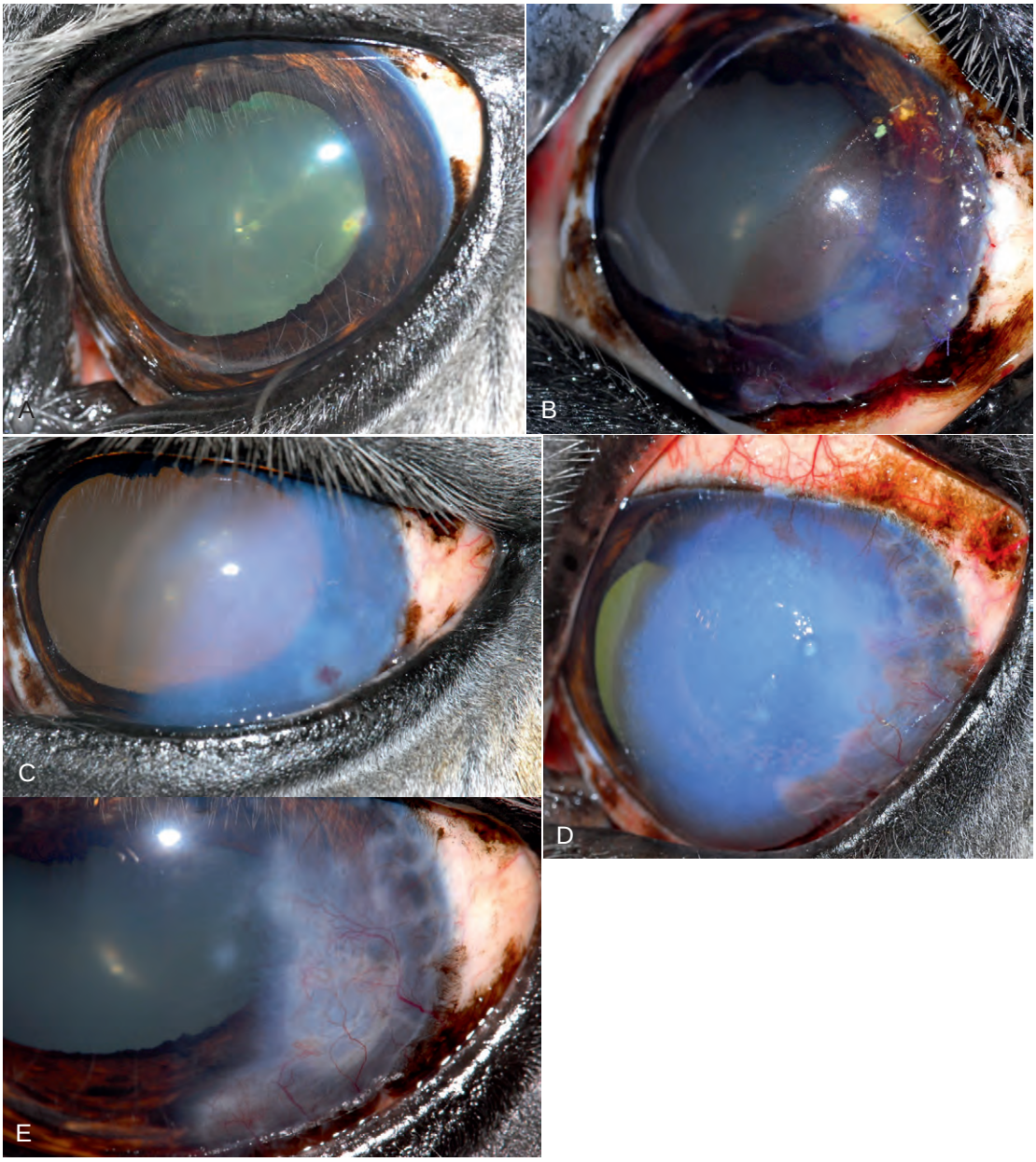


Figure 5-96. The following series of photographs are from the same horse, a 14-year-old Percheron mare that had been medically managed for a corneal stromal abscess beginning 3 months prior. **A,** Clinical photograph demonstrated a focal, ventrolateral paraxial corneal stromal abscess. Corneal and intraocular inflammation were minimal, however the abscess was recurring following medical therapy, and the eye was persistently painful. **B,** Immediately post-operative (Deep Lamellar Endothelial Keratoplasty, DLEK) photograph illustrating opacification and sutures in the area of the abscess, where the donor cornea was sutured in place. A double saw-tooth pattern encircles the adjacent limbus from approximately 3- to 6-o'clock, where the anterior corneal flap was sutured in place. The reddish haze to the ventromedial ⅓ of the cornea is due to blood seepage into the cornea along the plane of dissection of the anterior corneal flap. **C,** Seven days postoperative photograph showing improvement in degree of corneal edema. **D,** Five weeks post-operative photograph showing increase in corneal edema and return of bullae formation. Moderate perilimbal vascularization has progressed axially. **E,** Seven weeks postoperative photograph showing marked improvement of corneal edema and bullous keratopathy, with persistence of vascularization and fibrosis consistent with healing.

to the recipient cornea, using 8-0 or 9-0 absorbable suture such as polyglactin (see Fig. 5-97, *D*). The remainder of the graft is sutured with additional simple interrupted sutures, and a watertight seal is ensured by injection of sterile balanced saline solution at the limbus using a 27- or 30-gauge needle. The anterior stromal flap is replaced over the donor cornea and sutured in place with simple interrupted or simple continuous sutures of 8-0 or 9-0 absorbable suture (Fig. 5-98).

POSTOPERATIVE CARE

Postoperative care is similar to that for other grafting procedures, consisting of topical therapeutic antibiotics, topical antifungals in the presence of keratomycosis, and a topical therapeutic mydriatic-cycloplegic. Systemic antibiotics and antifungals may be indicated, as well as systemic NSAIDs. Topical antiproteases are generally not necessary, because PLK is not indicated for melting corneal disease. Serum or tetracyclines may be administered immediately postoperatively to minimize collagenolytic activity induced by surgical manipulation.

COMPLICATIONS

Complications associated with PLK are more pronounced with donor graft sizes greater than 6 mm and may include stromal hemorrhage, graft edema, corneal vascularization, graft dehiscence, synechiae, granulation tissue, and corneal ulceration.[266] In a series of nine horses receiving PLK for deep stromal abscesses, eight/nine had a positive visual outcome,[266] and in another report of 54 eyes receiving PLK for deep stromal abscesses, 53 (98.1%) had a positive visual outcome, with an average healing time of 30.8 ± 9.5 days.[291]

AMNIOTIC MEMBRANE GRAFTS

INDICATIONS

Amniotic membrane grafts supply antifibrotic, antiinflammatory, antiangiogenic, and growth factors, making it a viable option for surgical reconstruction of corneas affected by severe keratomalacia.[183] Additionally, use of amniotic membranes to cover the surgical site following superficial keratectomy for SCC is advocated to avoid infection, minimize pain, and limit scarring and symblepharon formation.[354] An advantage over use of conjunctival grafts in similar situations is the greater availability of amnion, which is harvested and stored frozen until use. Other biological and biosynthetic materials, such as porcine small-intestinal submucosa and A-cell, may be used for disease processes in which amnion is also indicated.

PROCEDURE

The placenta of a mare generally undergoing Cesarean section is collected and rinsed with normal phosphate-buffered saline solution containing 50 g/mL penicillin, 50 g/mL streptomycin, 100 g/mL neomycin, and 2.5 g/mL amphotericin B. The amnion, which consists of an epithelium, basement membrane, and stroma, is bluntly dissected from the vascularized chorion and placed epithelial side up on 0.45-µm nitrocellulose paper. The sample is rinsed again, and the amnion and nitrocellulose are cut into pieces, generally 4 × 4 to 5 × 5 cm. They are stored in Dulbecco's modified Eagle medium and glycerol at a ratio of 1:1 (vol/vol), containing 50 g/mL penicillin, 50 g/mL streptomycin, 100 g/mL neomycin, and 2.5 g/mL amphotericin B at −80°C for up to 12 months prior to use.[115] Prior to use, the amnion/nitrocellulose sample is thawed to room temperature and washed for 30 minutes to remove the glycerol (Fig. 5-99).

Following débridement and keratectomy of the patient's cornea, as indicated for the underlying disease process, an appropriately sized section of amnion is sutured into the keratectomy bed. Orientation of the amnion theoretically determines whether the amnion is incorporated into the cornea (epithelial side up, stromal side down) or sloughed (epithelial side down, stromal side up).[183] Practically, however, it is difficult at the time of surgery to differentiate between the two sides. The amnion is sutured into the keratectomy bed with simple interrupted or simple continuous suture pattern of 7-0 to 9-0 absorbable suture such as polyglactin (Fig. 5-100). Amnion may be sutured as a single layer, a double layer, or a single layer with an overlying graft of a different biosynthetic material, such as A-cell.[183]

POSTOPERATIVE CARE

Postoperative care is similar to that for other grafting procedures, consisting of topical therapeutic antibiotics, topical antifungals in the presence of keratomycosis, and a topical therapeutic mydriatic-cycloplegic. Systemic antibiotics and antifungals may be indicated, as well as systemic NSAIDs. Topical antiproteases are frequently administered postoperatively because amnion grafts are indicated for corneal melting, which may not be immediately controlled following placement of the graft. If oriented with the epithelial side down, the layers of amnion visibly slough, generally within 3 to 4 weeks of surgery,[183] whereas no sloughing occurs if oriented stromal side down.[354]

COMPLICATIONS

Complications associated with placement of an amnion graft include premature sloughing or dehiscence, failure to control melting or infection, and postoperative corneal scarring. Subjectively, amnion grafts have been reported to produce less corneal scarring than conjunctival grafts when used to cover SK beds following removal of corneolimbal SCC.[354] Of nine horses receiving amnion grafts in addition to SK, and in some cases strontium-90 irradiation for corneolimbal SCC, duration of tumor nonrecurrence was a mean of 226 days (range 21 to 778 days), and all had subjectively less scarring than those treated with conjunctival grafts.[354] Three horses with severe keratomalacia treated with amnion grafts were sighted and comfortable at last follow-up.[183]

FUTURE STUDY

Considering the significance of corneal disease in the horse, further research into the underlying processes and potential therapeutic options is vital to improving the prognosis for vision and globe retention in our patients. Greater understanding of equine corneal immunology is imperative, along with increasing the pharmacologic repertoire for medical management of corneal disease. Improving existing surgical procedures and developing new ones are also requisites to increasing favorable outcomes in cases requiring surgical correction.

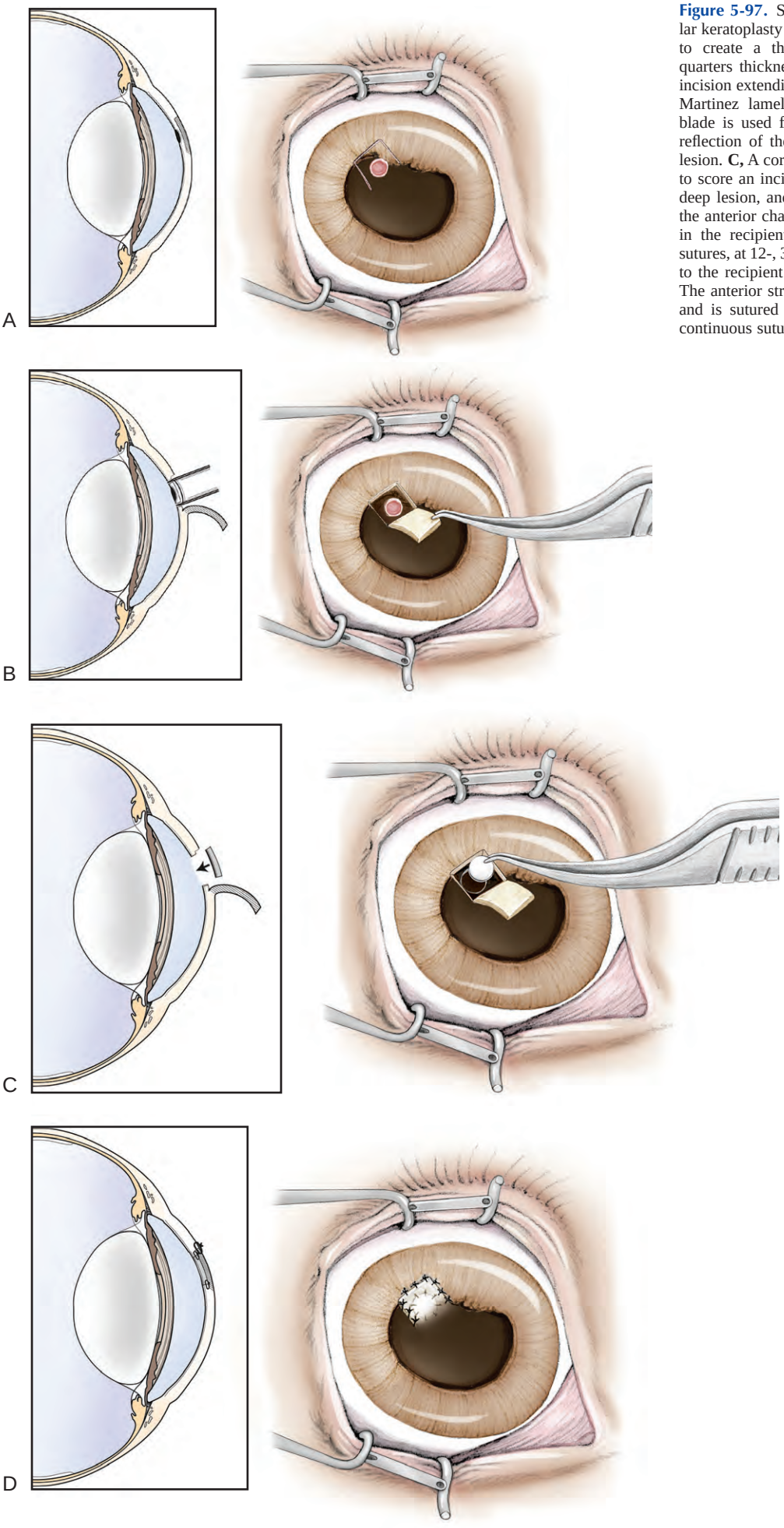


Figure 5-97. Surgical steps for performing posterior lamellar keratoplasty (PLK). **A,** A #64 microsurgical blade is used to create a three-sided (rectangular), one-half to three-quarters thickness incision over the deep lesion, with each incision extending 1 mm beyond the edge of the lesion. **B,** A Martinez lamellar corneal dissector or #64 microsurgical blade is used for lamellar dissection of the flap, allowing reflection of the flap and exposure of the underlying deep lesion. **C,** A corneal trephine or dermal biopsy punch is used to score an incision in the posterior stroma surrounding the deep lesion, and a #65 microsurgical blade is used to enter the anterior chamber. **D,** The donor corneal button is placed in the recipient site and four cardinal simple interrupted sutures, at 12-, 3-, 6-, and 9-o'clock, are placed from the graft to the recipient cornea, using 8-0 or 9-0 absorbable suture. The anterior stromal flap is replaced over the donor cornea, and is sutured in place with simple interrupted or simple continuous sutures.

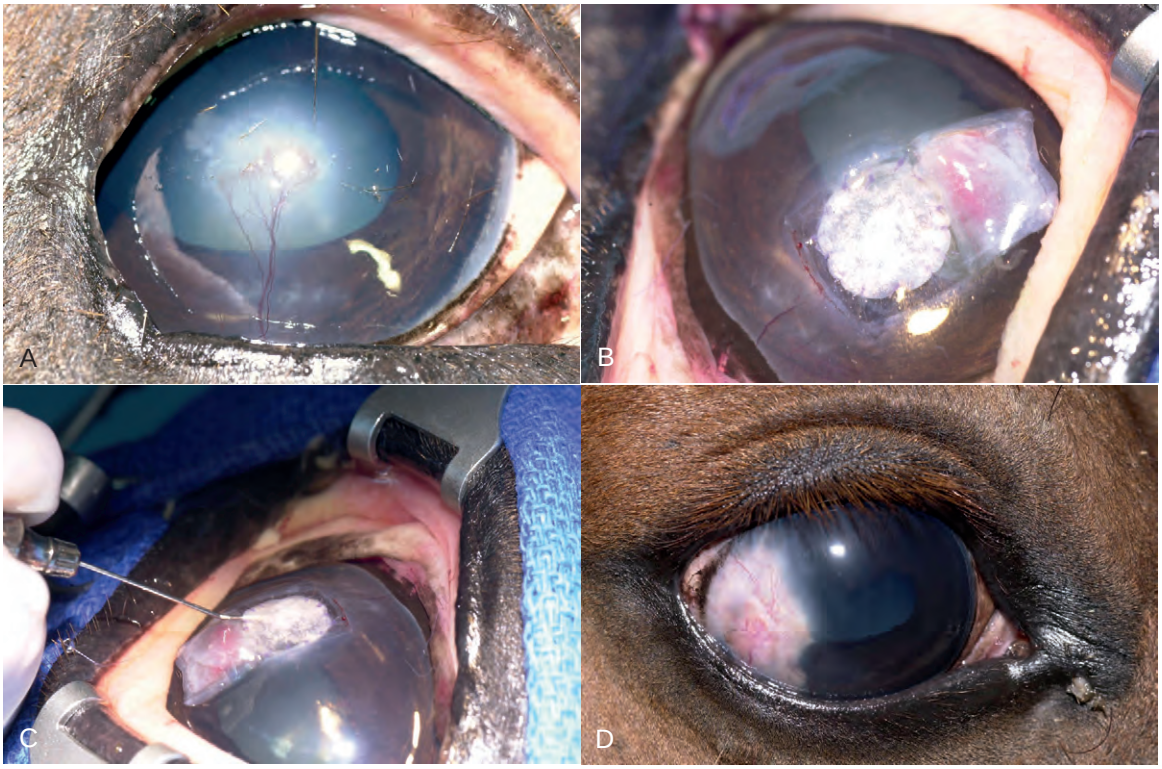


Figure 5-98. Intraoperative and postoperative photographs of posterior lamellar keratoplasty (PLK). **A,** A central deep corneal abscess. **B,** PLK flap created with placement of a porcine intestinal submucosa (Biosys) tissue graft in the full-thickness wound. **C,** Refilling of the anterior chamber prior to closure of overlying corneal flap. **D,** Appearance of eye 8 weeks later with extensive vascularization and fibrosis.

Figure 5-99. Photograph of amnion membrane prior to application in surgery.

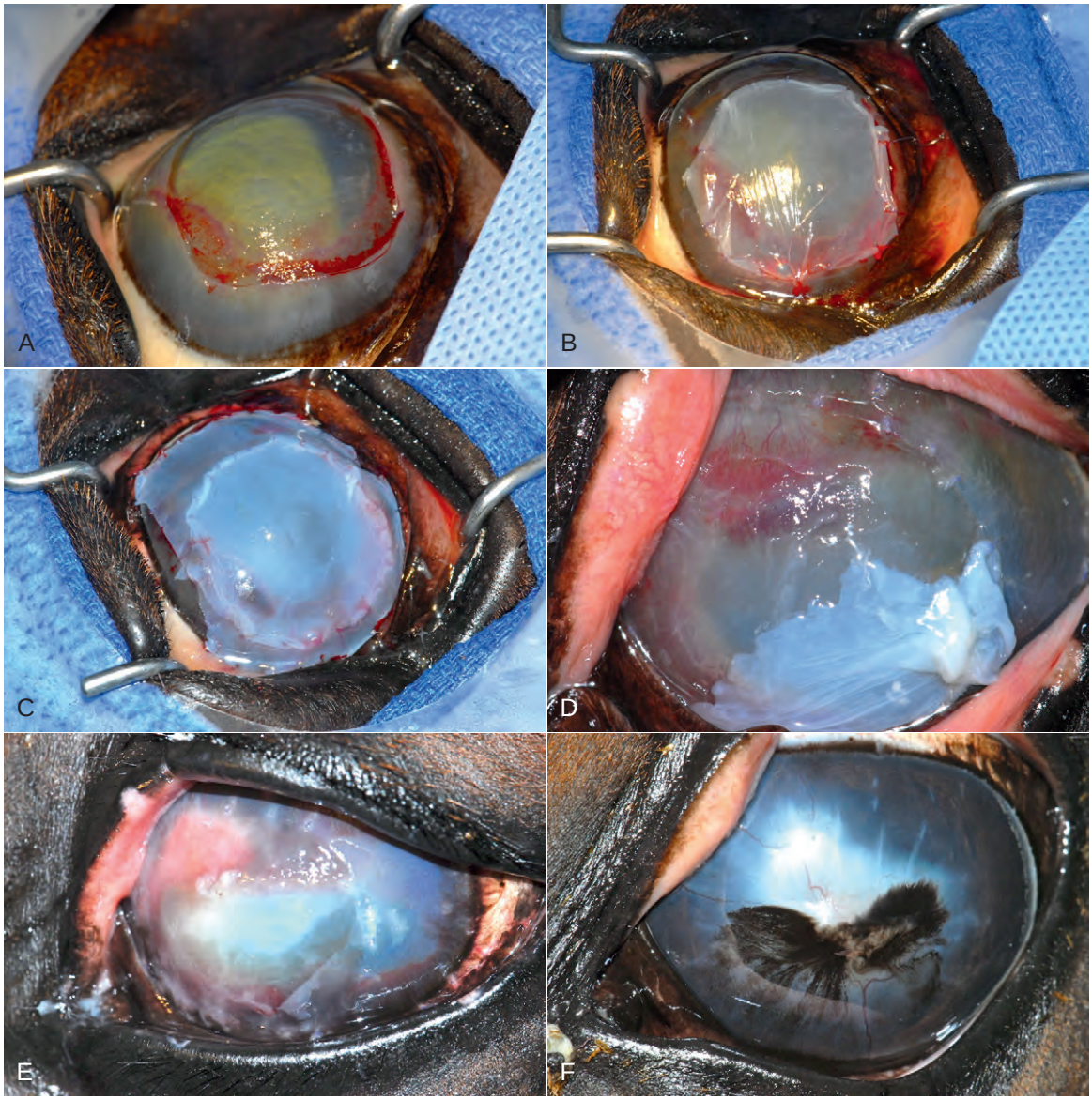


Figure 5-100. Series of intraoperative and postoperative photographs of the horse pictured in Fig. 5-41, *B*. **A,** Intraoperative photograph following surgical removal of the fungal plaque via superficial keratectomy. **B,** Intraoperative photograph following placement and suturing of single layer of amnion over superficial keratectomy bed. **C,** Immediately postoperative photograph showing double layer of amnion sutured over entire cornea. **D,** Four days postoperative photograph showing sloughing of posterior layer of amnion. Anterior layer had previously sloughed. **E,** Twelve days postoperative photograph of vascularized, infiltrated superficial keratectomy bed remaining following complete sloughing of both layers of amnion. Anterior chamber cannot be visualized with direct illumination of the globe. **F,** Eleven weeks postoperative photograph showing corneal fibrosis and pigmentation of greater than 50% of the cornea; anterior chamber is clear and eye is comfortable, with no signs of residual infection.

References

1. Lavach J: The handbook of equine ophthalmology, Ft Collins, 1987, Giddings Studio Publishing.
2. Ramsey D, Hauptman J, Petersen-Jones S: Corneal thickness, intraocular pressure, and optical corneal diameter in Rocky Mountain horses with cornea globosa or clinically normal corneas, Am J Vet Res 60:1317–1321, 1999.
3. Latimer C, Wyman M, Hamilton J: An ophthalmic survey of the neonatal horse, Equine Vet J (Supplement 2):9–14, 1983.
4. Plummer C, Ramsey D, Hauptman J: Assessment of corneal thickness, intraocular pressure, optical corneal diameter, and axial globe dimensions in Miniature horses, Am J Vet Res 64:661–665, 2003.
5. McMullen R, Gilger B: Keratometry, biometry and prediction of intraocular lens power in the equine eye, Vet Ophthalmol 9:357–360, 2006.
6. Woerdt Avd, Gilger B, Wilkie D, et al: Effect of auriculopalpebral nerve block and intravenous administration of xylazine on intraocular pressure and corneal thickness in horses, Am J Vet Res 56:155–158, 1995.

7. Andrew S, Ramsey D, Hauptman J, et al: Density of corneal endothelial cells and corneal thickness in eyes of euthanatized horses, Am J Vet Res 62:479–482, 2001.
8. Edelhauser H, Ubels J, Hejny C: The Cornea and the Sclera. In Kaufman P, Alm A, editors: Adler's Physiology of the eye, ed 10, St. Louis, Missouri, 2003, Mosby, pp 47–114.
9. Biros D, Brooks D, Brown M, et al: Regional and zonal variations in the sulfation patterns of chondroitin sulfate in normal equine corneal stroma, Am J Vet Res 63:143–147, 2002.
10. Whitley R, Burgess E, Moore C: Microbial isolates of the normal equine eye, Equine Vet J (Supplement 2), 1983.
11. Whitley R, Moore C: Microbiology of the equine eye in health and disease, Vet Clin North Am 6:451, 1984.
12. Moore C, Heller N, Majors L, et al: Prevalence of ocular microorganisms in hospitalized and stabled horses, Am J Vet Res 49:773–777, 1988.
13. Andrew S, Nguyen A, Jones G, et al: Seasonal effects on the aerobic bacterial and fungal conjunctival flora of normal thoroughbred brood mares in Florida, Vet Ophthalmol 6:45–50, 2003.
14. Gemensky-Metzler A, Wilkie D, Kowalski J, et al: Changes in bacterial and fungal ocular flora of clinically normal horses following experimental application of topical antimicrobial or antimicrobial-corticosteroids ophthalmic preparations, Am J Vet Res 66:800–811, 2005.
15. Rosa M, Cardozo L, Pereira J, et al: Fungal flora of normal eyes of healthy horses from the State of Rio de Janeiro, Brazil, Vet Ophthalmol 6:51–55, 2003.
16. Samuelson D, Andresen T, Gwin R: Conjunctival fungal flora in horses, cattle, dogs, and cats, J Am Vet Med Assoc 184:1240–1242, 1984.
17. Oliveira-Soto L, Efron N: Morphology of corneal nerves using confocal microscopy, Cornea 20:374, 2001.
18. Brooks D, Clark C, Lester G: Cochet-Bonnet aesthesiometer-determined corneal sensitivity in neonatal foals and adult horses, Vet Ophthalmol 3:133–137, 2000.
19. Kaps S, Richter M, Spiess B: Corneal esthesiometry in the healthy horse, Vet Ophthalmol 6:151–155, 2003.
20. Kalf K, Utter M, Wotman K: Evaluation of duration of corneal anesthesia induced with ophthalmic 0.5% proparacaine hydrochloride by use of a Cochet-Bonnet aesthesiometer in clinically normal horses, Am J Vet Res 69:1655–1658, 2008.
21. Marfurt C, Murphy C, Florczak J: Morphology and neurochemistry of canine corneal innervation, Invest Ophthalmol Vis Sci 42:2242–2251, 2001.
22. Hori J, Joyce N, Streilein J: Immune privilege and immunogenicity reside among different layers of the mouse cornea, Invest Ophthalmol Vis Sci 41:3032–3042, 2000.
23. Kaplan H, Niederkorn J: Regional immunity and immune privilege, Chem Immunol Allergy 92:11–26, 2007.
24. Cursiefen C: Immune privilege and angiogenic privilege of the cornea, Chem Immunol Allergy 92:50–57, 2007.
25. Matthews A: An overview of recent developments in corneal immunobiology and potential relevance in the etiogenesis of corneal disease in the horse, Vet Ophthalmol 11:66–76, 2008.
26. Dana R: Corneal antigen presentation: molecular regulation and functional implications, Ocul Surf 3:S169–S172, 2005.
27. Mo J-S, Wang W, Kaplan H: Impact of inflammation on ocular immune privilege, Chem Immunol Allergy 92:155–165, 2007.
28. Gilger B: Immunology of the ocular surface, Vet Clin North Am Small Anim Pract 38:223–231, 2008.
29. Hanna C, Bicknell D, O'Brien J: Cell turnover in the adult human eye, Arch Ophthalmol 65:695, 1961.
30. Cintron C, Kublin C, Covington H: Quantitative studies of corneal epithelial wound healing in rabbits, Curr Eye Res 1:507–516, 1981.
31. Gipson I, Spurr-Michaud S, Tisdale A, et al: Reassembly of the anchoring structures of the corneal epithelium during wound repair in the rabbit, Invest Ophthalmol Vis Sci 30:425, 1989.
32. Neaderland M, Riis R, Rebhun W, et al: Healing of experimentally induced corneal ulcers in horses, Am J Vet Res 48:427–430, 1987.
33. Lemp M: Cornea and sclera, Arch Ophthalmol 94:473, 1976.
34. Yee R, Geroski D, Matsuda M, et al: Correlation of corneal endothelial pump site density, barrier function, and morphology in wound repair, Invest Ophthalmol Vis Sci 26:1191, 1985.
35. Bourne W, Kaufman H: Specular microscopy of the human corneal endothelium in vivo, Am J Ophthalmol 81:319–323, 1976.
36. Imanishi J, Kamiyama K, Iguchi I, et al: Growth factors: importance in wound healing and maintenance of transparency of the cornea, Prog Retin Eye Res 19:113–129, 2000.
37. Tripathi R, Raja S, Tripathi B: Prospects for epidermal growth factor in the management of corneal disorders, Surv Ophthalmol 34:457–462, 1990.
38. Hoppenreijs V, Pels E, Vrensen G, et al: Platelet-derived growth factor: receptor expression in corneas and effects on corneal cells, Invest Ophthalmol Vis Sci 34:637–649, 1993.
39. Frazier K, Williams S, Kothapalli D, et al: Stimulation of fibroblast cell growth, matrix production, and granulation tissue formation by connective tissue growth factor, J Invest Dermatol 107:404–411, 1996.
40. Haber M, Cao Z, Panjwani N, et al: Effects of growth factors (EGF, PDGF-BB, TGF-β1) on cultured equine epithelial cells and keratocytes: implications for wound healing, Vet Ophthalmol 6:211–217, 2003.
41. Burling K, Seguin M, Marsh P, et al: Effect of topical administration of epidermal growth factor on healing of corneal epithelial defects in horses, Am J Vet Res 61:1150–1155, 2000.
42. Ollivier F, Brooks D, Schultz G, et al: Connective tissue growth factor in tear film of the horse: detection, identification and origin, Graefes Arch Clin Exp Ophthalmol 242:165–171, 2004.
43. Sassani J, Zagon I, McLaughlin P: Opioid growth factor modulation of corneal epithelium: uppers and downers, Curr Eye Res 26:249–262, 2003.
44. Zagon I, Sassani J, McLaughlin P: Re-epithelialization of the rabbit cornea is regulated by opioid growth factor, Brain Res 803:61–68, 1998.
45. Zagon I, Sassani J, McLaughlin P: Re-epithelialization of the rat cornea is accelerated by blockade of opioid receptors, Brain Res 798:254–260, 1998.
46. Zagon I, Sassani J, McLaughlin P: Re-epithelialization of the human cornea is regulated by endogenous opioids, Invest Ophthalmol Vis Sci 41:73–81, 2000.
47. Robertson S, Andrew S: Presence of opioid growth factor and its receptor in the normal dog, cat and horse cornea, Vet Ophthalmol 6:131–134, 2003.
48. Ollivier F, Gilger B, Barrie K, et al: Proteinases of the cornea and preocular tear film, Vet Ophthalmol 10:199–206, 2007.
49. Twining S, Fukuchi T, Yu B, et al: Corneal synthesis of alpha 1-proteainase inhibitor (alpha 1-antitrypsin), Invest Ophthalmol Vis Sci 35:458–462, 1994.
50. Twining S, Fukuchi T, Yue B, et al: Alpha-2 macroglobulin is present in and synthesized by the cornea, Invest Ophthalmol Vis Sci 35:3226–3233, 1994.
51. Sivak J, Fini M: MMPs in the eye: emerging roles for matrix metalloproteinases in ocular physiology, Prog Retin Eye Res 21:1–14, 2002.
52. Sack R, Beaton A, Sathe S, et al: Towards a closed eye model of the pre-ocular tear layer, Prog Retin Eye Res 19:649–668, 2000.
53. Strubbe D, Brooks D, Schultz G, et al: Evaluation of tear film proteinases in horses with ulcerative keratitis, Vet Ophthalmol 3:111–119, 2000.
54. Matsumoto K: Proteases in bacterial keratitis, Cornea 19:160–164, 2000.
55. Zhu W, Wojdyla K, Donlon K, et al: Extracellular proteases of *Aspergillus flavus*, Diagn Microbiol Infect Dis 13:491–497, 1990.
56. Kessler E, Kennah H, Brown S: Pseudomonas protease. Purification, partial characterization, and its effect on collage, proteoglycan, and rabbit corneas, Invest Ophthalmol Vis Sci 16:488–497, 1977.
57. Matsubara M, Girard M, Kublin C, et al: Differential roles for two gelatinolytic enzymes of the matrix metalloproteinase family in the remodeling cornea, Dev Biol 147:425–439, 1991.
58. Barletta J, Angella G, Balch K, et al: Inhibition of pseudomonal ulceration in rabbit corneas by a synthetic matrix metalloproteinase inhibitor, Invest Ophthalmol Vis Sci 37:20–28, 1996.
59. Watanabe H, Hattori S, Katsuda S, et al: Human neutrophil elastase: degradation of basement membrane components and immunolocalization in the tissues, J Biochem 108:753–759, 1990.
60. Sathe S, Sakata M, Beaton A, et al: Identification, origins and the diurnal role of the principle serine protease inhibitors in human tear fluid, Curr Eye Res 17:348–362, 1998.
61. Ollivier F, Brooks D, Setten GV, et al: Profiles of matrix metalloproteinase activity in equine tear fluid during corneal healing in 10 horses with ulcerative keratitis, Vet Ophthalmol 7:397–405, 2004.
62. Twining S: Regulation of proteolytic activity in tissues, Crit Rev Biochem Mol Biol 29:315–383, 1994.

63. Fini M, Girard M: Expression of collagenolytic/gelatinolytic metalloproteinases by normal cornea, Invest Ophthalmol Vis Sci 31:1779–1788, 1990.
64. Ye H, Azar D: Expression of gelatinases A and B, and TIMPs 1 and 2 during corneal wound healing, Invest Ophthalmol Vis Sci 39:913–921, 1998.
65. BenEzra D: Possible mediation of vasculogenesis by products of the immune system. In Silverstein A, O'Connor D, editors: Immunology and immunopathology of the eye, New York, 1978, Masson, p. 315.
66. Rochels R: Animal experiment studies on the role of inflammation mediators in corneal neovascularization, Doc Ophthalmol 57:215–262, 1984.
67. Chung E, Saban D, Chauhan S, et al: Regulation of blood vessel versus lymphatic vessel growth in the cornea, Invest Ophthalmol Vis Sci 50:1613–1816, 2009.
68. Klenkler B, Sheardown H: Growth factors in the anterior segment: role in tissue maintenance, wound healing and ocular pathology, Exp Eye Res 79:677–688, 2004.
69. Fujita S, Saika S, Kao W, et al: Endogenous TNFα Suppression of neovascularization in corneal stroma in mice, Invest Ophthalmol Vis Sci 48:3051–3055, 2007.
70. Gilger B: Diseases and surgery of the canine cornea and sclera. In Gelatt K, editor: Veterinary ophthalmology, ed 4, Ames, Iowa, 2007, Blackwell, pp 690–752.
71. Ytteborg J, Dohlman C: Corneal edema and intraocular pressure. II. Clinical results, Arch Ophthalmol 74:477–484, 1965.
72. Grahn B, Pinard C, Archer S, et al: Congenital ocular anomalies in purebred and crossbred Rocky and Kentucky Mountain horses in Canada, Can Vet J 49:675–681, 2008.
73. Ramsey D, Ewart S, Render J, et al: Congenital ocular abnormalities of Rocky Mountain horses, Vet Ophthalmol 2:47–59, 1999.
74. Latimer C, Wyman M: Neonatal ophthalmology, Vet Clin North Am Equine Pract 1:235–259, 1985.
75. Andersson L, Juras R, Ramsey D, et al: Equine multiple congenital ocular anomalies maps to a 4.9 megabase interval on horse chromosome 6, BMC Genet 9:88, 2008.
76. Townsend W: Congenital anomalies of the cornea. In Kaufman H, editor: The cornea, New York, 1988, Churchill Livingstone, pp 333–360.
77. Mann I: Developmental abnormalities of the eye, London, 1957, JB Lippincott.
78. Barnett K, Crispin S, Lavach J, et al: Equine ophthalmology: an atlas and text, ed 3, Edinburgh, 2004, Saunders.
79. Williams D, Barnett K: Bilateral optic disc colobomas and microphthalmos in a thoroughbred horse, Vet Rec 132:101–103, 1993.
80. Cook C: Embryogenesis of congenital eye malformations, Vet Comp Ophthalmol 5:109–123, 1995.
81. Spencer W: Conjunctiva. In Spencer W, editor: Ophthalmic pathology: an atlas and textbook, ed 4, Philadelphia, 1996, W.B. Saunders, pp 38–155.
82. Joyce J: Iridal hypoplasia (aniridia) accompanied by limbic dermoids in a group of related quarterhorses, Equine Vet J Supplement 2:26–28, 1990.
83. McLaughlin S, Brightman A: Bilateral ocular dermoids in a colt, Equine Pract 5:10–14, 1983.
84. Grahn B, Peiffer R: Fundamentals of veterinary ophthalmic pathology. In Gelatt K, editor: Veterinary ophthalmology, ed 4, St. Louis, 2007, Blackwell Publishing, pp 355–437.
85. Cook C: Ocular embryology and congenital malformations. In Gelatt K, editor: Veterinary ophthalmology, ed 4, Ames, Iowa, 2007, Blackwell Publishing, pp 3–36.
86. Munroe G: Congenital corneal vascularisation in a neonatal Thoroughbred foal, Equine Vet J 27:156–157, 1995.
87. Gelatt K: The eye. In Mansmann R, McAllister E, Pratt P, editors: Equine medicine and surgery, ed 3, Santa Barbara, Calif, 1982, American Veterinary Publications, pp 1280–1282.
88. Szutter L: Ophthalmoscopic examination of newborn domestic animals, Acta Vet Acad Sci Hung 11:183–193, 1961.
89. Solomon A, Rossenblatt M, Li D, et al: Doxycycline inhibition of interleukin-1 in the corneal epithelium, Invest Ophthalmol Vis Sci 41:2544–2557, 2000.
90. Kuzin I, Snyder J, Ugine G, et al: Tetracyclines inhibit activated B cell function, Int Immunol 13:921–931, 2001.
91. Bentley E, Murphy C: Thermal cautery of the cornea for treatment of spontaneous chronic corneal epithelial defects in dogs and horses, J Am Vet Med Assoc 224:250–253, 2004.
92. Rebhun W: Chronic corneal epithelial erosions in horses, Vet Med Small Anim Clin 78:1635–1638, 1983.
93. Michau T, Schwabenton B, Davidson M, et al: Superficial, nonhealing corneal ulcers in horses: 23 cases (1989–2003), Vet Ophthalmol 6:291–297, 2003.
94. Cooley P, Wyman M: Indolent-like corneal ulcers in 3 horses, J Am Vet Med Assoc 188:295–297, 1986.
95. Brunott A, Boeve M, Velden M: Grid keratotomy as a treatment for superficial nonhealing corneal ulcers in 10 horses, Vet Ophthalmol 10:162–167, 2007.
96. Hakanson N, Dubielzig R: Chronic superficial corneal erosions with anterior stromal sequestration in three horses, Vet Comp Ophthalmol 4:179–183, 1994.
97. Bentley E, Abrams G, Covitz D, et al: Morphology and immunohistochemistry of spontaneous chronic corneal epithelial defects (SCCED) in dogs, Invest Ophthalmol Vis Sci 42:2262–2269, 2001.
98. Bentley E, Campbell S, Woo H, et al: The effect of chronic corneal epithelial debridement on epithelial and stromal morphology in dogs, Invest Ophthalmol Vis Sci 43:2136–2142, 2002.
99. Murphy C, Marfurt C, McDermott A, et al: Spontaneous chronic corneal epithelial defects (SCCED) in dogs: clinical features, innervation, and effect of topical SP, with or without IGF-1. Invest Ophthalmol Vis Sci 42:2252–2261, 2001.
100. Fini M, Parks W, Rinehart W, et al: Role of matrix metalloproteinases in failure to re-epithelialize after corneal injury, Am J Pathol 149:1287–1302, 1996.
101. Garrana M, Zieske J, Assouline M, et al: Matrix metalloproteinases in epithelia from human recurrent corneal erosions, Invest Ophthalmol Vis Sci 40:1266–1270, 1999.
102. Morgan R, Abrams K: A comparison of six different therapies for persistent corneal erosions in dogs and cats, Vet Comp Ophthalmol 1:38–43, 1994.
103. Berman M: The pathogenesis of corneal epithelial defects, Acta Ophthalmol Suppl (Oxf) 192:55–64, 1989.
104. Wada S, Yoshinari M, Mizuno Y: Practical usefulness of a therapeutic soft contact lens for a corneal ulcer in a racehorse, Vet Ophthalmol 3:217–219, 2000.
105. Champagne E, Munger R: Multiple punctate keratotomy for the treatment of recurrent epithelial erosions in dogs, J Am Anim Hosp Assoc 28:213–216, 1992.
106. Chavkin M, Riis R, Scherlie P: Management of a persistent corneal erosion in a Boxer dog, Cornell Vet 80:347–356, 1990.
107. Katser D, Kincaid M, Fouraker B, et al: Recurrent corneal erosion: pathology of corneal puncture, Cornea 10:418–423, 1991.
108. Peiffer R: Superficial keratectomy in the management of indolent ulcers of the boxer cornea, Canine Pract 3:31–32, 1976.
109. Gelatt K, Samuelson D: Recurrent corneal erosions and epithelial dystrophy in the boxer dog, J Am Anim Hosp Assoc 18:453–460, 1982.
110. Lavach J, Severin G, Roberts S: Lacerations of the equine eye: a review of 48 cases, J Am Vet Med Assoc 184:1243–1248, 1984.
111. Chmielewski N, Brooks D, Smith P, et al: Visual outcome and ocular survival following iris prolapse in the horse: a review of 32 cases, Equine Vet J 29:31–39, 1997.
112. Rampazzo A, Eule C, Speier S, et al: Scleral rupture in dogs, cats, and horses, Vet Ophthalmol 9:149–155, 2006.
113. Ramsey D, Whiteley H, Gerding P, et al: Eosinophilic keratoconjunctivitis in a horse, J Am Vet Med Assoc 205:1308–1311, 1994.
114. Yamagata M, Wilkie D, Gilger B: Eosinophilic keratoconjunctivitis in seven horses, J Am Vet Med Assoc 209:1283–1286, 1996.
115. Andrew S, Willis A: Diseases of the cornea and sclera. In Gilger B, editor: Equine Ophthalmology, St. Louis, Missouri, 2005, Elsevier Saunders, pp 157–251.
116. Cutler T: Corneal epithelial disease, Vet Clin North Am Equine Pract 20:319–343, 2004.
117. Brooks D: Equine ophthalmology. In Gelatt K, editor: Veterinary ophthalmology, ed 3, Philadelphia, 1999, Lippincott Williams & Wilkins, pp 1052–1116.
118. Schmidt G, Krehbiel J, Coley S, et al: Equine ocular onchocerciasis: histopathologic study, Am J Vet Res 43:1371–1375, 1982.
119. Trocme S, Hallberg C, Gill K, et al: Effects of eosinophil granule proteins on human corneal epithelial cell viability and morphology, Invest Ophthalmol Vis Sci 38:593–599, 1997.

120. Nasisse M, Clover T, Moore C, et al: Detection of feline herpesvirus 1 DNA in corneas of cats with eosinophilic keratitis or corneal sequestration, Am J Vet Res 59:856–858, 1998.
121. McEwan B: The response of the eosinophil in acute inflammation in the horse. In Tascharner Cv, Halliwell R, editors: Advances in veterinary dermatology, London, 1990, Bailliere Tindall, pp 176–194.
122. Spiess A, Sapienza J, Mayordomo A: Treatment of proliferative feline eosinophilic keratitis with topical 1.5% cyclosporine: 35 cases, Vet Ophthalmol 12:132–137, 2009.
123. Trocme S, Gleich G, Kephart G, et al: Eosinophilic granule major basic protein inhibition of corneal epithelial wound healing, Invest Ophthalmol Vis Sci 35:3051–3056, 1994.
124. McClellan G, Archer F: Corneal stromal sequestration and keratoconjunctivitis sicca in a horse, Vet Ophthalmol 3:207–212, 2000.
125. Featherstone H, Franklin V, Sansom J: Feline corneal sequestrum: laboratory analysis of ocular samples from 12 cats, Vet Ophthalmol 7:229–238, 2004.
126. Cullen C, Wadowska D, Singh A, et al: Ultrastructural findings in feline corneal sequestra, Vet Ophthalmol 8:295–303, 2005.
127. Ejima H, Hara N, Kajigaya H: Detection of iron in a blackish lesion in a case of feline corneal sequestrum, J Vet Med Sci 55:1051–1052, 1993.
128. Souri E: The feline corneal nigrum, Vet Med Small Anim Clin 70:531–534, 1975.
129. Moore C, Corwin L, Collier L: Keratopathy induced by beta radiation therapy in a horse, Equine Vet J Suppl 2:112–116, 1983.
130. Slatter D, Nelson A, Smith G: Ocular sequelae of high-dose periocular gamma irradiation in a horse, Equine Vet J Suppl 2:110–111, 1983.
131. Theon A, Pascoe J: Iridium-192 interstitial brachytherapy for equine periocular tumours: treatment results and prognostic factors in 115 horses, Equine Vet J 27:117–121, 1994.
132. Plummer C, Smith S, Andrew S, et al: Combined keratectomy, strontium-90 irradiation and permanent bulbar conjunctival grafts for corneolimbal squamous cell carcinomas in horses (1990–2002): 38 horses, Vet Ophthalmol 10:37–42, 2007.
133. Singer B: Ocular effects of ionizing radiation: past and present problems, Br J Dermatol 63:455–456, 1979.
134. Collins B, Johnson P, Moore C, et al: Immune-mediated keratoconjunctivitis sicca in a horse, Vet Comp Ophthalmol 4:61–65, 1994.
135. Joyce J, Bratton G: Keratoconjunctivitis sicca secondary to fracture of the mandible, Vet Med Small Anim Clin 68:619–620, 1973.
136. Reilly L, Beech J: Bilateral keratoconjunctivitis sicca in a horse, Equine Vet J 26:171–172, 1994.
137. Spurlock S, Spurlock G, Wise M: Keratoconjunctivitis sicca associated with fracture of the stylohyoid bone in a horse, J Am Vet Med Assoc 194:258–259, 1989.
138. Spiess B, Wilcock B, Physick-Sheard P: Eosinophilic granulomatous dacryoadenitis causing bilateral keratoconjunctivitis sicca in a horse, Equine Vet J 21:226–228, 1989.
139. Schwarz B, Sallmutter T, Nell B: Keratoconjunctivitis sicca attributable to parasympathetic facial nerve dysfunction associated with hypothyroidism in a horse, J Am Vet Med Assoc 233:1761–1766, 2008.
140. Williams R, Manning J, RL Peiffer J: The Schirmer tear test in the equine: normal values and the contribution of the gland of the nictitating membrane, J Equine Med Surg 3:117–119, 1979.
141. Marts B, Bryan G, Prieur D: Schirmer tear test measurement and lysozyme concentration of equine tears, J Equine Med Surg 1:427–430, 1977.
142. Crispin S: Tear-deficient and evaporative dry eye syndromes of the horse, Vet Ophthalmol 3:87–92, 2000.
143. Kampen KV, James L: ophthalmic lesions in locoweed poisoning of cattle, sheep, and horses, Am J Vet Res 32:1293–1295, 1971.
144. Rothschild C, Sellon D, Bryan G, et al: Effects of trimethoprim-sulfadiazine on tear production and the fluctuations of Schirmer tear test values in horses, Vet ophthalmol 7:385–390, 2004.
145. Shamir M, Ofri R: Comparative neuro-ophthalmology. In Gelatt K, editor: Veterinary ophthalmology, ed 4, Ames, Iowa, 2007, Blackwell Publishing, pp 1406–1469.
146. Herring I: Clinical pharmacology and therapeutics. In Gelatt K, editor: Vet Ophthalmol, ed 4, Ames, Iowa, 2007, Blackwell, pp 332–354.
147. Wolf E, Merideth R: Parotid duct transposition in the horse, Equine Vet Sci 1:143–145, 1981.
148. Rebhun W: Chemical keratitis in a horse, Vet Med Small Anim Clin 75:1537–1539, 1980.
149. Schrage N, Langefeld S, Zschocke J, et al: Eye burns: an emergency and continuing problem, Burns 26:689–699, 2000.
150. Kuckelhorn R, Schrage N, Keller G, et al: Emergency treatment of chemical and thermal eye burns, Acta Ophthalmol Scand 80:4–10, 2002.
151. Haddox J, Pfister R, Yuille-Barr D: The efficacy of topical citrate after alkali injury is dependent on the period of time it is administered, Invest Ophthalmol Vis Sci 30:1062–1068, 1989.
152. Borchers K, Wolfinger U, Goltz M, et al: Distribution and relevance of equine herpesvirus type 2 (EHV-2) infections, Arch Virol 142:917–928, 1997.
153. Kershaw O, Oppen T, Glitz F, et al: Detection of equine herpesvirus type 2 (EHV-2) in horses with keratoconjunctivitis, Virus Res 80:93–99, 2001.
154. Borchers K, Ebert M, Fetsch A, et al: Prevalence of equine herpesvirus type 2 (EHV-2) DNA in ocular swabs and its cell tropism in equine conjunctiva, Vet Microbiol 118:260–266, 2006.
155. Collinson P, O'Reilly J, Ficorilli N, et al: Isolation of equine herpesvirus type 2 (equine gammaherpesvirus 2) from foals with keratoconjunctivitis, J Am Vet Med Assoc 205:329–331, 1994.
156. Miller T, Gaskin J, Whitley R, et al: Herpetic keratitis in a horse, Equine Vet J Suppl 1:15–17, 1990.
157. Matthews A, Handscombe M: Superficial keratitis in the horse: treatment with the antiviral drug idoxuridine, Equine Vet J Suppl 2:29–31, 1983.
158. Brooks D: Inflammatory stromal keratopathies: medical management of stromal keratomalacia, stromal abscesses, eosinophilic keratitis, and band keratopathy in the horse, Vet Clin North Am Equine Pract 20:345–360, 2004.
159. Rizvi S, Slater J, Wolfinger U, et al: Detection and distribution of equine herpesvirus 2 DNA in the central and peripheral nervous systems of ponies, J Gen Virol 78:1115–1118, 1997.
160. Borchers K, Wolfinger U, Ludwig H, et al: Virological and molecular biological investigations into equine herpes virus types 2 (EHV-2) experimental infections, Virus Res 55:101–106, 1998.
161. Garre B, Shebany K, Gryspeerdt A, et al: Pharmacokinetics of acyclovir after intravenous infusion of acyclovir and after oral administration of acyclovir and its prodrug valacyclovir in healthy adult horses, Antimicrob Agents Chemother 51:4308–4314, 2007.
162. Garre B, Meulen Kvd, Nugent J, et al: In vitro susceptibility of six isolates of equine herpesvirus 1 to acyclovir, ganciclovir, cidofovir, adefovir, PMEDAP and foscarnet, Vet Microbiol 122:43–51, 2007.
163. Garre B, Gryspeerdt A, Croubels S, et al: Evaluation of orally administered valacyclovir in experimentally EHV1-infected ponies, Vet Microbiol 135:214–221, 2009.
164. Bentz B, Maxwell L, Erkert R, et al: Pharmacokinetics of acyclovir after single intravenous and oral administration to adult horses, J Vet Intern Med 20:589–594, 2006.
165. Regnier A: Clinical pharmacology and therapeutics. Part 2: Antimicrobials, antiinflammatory agents, and antiglaucoma drugs. In Gelatt K, editor: Veterinary Ophthalmology, ed 4, Ames, Iowa, 2007, Blackwell, pp 288–331.
166. Moore C, Fales W, Whittington P, et al: Bacterial and fungal isolates from Equidae with ulcerative keratitis, J Am Vet Med Assoc 182:600–603, 1983.
167. McLaughlin S, Brightman A, Helper L, et al: Pathogenic bacteria and fungi associated with extraocular disease in the horse, J Am Vet Med Assoc 182:241–242, 1983.
168. Utter M, Davidson E, Wotman K: Clinical features and outcomes of severe ulcerative keratitis with medical and surgical management in 41 horses (2000–2006), Equine Vet Educ 21:321–327, 2009.
169. Keller R, Hendrix D: Bacterial isolates and antimicrobial susceptibilities in equine bacterial ulcerative keratitis (1993–2004), Equine Vet J 37:207–211, 2005.
170. Sauer P, Andrew S, Lassaline M, et al: Changes in antibiotic resistance in equine bacterial ulcerative keratitis (1991–2000): 65 horses, Vet Ophthalmol 6:309–313, 2003.
171. Moore C, Collins B, Fales W: Antibacterial susceptibility patterns for microbial isolates associated with infectious keratitis in horses: 63 cases (1986–1994), J Am Vet Med Assoc 207:928–933, 1995.
172. Rebhun W, Cho J, Gaarder J, et al: Presumed clostridial and aerobic bacterial infections of the cornea in two horses, J Am Vet Med Assoc 214:1519–1522, 1999.
173. Adamson P, Jang S: Ulcerative keratitis associated with *Salmonella arizonae* infection in a horse, J Am Vet Med Assoc 186:1219–1220, 1985.
174. Divers T, George L: Hypopyon and descemetocele associated with *Pseudomonas* ulcerative keratitis in a horse: a case report and review, Equine Vet Sci 2:104, 1982.

175. Rebhun W: Bacterial ulcers of the equine cornea, Equine Pract 3:40–48, 1981.
176. Gelatt K: *Pseudomonas* ulcerative keratitis and abscess in a horse, Vet Med Small Anim Clin 1309–1310, 1974.
177. Cullen C, Grahn B: Diagnostic ophthalmology, Can Vet J 41:867–868, 2000.
178. Curiel JdS, Murphy C, Jang S, et al: Nutritionally variant streptococci associated with corneal ulcers in horses: 35 cases (1982–1988), J Am Vet Med Assoc 197:624–626, 1990.
179. Brooks D, Andrew S, Biros D, et al: Ulcerative keratitis caused by beta-hemolytic *Streptococcus equi* in 11 horses, Vet Ophthalmol 3:121–125, 2000.
180. Sanchez S, Studer M, Currin P, et al: *Listeria* keratitis in a horse, Vet Ophthalmol 4:217–219, 2001.
181. Higgins R, Biberstein E, Jang S: Nutritionally variant streptococci from corneal ulcers in horses, J Clin Microbiol 20:1130–1134, 1984.
182. Ledbetter E, Scarlett J: Isolation of obligate anaerobic bacteria from ulcerative keratitis in domestic animals, Vet Ophthalmol 11:114–122, 2008.
183. Lassaline M, Brooks D, Ollivier F, et al: Equine amniotic membrane transplantation for corneal ulceration and keratomalacia in three horses, Vet Ophthalmol 8:311–317, 2005.
184. Sweeney C, Irby N: Topical treatment of *Pseudomonas* sp.–infected corneal ulcers in horses: 70 cases (1977–1994), J Am Vet Med Assoc 209:954–957, 1996.
185. Nasisse M, Nelms S: Equine ulcerative keratitis, Vet Clin North Am Equine Pract 8:537–557, 1992.
186. Hamor R, Whelan N: Equine infectious keratitis, Vet Clin North Am Equine Pract 15:623–646, 1999.
187. Ferrer C, Rodriguez-Prats J, Abad J, et al: Unusual anaerobic bacteria in keratitis after laser in situ keratomileusis: diagnosis using molecular biology methods, J Cataract Refract Surg 30:1790–1794, 2004.
188. Stern G, Hodes B, Stock E: Clostridium perfringens corneal ulcer, Arch Ophthalmol 97:661–663, 1979.
189. Massa K, Murphy C, Hartmann F, et al: Usefulness of aerobic microbial cultures and cytologic evaluation of corneal specimens in the diagnosis of infectious ulcerative keratitis in animals, J Am Vet Med Assoc 215:1671–1674, 1999.
190. Matsubara M, Zieske J, Fini M: Mechanism of basement membrane dissolution preceding corneal ulceration, Invest Ophthalmol Vis Sci 32:3221–3237, 1991.
191. Slansky H, Gnadinger M, Itoi M, et al: Collagenase in corneal ulcerations, Arch Ophthalmol 82:108–111, 1969.
192. Hibbetts K, Hines B, Williams D: An overview of proteinase inhibitors, J Vet Intern Med 13:302–308, 1999.
193. Brown S: Collagenase and corneal ulcers, Invest Ophthalmol Vis Sci 10:203, 1971.
194. Aarestrup F, Scott N, Sordillo L: Ability of *Staphylococcus aureus* coagulase genotypes to resist neutrophil bactericidal activity and phagocytosis, Infect Immunol 62:5679–5682, 1994.
195. Rause J, Love D: Characterization of coagulase-positive *Staphylococcus intermedius* and *Staphylococcus aureus* isolated from veterinary clinical specimens, J Clin Microbiol 18:789–792, 1983.
196. Callegan M, Engel L, Hill J, et al: Corneal virulence of *Staphylococcus aureus:* roles of alpha-toxin and protein A in pathogenesis, Infect Immunol 62:2478–2882, 1994.
197. Dajcs J, Thibodeaux B, Girgis D, et al: Corneal virulence of *Staphylococcus aureus* in an experimental model of keratitis, DNA Cell Biol 21:375–382, 2002.
198. Loeffler D, Norcross N: Enzyme-linked immunosorbent assay for detection of milk immunoglobulins to leukocidin toxin of *Staphylococcus aureus*, Am J Vet Res 46:1728–1732, 1985.
199. Stern G, Lubniewski A, Allen C: The interaction between *Pseudomonas aeruginosa* and the corneal epithelium: an electron microscopic study, Arch Ophthalmol 103:1221–1225, 1985.
200. Reichert R, Das N, Zam Z: Adherence properties of *Pseudomonas pili* to epithelial cells of the human cornea, Curr Eye Res 2:289–293, 1982–1983.
201. Twining S, Kirschner S, Mahnke L: Effect of *Pseudomonas aeruginosa* elastase, alkaline protease, and exotoxin A on corneal proteinases and proteins, Invest Ophthalmol Vis Sci 34:2699–2712, 1993.
202. Bachman J, Gabriel H: A 10-year case report and current clinical review of chronic beta-hemolytic streptococcal keratoconjunctivitis, Optometry 73:303–310, 2002.
203. Jones S, Cohne E, Arentsen J, et al: Ocular streptococcal infections, Cornea 7:295–299, 1988.
204. Francois J, Rijsselaere M: Corticosteroids and ocular mycoses: Experimental study, Ann Ophthalmol 6:207, 1974.
205. Srinivasan M, Lalitha P, Mahalakshmi R, et al: Corticosteroids for bacterial corneal ulcers, Br J Ophthalmol 93:198–202, 2009.
206. Lev M, Keudell K, Milford A: Succinate as a growth factor for *Bacteroides melaninogenicus*, J Bacteriol 108:15–178, 1971.
207. Tofte R, Peterson P, Schemlling D, et al: Opsonization of four Bacteroides species. Role of the classical complement pathway and immunoglobulin, Infect Immun 27:784–792, 1980.
208. Smith G, Barton S, Wallace L: Further observations on enhancement of the infectivity of *Fusobacterium necrophorum* by other bacteria, Epidemiol Infect 106:305–310, 1991.
209. Suzuki T, Sano Y, Sasaki O, et al: Ocular surface inflammation induced by *Propionibacterium acnes*, Cornea 21:812–817, 2002.
210. Hatheway C: Toxigenic clostridia, Clin Microbiol Rev 3:66–98, 1990.
211. Csukas Z, Banizs B, Rozgonyi F: Studies on the cytotoxic effects of *Propionibacterium acnes* strains isolated from the cornea, Microb Pathog 36:171–174, 2004.
212. Schlech B, Alfonso E: Overview of the potency of moxifloxacin ophthalmic solution 0.5% (VIGAMOX), Surv Ophthalmol 50:7–15, 2005.
213. Soussy C, Nguyen J, Goldstein F, et al: In vitro antibacterial activity of moxifloxacin against hospital isolates: a multicentre study, Clin Microbiol Infect 9:997–1005, 2003.
214. Asbell P, Colby K, Deng S, et al: Ocular TRUST: nationwide antimicrobial susceptibility patterns in ocular isolates, Am J Ophthalmol 145:951–958, 2008.
215. Afshari N, Ma J, Duncan S, et al: Trends in resistance to ciprofloxacin, cefazolin, and gentamicin in the treatment of bacterial keratitis, J Ocul Pharmacol Ther 24:217–223, 2008.
216. Duggirala A, Joseph J, Sharma S, et al: Activity of newer fluoroquinolones against gram-positive and gram-negative bacteria isolated from ocular infections: an in vitro comparison, Indian J Ophthalmol 55:15–19, 2007.
217. Williams M, Spiess B, Pascoe P, et al: Systemic effects of topical and subconjunctival ophthalmic atropine in the horse, Vet Ophthalmol 3:193–199, 2000.
218. Smith V, Cook S: Doxycycline: a role in ocular surface repair, Br J Ophthalmol 88:619–625, 2004.
219. Gilmour M, Clarke C, MacAllister G, et al: Ocular penetration of oral doxycycline in the horse, Vet Ophthalmol 8:331–335, 2005.
220. Davis J, Salmon J, Papich M: Pharmacokinetics and tissue distribution of doxycycline after oral administration of single and multiple doses in horses, Am J Vet Res 67:310–316, 2006.
221. Baker A, Plummer C, Szabo N, et al: Doxycycline levels in preocular tear film of horses following oral administration, Vet Ophthalmol 11:381–385, 2008.
222. Berman M: Corneal ulceration and the serum anti-proteases. I. Alpha 1-antitrypsin, Invest Ophthalmol Vis Sci 12:759–770, 1973.
223. Berman M: Corneal ulceration and the serum antiproteases. II. Complexes of corneal collagenases and alpha-macroglobulins, Exp Eye Res 20:231–244, 1975.
224. Ollivier F, Brooks D, Kallberg M, et al: Evaluation of various compounds to inhibit activity of matrix metalloproteinases in the tear film of horses with ulcerative keratitis, Am J Vet Res 64:1081–1087, 2003.
225. D'Agostino P, Arcoleo F, Barbera C, et al: Tetracycline inhibits the nitric oxide synthase activity induced by endotoxin culture murine macrophages, Eur J Pharmacol 346:283–290, 1998.
226. Hanamaaijer R, Visser H, Koolwijk P, et al: Inhibition of MMP synthesis by doxycycline and chemically modified tetracyclines (CMTs) in human endothelial cells, Adv Dent Res 12:114–118, 1998.
227. Durson D, Kim M, Solomon A, et al: Treatment of recalcitrant recurrent corneal erosions with inhibitors of matrix metalloproteinase-9, doxycycline and corticosteroids, Am J Ophthalmol 132:8–13, 2001.
228. Hao J, Nagano T, Nakamura M, et al: Galardin inhibits collagen degradation by rabbit keratocytes by inhibiting the activation of pro-matrix metalloproteinases, Exp Eye Res 68:565–572, 1999.
229. Hodgson D, Jacobs K: Two cases of fusarium keratomycosis in the horse, Vet Rec 110:520–522, 1982.
230. Frauenfelder H, McIlwraith W: Heparin treatment of an equine corneal ulcer, Equine Vet J 12:88–89, 1980.
231. Ueda Y, Homma J, Abe C: Effects of immunization of horses with common antigen (OEP), protease toxoid, and elastase toxoid on corneal

ulceration due to *Pseudomonas aeruginosa*, Nippon Juigaku Zasshi 44, 1982.
232. Ueda Y, Sanai Y, Homma J: Therapeutic effect of intracorneal injection of immunoglobulins on corneal ulcers in horses experimentally infected with Pseudomonas aeruginosa, Nippon Juigaku Zasshi 44:301–308, 1982.
233. Baum J, Barza M: Topical vs subconjunctival treatment of bacterial corneal ulcers, Ophthalmology 90:162–168, 1983.
234. Matthews A: Ophthalmic antimicrobial therapy in the horse, Equine Vet Educ 21:271–280, 2009.
235. Galan A, Martin-Suarez E, Gallardo J, et al: Clinical findings and progression of 10 cases of equine ulcerative keratomycosis (2004–2007), Equine Vet Educ 21:236–242, 2009.
236. Coad C, Robinson N, Wilhelmus K: Antifungal sensitivity testing for equine keratomycosis, Am J Vet Res 46:676–678, 1985.
237. Grahn B: Equine keratomycosis: clinical and laboratory findings in 23 cases, Vet Comp Ophthalmol 3:2–7, 1993.
238. Mitchell J, Attleberg M: Fusarium keratomycosis in the horse, Vet Med Small Anim Clin 68:1257–1260, 1973.
239. Bistner S, Riis R: Clinical aspects of mycotic keratitis in the horse, Cornell Vet 69:364–372, 1979.
240. Kern T, Brooks D, White M: Equine keratomycosis: current concepts of diagnosis and therapy, Equine Vet J Suppl 2:22–38, 1983.
241. Gwin R: Equine fungal keratitis: diagnosis and treatment, Equine Vet Sci 1:66–68, 1981.
242. Beech J, Sweeney C: Keratomycoses in 11 horses, Equine Vet J (Suppl 2):39–44, 1983.
243. Friedman D, Schoster J, Pickett J, et al: *Pseudallescheria boydii* keratomycosis in a horse, J Am Vet Med Assoc 195:616–618, 1989.
244. Gaarder J, Rebhun W, Ball M, et al: Clinical appearances, healing patterns, risk factors, and outcomes of horses with fungal keratitis: 53 cases (1978–1996), J Am Vet Med Assoc 213:105–112, 1998.
245. Andrew S, Brooks D, Smith P, et al: Equine ulcerative keratomycosis: visual outcome and ocular survival in 39 cases (1987–1996), Equine Vet J 30:109–116, 1998.
246. Barton M: Equine keratomycosis, Compend Contin Educ Vet 14:936–944, 1992.
247. Brooks D, Andrew S, Dillavou C, et al: Antimicrobial susceptibility patterns of fungi isolated from horses with ulcerative keratomycosis, Am J Vet Res 59:138–142, 1998.
248. Ball M, Rebhun W, Gaarder J, et al: Evaluation of itraconazole-dimethyl sulfoxide ointment for treatment of keratomycosis in nine horses, J Am Vet Med Assoc 211:199–203, 1997.
249. Aho R, Tala M, Kivalo M: Mycotic keratitis in a horse caused by *Aspergillus fumigatus*, the first reported case in Finland, Acta Vet Scand 32:373–376, 1991.
250. Hendrix D, Ward D, Guglick M: Disseminated candidiasis in a neonatal foal with keratomycosis as the initial sign, Vet Comp Ophthalmol 7:10–13, 1997.
251. Hendrix D, Chmielewski N, Smith P, et al: Keratomycosis in four horses caused by *Cylindrocarpon destructans*, Vet Comp Ophthalmol 6:252–257, 1996.
252. Chopin J, Sigler L, Connole M, et al: Keratomycosis in a Percheron cross horse caused by *Cladorrhinum bulbillosum*, J Med Vet Mycol 35:53–55, 1997.
253. Foley J, Norris C, Jang S: Paecilomycosis in dogs and horses and a review of the literature, J Vet Intern Med 16:238–243, 2002.
254. Richter M, Hauser B, Kaps S, et al: Keratitis due to *Histoplasma* spp. in a horse, Vet Ophthalmol 6:99–103, 2003.
255. Welch P, Gabal M, Betts D, et al: In vitro analysis of antiangiogenic activity of fungi isolated from clinical cases of equine keratomycosis, Vet Ophthalmol 3:145–151, 2000.
256. Ledbetter E, Patten V, Scarlett J, et al: In vitro susceptibility patterns of fungi associated with keratomycosis in horses of the northeastern United States: 68 cases (1987–2006), J Am Vet Med Assoc 231:1086–1091, 2007.
257. Betbeze C, Wu C, Krohne S, et al: In vitro fungistatic and fungicidal activities of silver sulfadiazine and natamycin on pathogenic fungi isolated from horses with keratomycosis, Am J Vet Res 67:1788–1793, 2006.
258. Sansom J, Featherstone H, Barnett K: Keratomycosis in six horses in the United Kingdom, Vet Rec 156:13–17, 2005.
259. Brooks D, Andrew S, Denis H, et al: Rose bengal positive epithelial microerosions as a manifestation of equine keratomycosis, Vet Ophthalmol 3:83–86, 2000.
260. Hendrix D, Brooks D, Smith P, et al: Corneal stromal abscesses in the horse: a review of 24 cases, Equine Vet J 27:440–447, 1995.
261. Gaudio P, Gopinathan U, Sangwan V, et al: Polymerase chain reaction based detection of fungi in infected corneas, Br J Ophthalmol 86:755–760, 2002.
262. Ferrer C: Polymerase chain reaction diagnosis in fungal keratitis caused by *Alternaria alternate*, Am J Ophthalmol 133:398–399, 2002.
263. Rao N, Riggio D, Delmage J, et al: Adherence of *Candida* to corneal surface, Curr Eye Res 4:851–856, 1985.
264. Thomas P: Fungal infections of the cornea, Eye 17:852–862, 2003.
265. Thomas P: Current perspectives on ophthalmic mycoses, Clin Microbiol Rev 16:730–797, 2003.
266. Andrew S, Brooks D, Biros D, et al: Posterior lamellar keratoplasty for treatment of deep stromal abscesses in nine horses, Vet Ophthalmol 3:99–103, 2000.
267. Hamilton H, McLaughlin S, Whitley E, et al: Histological findings in corneal stromal abscesses of 11 horses: correlation with cultures and cytology, Equine Vet J 26:448–453, 1994.
268. Wilson F: Adverse external ocular effects of topical ophthalmic medications, Surv Ophthalmol 24:57–88, 1979.
269. Moore C, Heller N, Majors L, et al: Prevalence of ocular microorganisms in hospitalized and stabled horses, Am J Vet Res 49:773–777, 1988.
270. O'Day D: Influence of the corneal epithelium on the efficacy of topical antifungal agents, Invest Ophthalmol Vis Sci 25:855, 1984.
271. Mauger T, Craig E: Havener's ocular pharmacology, ed 9, St. Louis, Mo., 1994, C.V. Mosby.
272. O'Day D, Head W, Robinson R, et al: Corneal penetration of topical amphotericin B and natamycin, Curr Eye Res 5:877–882, 1986.
273. Scotty N, Brooks D, Rose C: In vitro efficacy of an ophthalmic drug combination against corneal pathogens of horses, Am J Vet Res 69:101–107, 2008.
274. Foster C, Lass J, Moran-Wallace K, et al: Ocular toxicity of topical antifungal agents, Arch Ophthalmol 99:1081–1084, 1981.
275. Clode A, Davis J, Salmon J, et al: Evaluation of concentration of voriconazole in aqueous humor after topical and oral administration in horses, Am J Vet Res 67:296–301, 2006.
276. Ball M, Rebhun W, Trepanier L, et al: Corneal concentrations and preliminary toxicological evaluation of an itraconazole/dimethyl sulphoxide ophthalmic ointment, J Vet Pharmacol Ther 20:100–104, 1997.
277. Davis J, Salmon J, Papich M: Pharmacokinetics and tissue distribution of itraconazole after oral and intravenous administration to horses, Am J Vet Res 66:1694–1701, 2005.
278. Latimer F, Colitz C, Campbell N, et al: Pharmacokinetics of fluconazole following intravenous and oral administration and body fluid concentrations of fluconazole following repeated oral dosing in horses, Am J Vet Res 62:1606–1611, 2001.
279. Colitz C, Latimer F, Cheng H, et al: Pharmacokinetics of voriconazole following intravenous and oral administration and body fluid concentrations of voriconazole following repeated oral administration in horses, Am J Vet Res 68:1115–1121, 2007.
280. Marangon F, Miller D, Giaconi J, et al: In vitro investigation of voriconazole susceptibility for keratitis and endophthalmitis fungal pathogens, Am J Ophthalmol 137:820–825, 2004.
281. Johnson E, Szekely A, Warnock D: In-vitro activity of voriconazole, itraconazole, and amphotericin B against filamentous fungi, J Antimicrob Chemother 42:741–745, 1998.
282. Sarro AD, Camera EL, Fera M: New and investigational triazole agents for the treatment of invasive fungal infections, J Chemother 20:661–671, 2008.
283. Page A, Liles W: Posaconazole: A new agent for the prevention and management of severe, refractory, or invasive fungal infections, Can J Infect Dis Med Microbiol 19:297–305, 2008.
284. Collins M, Ethell M, Hodgson D: Management of mycotic keratitis in a horse using a conjunctival pedicle graft, Australian Veterinary Journal 71:298–299, 1994.
285. Weinstein W, Moore P, Sanchez S, et al: In vitro efficacy of a buffered chelating solution as an antimicrobial potentiator for antifungal drugs against fungal pathogens obtained from horses with mycotic keratitis, Am J Vet Res 67:562–568, 2006.
286. Denis H: Equine corneal surgery and transplantation, Vet Clin North Am Equine Pract 20:361–380, 2004.
287. Alexander G, Chester Z: Use of free conjunctival grafts in horses: ten cases, Aust Vet J 82:204–208, 2004.
288. Bussieres M, Krohne S, Stiles J, et al: The use of porcine small intestinal submucosa for the repair of full-thickness corneal defects in dogs, cats and horses, Vet Ophthalmol 7:352–359, 2004.

289. Wilkie D, Whittaker C: Surgery of the cornea, Vet Clin North Am Small Anim Pract 27:1067–1107, 1997.
290. Plummer C, Kallberg M, Ollivier F, et al: Deep lamellar endothelial keratoplasty in 10 horses, Vet Ophthalmol 11:35–43, 2008.
291. Brooks D, Plummer C, Kallberg M, et al: Corneal transplantation for inflammatory keratopathies in the horse: visual outcome in 206 cases (1993–2007), Vet Ophthalmol 11:123–133, 2008.
292. Matthews A: Cornea. In: Barnett K, Crispin S, Lavach J, et al, editors: Equine Ophthalmology: An Atlas and Text, ed 2, Edinburgh, 2004, Saunders, pp 98–135.
293. Matthews A: Nonulcerative keratopathies in the horse, Equine Vet Educ 12:271–278, 2000.
294. Gilger B, Michau T, Salmon J: Immune-mediated keratitis in horses: 19 cases (1998–2004), Vet Ophthalmol 8:233–239, 2005.
295. Clark R: Anti-inflammatory functions of glucocorticoid-induced genes, Mol Cell Endocrinol 275:79–97, 2007.
296. Smoak K, Cidlowski J: Mechanisms of glucocorticoid receptor signalling during inflammation, Mech Ageing Dev 125:679–706, 2004.
297. Lowenberg M, Stahn C, Hommes D, et al: Novel insights into the mechanisms of glucocorticoid action and the development of new glucocorticoid receptor ligands, Steroids 73:1025–1029, 2008.
298. Zeyda M, Geyeregger R, Poglitsch M, et al: Impairment of T cell interactions with antigen-presenting cells by immunosuppressive drugs reveals involvement of calcineurin and NF-κβ in immunological synapse formation, J Leukoc Biol 81:319–327, 2007.
299. Chinenov Y, Rogatsky I: Glucocorticoids and the innate immune system: crosstalk with the toll-like receptor signalling network, Mol Cell Endocrinol 275:30–42, 2007.
300. Wekerie T: T-regulatory cells—what relationship with immunosuppressive agents? Transpl Proc 40:S13–S16, 2008.
301. Kim H-S, Luo L, Pflugfelder S, et al: Doxycycline inhibits TGF-β1 induced MMP-9 via SMAD and MAPK pathways in human corneal epithelial cells, Invest Ophthalmol Vis Sci 46:840–848, 2004.
302. Brooks D, Millichamp N, Peterson M, et al: Nonulcerative keratouveitis in five horses, J Am Vet Med Assoc 196:1985–1991, 1990.
303. Gratzek A, Kaswan R, Martin C, et al: Ophthalmic cyclosporine in equine keratitis and keratouveitis: 11 cases, Equine Vet J 27:327–333, 1995.
304. Wada S, Yoshinari M, Katayama Y, et al: Nonulcerative keratouveitis as a manifestation of leptospiral infection in a horse, Vet Ophthalmol 6:191–195, 2003.
305. Mondino B: Inflammatory diseases of the peripheral cornea, Ophthalmology 95:577–590, 1988.
306. Rebhun W: Corneal stromal abscesses in the horse, J Am Vet Med Assoc 181:677–679, 1982.
307. Vengayil S, Panda A, Satpathy G, et al: Polymerase chain reaction-guided diagnosis of mycotic keratitis: a prospective evaluation of its efficacy and limitations, Invest Ophthalmol Vis Sci 50:152–156, 2009.
308. Robert P, Adenis J: Comparative review of topical ophthalmic antibacterial preparations, Drugs 61:175–185, 2001.
309. Hendrix D, Stuffle J, Cox S: Pharmacokinetics of topically applied ciprofloxacin in equine tears, Vet Ophthalmol 10:344–347, 2007.
310. Andrew S: Corneal stromal abscess in a horse, Vet Ophthalmol 2:207–211, 1999.
311. Cello R: Ocular onchocerciasis in the horse, Equine Vet J 148–154, 1971.
312. Moran C, James E: Equine ocular pathology ascribed to *Onchocerca cervicalis* infection: a re-examination, Trop Med Parasitol 38:287–288, 1987.
313. Collobert C, Bernard N, Lamidey C: Prevalence of *Onchocerca* species and *Thelazia lacrimalis* in horses examined post mortem in Normandy, Vet Rec 136:463–465, 1995.
314. Lyons E, Drudge J, Tolliver S: Verification of ineffectual activity of ivermectin against adult *Onchocerca* spp. in the ligamentum nuchae of horses, Am J Vet Res 49:983–985, 1988.
315. Rebhun W: Corneal dystrophies and degenerations in horses, Comp Cont Ed Eq 14:945–949, 1992.
316. Millichamp N, Carter G, Dziezyc J: Idiopathic corneal edema in a horse, Equine Vet J (Supplement 10):12–14, 1990.
317. Ledbetter E, Munger R, Ring R, et al: Efficacy of two chondroitin sulfate ophthalmic solutions in the therapy of spontaneous chronic corneal epithelial defects and ulcerative keratitis associated with bullous keratopathy in dogs, Vet Ophthalmol 9:77–87, 2006.
318. Dice P, Severin G, Limb W: Experimental autogenous and homologous corneal transplantation in the dog, J Am Anim Hosp Assoc 9:265–269, 1973.
319. Keller W, Blanchard G, Kuhns E: The clinical application of homologous corneal and scleral grafts in the dog, J Am Anim Hosp Assoc 9:265–269, 1973.
320. Michau T, Gilger B, Maggio F, et al: Use of thermokeratoplasty for treatment of ulcerative keratitis and bullous keratopathy secondary to corneal endothelial disease in dogs: 13 cases (1994–2001), J Am Vet Med Assoc 222:607–612, 2003.
321. Spencer W: Cornea. In Spencer W, editor: Ophthalmic pathology: an atlas and textbook, ed 4, Philadelphia, 1996, W.B. Saunders, p 239.
322. O'Connor G: Calcific band keratopathy, Trans Am Ophthalmol Soc 70:58–81, 1972.
323. Taravella M, Stulting R, Mader T, et al: Calcific band keratopathy associated with the use of topical steroid-phosphate preparations, Arch Ophthalmol 112:608–613, 1994.
324. Lavach J, Severin G: Neoplasia of the equine eye, adnexa, and orbit: a review of 68 cases, J Am Vet Med Assoc 170:202–203, 1977.
325. Dugan S, Curtis C, Roberts S, et al: Epidemiologic study of ocular/adnexal squamous cell carcinoma in horses, J Am Vet Med Assoc 198:251–256, 1991.
326. Kafarnik C, Rawlings M, Dubielzig R: Corneal stromal invasive squamous cell carcinoma: a retrospective morphological description in 10 horses, Vet Ophthalmol 12:6–12, 2009.
327. King R, Priehs D, Gum G, et al: Therapeutic management of ocular squamous cell carcinoma in the horse: 43 cases (1979–1989), Equine Vet J 23:449–452, 1991.
328. Mosunic C, Moore P, Carmichael K, et al: Effects of treatment with and without adjuvant radiation therapy on recurrence of ocular and adnexal squamous cell carcinoma in horses: 157 cases (1985–2002), J Am Vet Med Assoc 225:1733–1738, 2004.
329. Walker M, Goble D, Geiser D: Two-year non-recurrence rates for equine ocular and periorbital squamous cell carcinoma following radiotherapy, Vet Radiol 27:146–148, 1986.
330. Smith K, Scase T, Miller J, et al: Expression of cyclooxygenase-2 by equine ocular and adnexal squamous cell carcinoma, Vet Ophthalmol 11:8–14, 2008.
331. Bosch G, Klein W: Superficial keratectomy and cryosurgery as therapy for limbal neoplasms in 13 horses, Vet Ophthalmol 8:241–246, 2005.
332. Schwink K: Factors influencing morbidity and outcome of equine ocular squamous cell carcinoma, Equine Vet J 19:198–200, 1987.
333. Rayner S, Zyl NV: The use of mitomycin C as an adjunctive treatment for equine ocular squamous cell carcinoma, Aust Vet J 84:43–46, 2006.
334. Rebhun W: Treatment of advanced squamous cell carcinomas involving the equine cornea, Vet Surg 19:297–302, 1990.
335. Schoster J: Using combined excision and cryotherapy to treat limbal squamous cell carcinoma, Vet Med 87:357–365, 1992.
336. English R, Nasisse M, Davidson M: Carbon dioxide laser ablation for treatment of limbal squamous cell carcinoma in horses, J Am Vet Med Assoc 196:439–442, 1990.
337. Monlux A, Anderson W, Davis C: The diagnosis of squamous cell carcinoma of the eye ('cancer eye') in cattle, Am J Vet Res 18:5–34, 1957.
338. Dugan S, Roberts S, Curtis C, et al: Prognostic factors and survival of horses with ocular/adnexal squamous cell carcinoma: 147 cases (1978–1988), J Am Vet Med Assoc 198:298–303, 1991.
339. Teifke J, Lohr C: Immunohistochemical detection of P53 overexpression in paraffin wax-embedded squamous cell carcinomas of cattle, horses, cats and cogs, J Comp Pathol 114:205–210, 1996.
340. Pazzie K, Kraegel S, Griffey S, et al: Analysis of the equine tumor suppressor gene p53 in the normal horse and in eight cutaneous squamous cell carcinoma, Cancer Lett 107:125–130, 1996.
341. Heeney J, Valli V: Bovine ocular squamous cell carcinoma: an epidemiological perspective, Can J Comp Med 49:21–26, 1985.
342. Rassnick K, Njaa B: Cyclooxygenase-2 immunoreactivity in equine ocular squamous-cell carcinoma, J Vet Diagn Invest 19:436–439, 2007.
343. Madewell B, Theilen G: Tumors of the skin and subcutaneous tissues. In Madewell B, Theilen G, editors: Veterinary cancer medicine, ed 2, Philadelphia, 1987, Lea & Febiger, pp 233–266.
344. Kagoura M, Toyoda M, Matsui C, et al: Immunohistochemical expression of cyclooxygenase-2 in skin cancer, J Cutan Pathol 28:298–302, 2001.
345. Almeida EPd, Piche C, Sirois J, et al: Expression of cyclo-oxygenase-2 in naturally occurring squamous cell carcinomas in dogs, J Histochem Cytochem 49:867–875, 2001.
346. Beam S, Rassnck K, Moore A: An immunohistochemical study of cyclooxygenase-2 expression in various feline neoplasms, Vet Pathol 40:496–500, 2003.

347. Knottenbelt C, Mellor D, Nixon C, et al: Cohort study of COX-1 and COX-2 expression in canine rectal and bladder tumours, J Small Anim Pract 47:196–200, 2006.
348. Mohammed S, Dhawan D, Abraham S, et al: Cyclooxygenase inhibitors in urinary bladder cancer: in vitro and in vivo effects, Mol Cancer Ther 5:329–336, 2006.
349. McInnis C, Giuliano E, Johnson P, et al: Immunohistochemical evaluation of cyclooxygenase expression in corneal squamous cell carcinoma in horses, Am J Vet Res 68:165–170, 2007.
350. Paterson S: Treatment of superficial ulcerative squamous cell carcinoma in three horses with topical 5-fluorouracil, Vet Rec 141:626–628, 1997.
351. Moore A, Beam S, Rassnick K, et al: Long-term control of mucocutaneous squamous cell carcinoma and metastases in a horse using piroxicam, Equine Vet J 35:715–718, 2003.
352. Woerdt Avd, Gilger B, Wilkie D: Penetrating keratoplasty for treatment of recurrent squamous cell carcinoma of the cornea in a horse, J Am Vet Med Assoc 208:1692–1694, 1996.
353. Grier R, Jr, Brewed WG, Jr, Paul S, et al: Treatment of bovine and equine ocular squamous cell carcinoma by radiofrequency hyperthermia, J Am Vet Med Assoc 177:55–61, 1980.
354. Ollivier F, Kallberg M, Plummer C, et al: Amniotic membrane transplantation for corneal surface reconstruction after excision of corneolimbal squamous cell carcinomas in nine horses, Vet Ophthalmol 9:404–413, 2006.
355. Merriam G: The effects of beta radiation on the eye, Radiology 66:240-244, 1956.
355a. Fraunfelder H, Blevins WE, Page HE: ^{90}Sr for treatment of periocular squamous cell carcinoma in the horse, Jour Am Vet Med Assoc 180:307–309, 1982.
356. Bolton J, Lees M, Robinson W, et al: Ocular neoplasms of vascular origin in the horse, Equine Vet J (Supplement 10):73–75, 1990.
357. Gelatt KN, Myers VS Jr, Perman V, et al: Conjunctival squamous cell carcinoma in the horse, Jour Am Vet Med Assoc 165(7):617–620, 1974.
358. Crawley G, Bryan G, Gogolewski R: Ocular hemangioma in a horse, Equine Pract 9:11–13, 1987.
359. Hacker D, Moore P, Buyukmihci N: Ocular angiosarcoma in four horses, J Am Vet Med Assoc 189:200–203, 1986.
360. Moore P, Hacker D, Buyukmihci N: Ocular angiosarcoma in the horse: morphological and immunohistochemical studies, Vet Pathol 23:240–244, 1986.
361. Vestre W, Turner T, Carlton W: Conjunctival hemangioma in a horse, J Am Vet Med Assoc 180:1481–1482, 1982.
362. Puff C, Herder V, Philipp A, et al: Lymphangiosarcoma in the nictitating membrane of a horse, J Vet Diagn Invest 20:108–110, 2008.
363. Hirst L, Jube D, Stoskopf M, et al: Benign epibulbar melanocytoma in a horse, J Am Vet Med Assoc 183:333–334, 1983.
364. McMullen R, Clode A, Pandiri A, et al: Epibulbar melanoma in a foal, Vet Ophthalmol 11:44–50, 2008.
365. Hamor R, Ramsey D, Wiedmeyer C, et al: Melanoma of the conjunctiva and cornea in a horse, Vet Comp Ophthalmol 7:52–55, 1997.
366. Valentine B: Equine melanocytic tumors: a retrospective study of 53 horses (1988–1991), J Vet Intern Med 9:291–297, 1995.
367. Kaskel P, Kind P, Sander S, et al: Trauma and melanoma formation: a true association? Br J Dermatol 143:749–753, 2000.
368. Donaldson D, Sansom J, Scase T, et al: Canine limbal melanoma: 30 cases (1992-2004). Part 1. Signalment, clinical and histological features and pedigree analysis, Vet Ophthalmol 9(2):115–119, 2006.
369. Goetz T, Ogilvie G, Keegan K, et al: Cimetidine for treatment of melanomas in three horses, J Amer Vet Med Assoc 196:449–452, 1990.
370. Ucar K: The effects of histamine H2 receptor antagonists on melanogenesis and cellular proliferation in melanoma cells in culture, Biochem Biophys Research Comm 177:545–550, 1991.
371. MacGillivray K, Sweeney R, Piero FD: Metastatic melanoma in horses, J Vet Intern Med 16:452–456, 2002.
372. Finocchiaro L, Riveros M, Glikin G: Cytokin-enhanced vaccine and suicide gene therapy as adjuvant treatments of metastatic melanoma in a horse, Vet Rec 164:278–279, 2009.
373. Blogg J, Durron A, Stanley R: Use of third eyelid grafts to repair full-thickness defects in the cornea and sclera, J Amer Animal Hosp Assoc 25:505–512, 1989.
374. Wilkie D, Wolf E: Treatment of epibulbar melanocytoma in a dog, using full-thickness eyewall resection and synthetic graft, J Amer Vet Med Assoc 198:1019–1022, 1991.
375. Martin C: Canine epibulbar melanomas and their management, J Amer Animal Hosp Assoc 17:83–90, 1981.
376. Kanai K, Kanemaki N, Matsuo S, et al: Excision of a feline limbal melanoma and use of nictitans cartilage to repair the resulting corneoscleral defect, Vet Ophthalmol 9(4):255–258, 2006.
377. Lewin G: Repair of a full-thickness corneoscleral defect in a German shepherd dog using porcine small intestinal submucosa, J Sm Animal Pract 40:340–342, 1999.
378. Harling D, Peiffer RL Jr, Cook C, et al: Feline limbal melanoma: four cases, J Amer Animal Hosp Assoc 22:795–802, 1986.
379. Sullivan T, Nasisse M, Davidson M, et al: Photocoagulation of limbal melanoma in dogs and cats: 15 cases (1989-1993), J Amer Vet Med Assoc 208:891–894, 1996.
380. Jakobiec F, Brownstein S, Wilkinson R, et al: Combined surgery and cryotherapy for diffuse malignant melanoma of the conjunctiva, Archives of Ophthalmology 98:1390–1396, 1980.
381. Donaldson D, Sansom J, Adams V: Canine limbal melanoma: 30 cases (1992-2004). Part 2. Treatment with lamellar resection and adjunctive strontium-90β plesiotherapy – efficacy and morbidity, Vet Ophthalmol 9:179–185, 2006.
382. Wilcock B: Neoplastic diseases of the skin. In Jubb K, Kennedy P, Palmer N, editors: Pathology of domestic animals, Orlando, FL, 1985, Academic Press, pp 519–520.
383. Martin C, Leipold H: Mastocytoma of the globe in a horse, J Am Anim Hosp Assoc 8:32–34, 1972.
384. Bosch G, Klein W. Superficial keratectomy and cryosurgery as therapy for limbal neoplasms in 13 horses, Vet Ophthalmol 8(4):241–246, 2005.
385. Ward D, Lakritz J, Bauer R: Scleral mastocytosis in a horse, Equine Vet J 25:79–80, 1993.
386. Hum S, Bowers J: Ocular mastocytosis in a horse, Aust Vet J 66:32, 1989.
387. Prasse K, Lundvall R, Cheville N: Generalized mastocytosis in a foal, resembling urticaria pigmentosa of man, J Am Vet Med Assoc 166:68–70, 1975.
388. Rebhun W, Piero FD: Ocular lesions in horses with lymphosarcoma: 21 cases (1977–1997), J Am Vet Med Assoc 212:852–854, 1998.
389. Germann S, Richter M, Schwarzwald C, et al: Ocular and multicentric lymphoma in a young racehorse, Vet Ophthalmol 11:51–56, 2008.
390. Woerdt Avd, Gilger B, Wilkie D: Penetrating keratoplasty for treatment of recurrent squamous cell carcinoma of the cornea in a horse, J Amer Vet Med Assoc 208(10):1692–1694, 1996.
391. Riedl M, Maca S, Amon M, et al: Intraocular ointment after small-incision cataract surgery causing chronic uveitis and secondary glaucoma, J Cataract Refract Surg 29:1022–1025, 2003.
392. Gelatt K, Gelatt J: Handbook of small animal ophthalmic surgery, New York, 1994, Pergamon.
393. Whittaker C, Smith P, Brooks D: Therapeutic penetrating keratoplasty for deep corneal stromal abscesses in eight horses, Vet Comp Ophthalmol 7:19–28, 1997.

Chapter 6

Diseases of the Uvea

Steven R. Hollingsworth

With the exception of uveitis and neoplasia, abnormalities of the equine uveal tract are relatively uncommon and often of minimal consequence to vision or comfort. However, some innocuous conditions can mimic serious disease, so proper assessment is important to prevent misinterpretation and inappropriate clinical action. This chapter will discuss diseases of the equine uvea, with the exception of equine recurrent uveitis (ERU), which is covered specifically in Chapter 8.

CLINICAL ANATOMY AND PHYSIOLOGY

The uveal tract is comprised of three components: the iris, ciliary body, and choroid and is anatomically similar to that of other species in most clinically relevant aspects. As in most herbivores, the adult equine pupil is horizontally oval. The anterior surface of the iris is without a contiguous epithelial layer and is composed of connective tissue interspersed with fibroblasts and melanocytes. Beneath this surface layer is the iris stroma, which consists of chromatophores, fibroblasts, and collagen fibers that cradle a plexus of blood vessels. Within the central stroma and circumferentially oriented along the pupillary margin is the parasympathetically innervated iris sphincter muscle. Immediately posterior to the iris stroma is the iris dilator muscle, which is radially oriented and sympathetically innervated. The posterior aspect of the iris is lined with a double layer of densely melanotic epithelial cells (Fig. 6-1). The dorsal aspect of the pupillary margin is capped with a cystic extension of the posterior epithelium, the corpora nigra (or granula iridica) (Fig. 6-2).

The ciliary body is posterior to the base of the iris and is approximately triangular in cross-section. As viewed from the vitreous cavity, the ciliary body is divided into the anteriorly positioned pars plicata and the posteriorly positioned pars plana. As the name suggests, the pars plicata is characterized by a folded or pleated appearance, although the number, prominence, and shape of the ciliary processes vary among species. In general, species with large anterior chambers, such as horses, have more processes than those with small anterior chambers. Carnivores' ciliary processes tend to be long and thin, whereas those of herbivores, including the horse, resemble blunted ridges.[1] From the ciliary processes, zonular fibers extend and connect to the equatorial region of the lens. The pars plana is a relatively smooth, flat portion that extends from the pars plicata to the most peripheral extension of the retina (the ora ciliaris retinae). The width of the pars plana varies and is widest dorsolaterally.[2] The entire inner surface of the ciliary body (the surface in contact with the vitreous body) is lined with a double row of epithelial cells. The innermost epithelial cell layer (from the perspective of the vitreous cavity) is nonpigmented and referred to as the nonpigmented epithelium (NPE) of the ciliary body. The NPE is confluent at the ora ciliaris retinae with the sensory retina, and at the posterior base of the iris with the innermost layer of the posterior iris epithelium. The second epithelial cell layer is heavily melanotic and is referred to as the pigmented epithelium of the ciliary body. The pigmented epithelium lies immediately under the NPE and is contiguous with the retinal epithelium at the ora ciliaris retinae and at the posterior base of the iris with the outermost layer of the posterior iris epithelium. Tight junctions between NPE cells are thought to represent the epithelial portion of the blood-aqueous barrier.[3] Deep to the two-layer ciliary body epithelium, each ciliary process has a central portion of connective tissue and a vascular plexus which is fenestrated, allowing leakage of plasma into the ciliary body stroma (Fig. 6-3). The epithelial portion of the blood-aqueous barrier filters this plasma, removing virtually all protein and cells. Thus the aqueous humor represents an ultrafiltrate of plasma. In addition to this filtration function, the NPE contains carbonic anhydrase, which catalyzes the active transport–mediated portion of aqueous humor production (Fig. 6-4).[1] Beneath the ciliary processes, lying on the internal surface of the sclera and forming the base of the ciliary body triangle, is the ciliary body musculature. Virtually all mammals have circumferentially oriented, parasympathetically innervated, smooth ciliary body muscles. When these

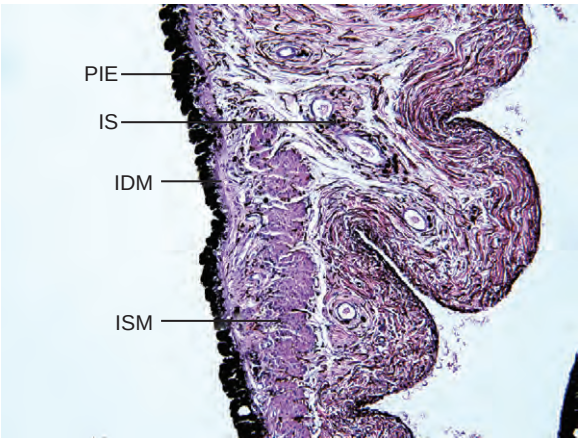


Figure 6-1. Photomicrograph of normal equine iris. *IDM*, Iris dilator muscle; *IS*, iris stroma; *ISM*, iris sphincter muscle; *PIE*, posterior iris epithelium (×4).

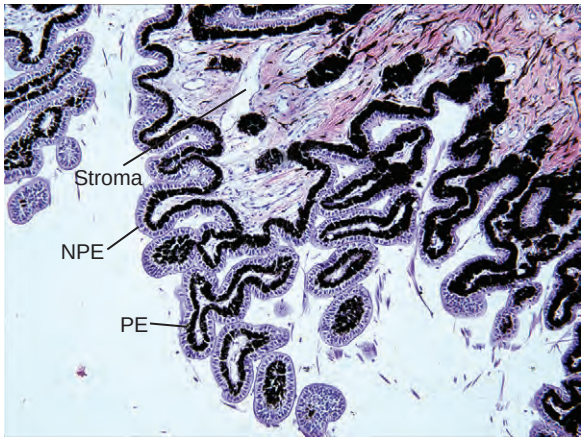


Figure 6-3. Photomicrograph of normal equine ciliary body. *NPE*, Nonpigmented ciliary body epithelium; *PE*, pigmented ciliary body epithelium (×4).

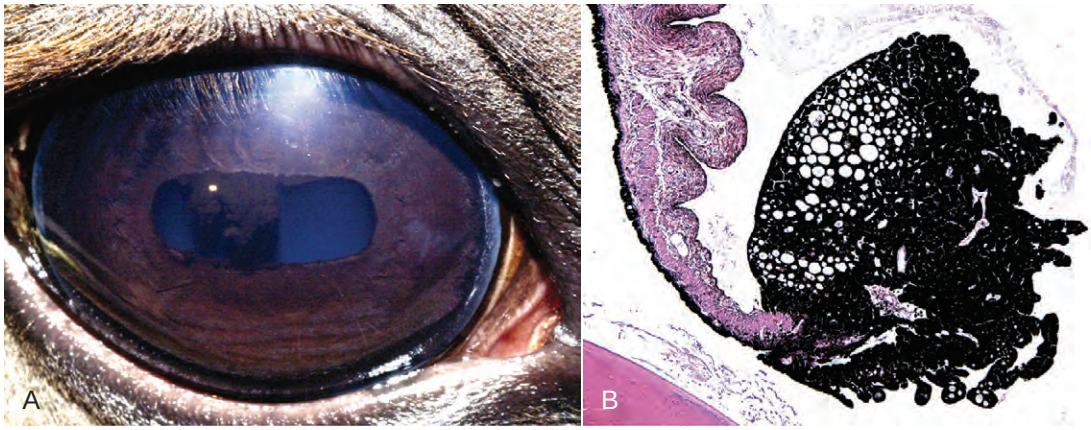
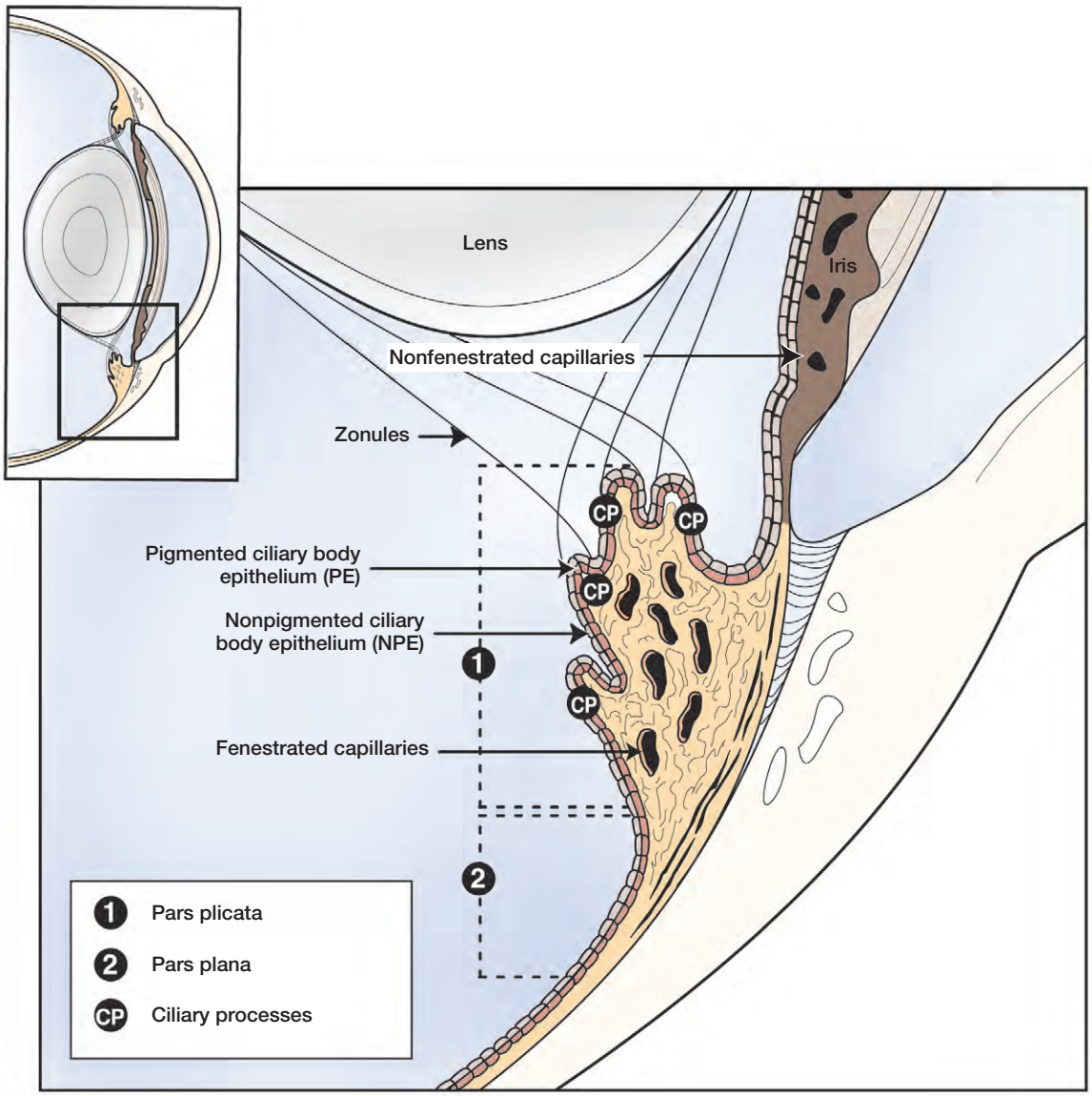


Figure 6-2. **A,** Clinical photograph of the normal equine eye with normal large dorsal corpora nigra. **B,** Photomicrograph of normal equine corpora nigra as a cystic extension of the posterior iris epithelium (×2).

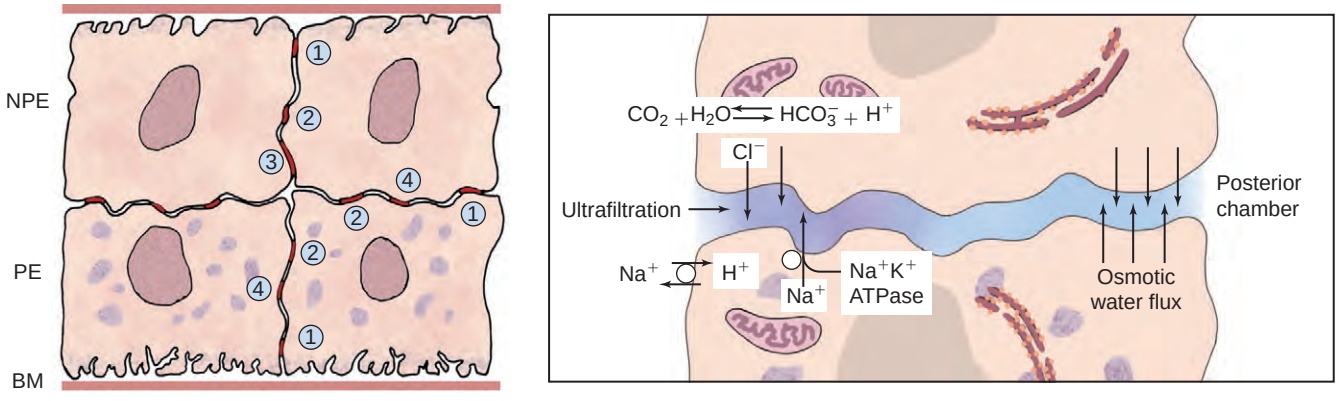
muscles are contracted, the zonular fibers are relaxed, which in turn allows the lens to passively thicken. This mechanism is responsible for accommodation in mammals. However, most nonprimate mammals have poorly developed ciliary body musculature and therefore poor accommodative ability.

Anterior to the ciliary body musculature and visible at the juncture of the base of the anterior face of the iris and the limbus is the ciliary cleft. Spanning the opening of this cleft are strands of connective tissue called *pectinate ligaments*, which extend from the base of the iris to insert on the inner aspect of the limbus. The ciliary cleft is posterior to the pectinate ligaments and filled with a spongelike network of connective tissue beams, the trabecular meshwork. In the horse, these beams are completely lined with endothelial cells called *trabecular cells*.[1] The ciliary cleft is the location of aqueous humor outflow. Any process that interferes with normal outflow can lead to increased intraocular pressure (see the discussion of equine glaucoma in Chapter 9).

The *choroid* is the posterior component of the uveal layer and has two main components. Covering the inner surface of the sclera is a thick plexus of vessels embedded in densely melanotic connective tissue that radiate out from the area of the optic disc. Most of these vessels are veins that unite to form the vortex veins near the equator. View of the choroidal vessels is usually obscured ventrally by melanin in the retinal epithelium and dorsally by the tapetum, but may be seen in lightly pigmented individuals (Fig. 6-5).[4-6] The tapetum occupies roughly the dorsal half of the fundus and is located immediately interior to the choroidal vasculature. The tapetum varies in color but is usually blue-green to yellow, and is often associated with iris and coat color. While cellular in carnivores, the tapetum in herbivores is made up of highly organized collagenous fibers. In the tapetal area, capillaries from the choroidal arteries run through the tapetal fibers to provide nutrition to the retina. When viewed end-on ophthalmoscopically, these vessels appear as multiple small dots throughout the tapetal area and are called the *stars of Winslow* (Fig. 6-6). Because the horse has a paurangiotic retinal vascular pattern, the choroid is responsible for supplying nutrition to the entire retina, with the exception of the peripapillar area.



A



B

Figure 6-4. **A,** Ciliary body anatomy. **B,** Note the tight junctions between the lateral borders of the nonpigmented ciliary body epithelium (NPE), which represents the epithelial portion of the blood-aqueous barrier. Note the active transport of sodium and bicarbonate ions (by the action of the enzyme carbonic anhydrase), which contributes to the production of aqueous. These enzyme systems are located in the lateral wall of the ciliary body NPE.

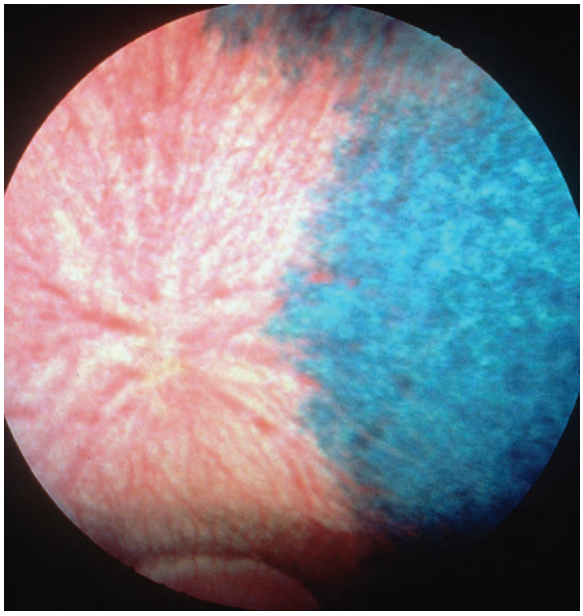


Figure 6-5. Note geographic absence of tapetum dorsal to optic disc, allowing for visualization of the choroidal vasculature and vortex vein area.

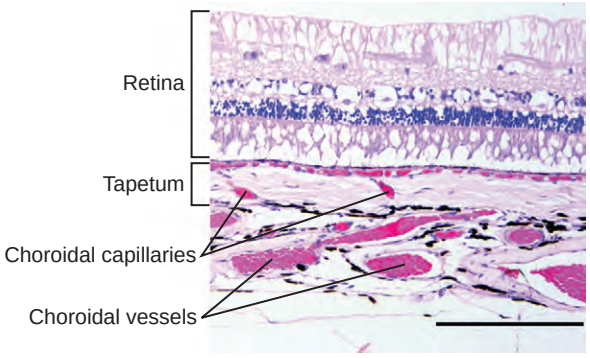


Figure 6-6. Photomicrograph of normal equine choroid (bar = 200 µm; ×100). (Photomicrograph courtesy Dr. Christopher M. Reilly.)

IMPACT OF UVEAL DISEASE ON THE EQUINE INDUSTRY

Complications associated with equine recurrent uveitis are the number-one cause of blindness in horses worldwide, with annual costs in the United States estimated up to $1 billion.[7] The conditions covered in this chapter occur infrequently and sporadically and have little impact on the equine industry from a strictly financial perspective. The importance of veterinarians correctly understanding and managing these diseases is related to the well-being of the individual patient.

CONGENITAL DISEASES

ANIRIDIA

Although the term *aniridia* implies complete absence of an iris, it has been applied to a clinical condition reported in horses in which only a rudimentary, nonfunctional ridge of iridal tissue is present (Fig. 6-7). Aniridia was first reported in 1955 in a Belgian Draft stallion and 65 of his offspring who were similarly affected.[8] The author concluded that aniridia was a heritable defect passed via an autosomal-dominant mode. Subsequently, aniridia was described in a Quarter Horse stallion.[9] In an ensuing study, eight offspring of that stallion were followed, and seven demonstrated aniridia.[10] The authors concluded the mode of inheritance was similar to that of the Belgian draft stallion. Since then, aniridia has been observed sporadically, being specifically reported in a Thoroughbred colt[11] and a Welsh/Thoroughbred cross filly.[12]

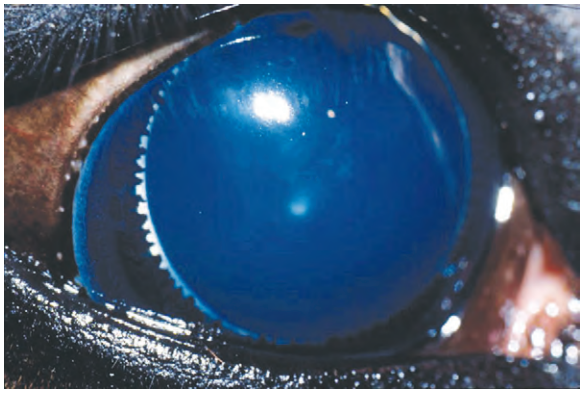


Figure 6-7. Aniridia in a horse. Notice the ciliary body processes and edge of the lens, which are not visible in normal horses. (Photograph courtesy Dr. Michelle Willis.)

Horses affected with aniridia are usually presented within the first few months of age because the client has noticed such signs as an unusual appearance of both eyes, excessive squinting in bright sunlight, and/or overreacting to flashes of light. On ophthalmic examination, the pupils are widely dilated and nonresponsive. The extent of the pupillary dilation is so marked that the lens equator and ciliary body processes are visible. The corpora nigra is absent. Virtually every reported case of aniridia has been accompanied by what is described as corneal vascularization and nodular changes along the dorsal and sometimes the ventral aspect of the limbus.[9-12] When affected globes have been available for histopathologic examination, fine hairs have been found growing from the corneal nodules. These have been identified as dermoids. Cataractous changes are also a frequent accompanying sign with aniridia. The cataracts are usually focal and found in the anterior cortex. They are sometimes present at the time of initial examination but may not arise until later and tend to be slowly progressive. Persistent pupillary membrane (PPM) was reported in one patient.[12] Findings on posterior segment examinations in horses with aniridia have been uniformly unremarkable.

The diagnosis of aniridia is straightforward and based on clinical signs alone (see Fig. 6-7). No treatment is available. Many horses with aniridia have performed well in racing or other activities.[11,12]

ANTERIOR SEGMENT DYSGENESIS/ PERSISTENT PUPILLARY MEMBRANE

The term *anterior segment dysgenesis* is used to describe several syndromes with different clinical presentations. Ophthalmic structures potentially affected by anterior segment dys-

genesis include the cornea, iridocorneal angle, iris, ciliary body, lens, and retina, as well as the globe itself as manifested by microphthalmos or buphthalmos.[13-16] The severity of signs associated with anterior segment dysgenesis varies greatly. Because most of the structures of the anterior segment are derived from the neural crest, alterations in the differentiation and migration of this layer lead to the signs associated with anterior segment dysgenesis.[15] Specific reported malformations involving the anterior uvea include miosis, iris hypoplasia, iris and ciliary body cysts, and persistent pupillary membranes (PPMs). Of these, the most common clinical manifestation of anterior segment dysgenesis in domestic species, including the horse, is PPMs.[15] During embryonic development, a vascular plexus called the *pupillary membrane* covers the anterior surface of the iris and the pupillary aperture. This membrane rarifies near the end of gestation, but remnants can often be found in neonatal foals.[16,17] When such strands persist into adulthood, they are called *PPMs*. In adult horses, it is not uncommon to find small PPMs that originate from the collarette region of the iris and extend a few millimeters. Usually these strands terminate either as a free end in the aqueous or attach to the anterior surface of the iris (Fig. 6-8). Occasionally, PPMs attach to the anterior lens capsule or posterior surface of the cornea. In such instances, opacification is usually seen where the PPMs attach. Such opacities would be present from birth. However, in most equine patients, the distal ends of the PPMs are free floating or attached to adjacent iris. In such instances, no secondary signs are found. In a recent study, the histopathologic changes of apparent PPMs extending from the iris to the posterior surface of the cornea in a 9-week-old Springer spaniel puppy were examined.[18] The area of attachment to the posterior cornea was characterized by disruption of Descemet's membrane and the corneal endothelium. These findings are identical to a developmental disease in humans referred to as *Peters anomaly*. The authors suggested that this condition should be differentiated from PPMs, which terminate by attaching to adjacent iris or as free floating in the aqueous.

The diagnosis of PPMs is made on the basis of clinical appearance. In horses, opacities associated with PPMs rarely cause significant visual deficits, and treatment is not usually indicated.

ANTERIOR UVEAL CYSTS

The cysts discussed here may not be congenital but are included in this section because they have been noted in horses of many different ages, including young horses, and may be present as very small cysts at birth, only to enlarge and become apparent later in life. Anterior uveal cysts may be found in four locations: (1) the corpora nigra, (2) along the margin of the pupil or free floating in the anterior chamber, (3) attached to the ciliary body, and (4) within the iris stroma.

The corpora nigra normally protrudes from the dorsal aspect and to a lesser degree the ventral aspect of the pupillary margin. It is a vacuolated extension of the posterior iris epithelium. Because many horses that have cystic corpora nigra are middle aged or older, it is believed that the condition is not congenital. The cause (or causes) of cystic corpora nigra is not known, but it does not seem to be related to past or present intraocular inflammation.[19]

When the corpora nigra becomes cystic, its normally roughened appearance becomes smooth and spherical (Fig. 6-9). The condition may be unilateral or bilateral, and the size of the cysts can vary markedly. Most are sufficiently small that they do not cause significant interference with vision. However, depending on the specific location, even moderate-sized cysts can partially inhibit the visual field, especially when the horse is in bright light and the pupil is miotic. For this reason, horses with cystic corpora nigra should be initially evaluated without pharmacologic dilation and under conditions of bright illumination so the extent of pupillary aperture blockage can be accurately assessed.

Differential diagnoses include inflammatory or neoplastic changes to the iris in the area of the corpora nigra. Although ultrasonography could be used to differentiate cystic corpora nigra from inflammatory or neoplastic infiltrates, this is rarely necessary because the clinical appearance is usually sufficiently characteristic.

Although treatment is not ordinarily necessary, the most effective and noninvasive treatment is deflation of the cystic corpora nigra with a laser. In a series of eight horses with signs including loss of vision, being startled when approached from the affected side, head shaking, and poor jumping performance, treatment with an ophthalmic neodymium-yttrium aluminum garnet (Nd:YAG) laser was effective in resolving the vision

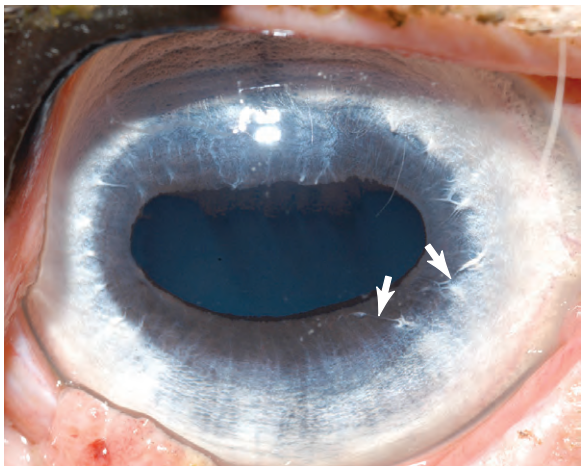


Figure 6-8. Persistent pupillary membranes *(arrows)* in adult horse.

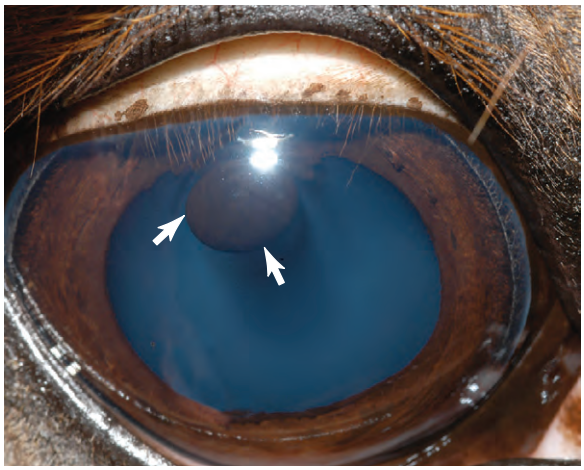


Figure 6-9. Cystic corpora nigra *(arrows)*.

problems in all horses.[19] This procedure does not require general anesthesia; only sedation and an auriculopalpebral nerve block are needed. After surgery, some horses required a short course of topical antiinflammatory and mydriatic medication, but most of the horses were comfortable without treatment. An 810-nm diode laser delivered through an indirect ophthalmoscope headset has also been used successfully to shrink cysts in dogs, cats, and horses.[20]

Iridal cysts may be found distinctly separate from the corpora nigra along the margin of the pupil or free floating in the anterior chamber. These cysts are believed to develop in a manner similar to iridal cysts in dogs and represent a failure of the two layers of neuroectoderm to completely fuse, thus allowing fluid to accumulate in areas between the two-layered posterior iris epithelium. Because iridal cysts can enlarge, it has been theorized that some of the posterior iridal epithelial cells that compose the lining of the cyst retain secretory ability.[21]

The clinical appearance of these cysts is spherical to oval and smooth. Although they can occasionally be transilluminated, most appear opaque (Fig. 6-10). Sometimes the cysts will spontaneously rupture and leave a circular area of pigmentation on the anterior lens capsule or the posterior surface of the cornea.

As with cysts of the corpora nigra, these must be differentiated from inflammatory or neoplastic masses, but this is rarely a problem because of the characteristic clinical appearance. Treatment is not commonly indicated because these iridal cysts seldom cause pain or visual impairment. Should removal be deemed necessary, they can be deflated with an Nd:YAG laser as described for cysts of the corpora nigra (Fig. 6-11).[19] Alternatively, a 25- to 27-gauge needle attached to a tuberculin syringe can be introduced into the anterior chamber at the limbus. The needle is used to perforate the cyst wall while gentle pressure from the syringe collapses the cyst.[21] This procedure is invasive and requires postoperative treatment with topical antiinflammatory and mydriatic medications for the resultant uveitis.

Ciliary body cysts are believed to originate in a manner similar to that of iridal cysts, except in this instance, the failure of the two layers of the neuroectoderm to fuse is in the area of the ciliary body, so these cyst walls are made up of NPE (Fig. 6-12).[13,22] Other potential causes of ciliary body cysts include inflammatory processes, traction from zonules, anterior segment dysgenesis, and age.

Because the walls of these cysts are usually lined with NPE, they can be transilluminated. They tend to be oval and relatively large, often extending from the pars plicata to the ora ciliaris retinae (Fig. 6-13). Their most common location is ventrolaterally, and they can be difficult to detect without pharmacologic mydriasis.[13,22]

Figure 6-10. Iris cyst along pupillary margin. (Photograph courtesy Dr. David J. Maggs.)

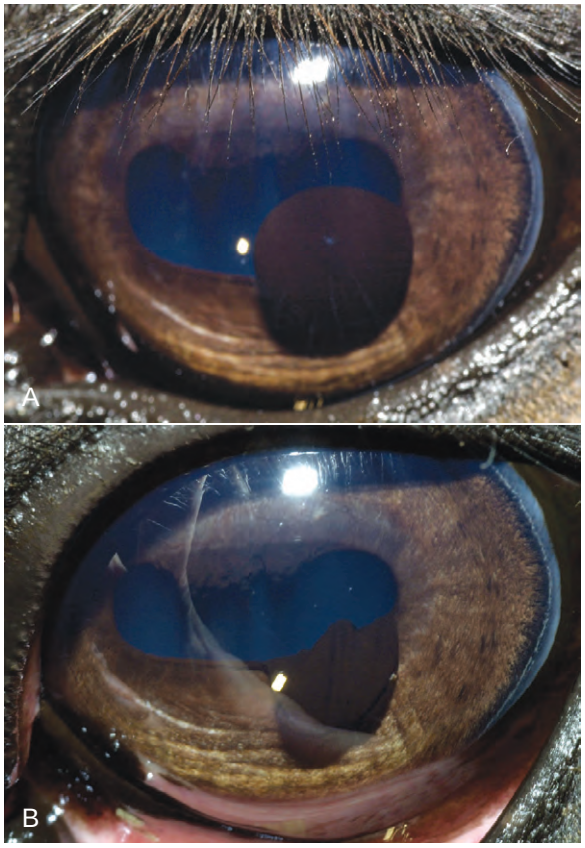


Figure 6-11. A, Iris cyst in lower leaf of the iris immediately before application of an ophthalmic neodymium-yttrium aluminum garnet (Nd:YAG) laser. **B,** Iris cyst in lower leaf of the iris immediately after application of an ophthalmic Nd:YAG laser, demonstrating deflation of the cyst. (Photograph courtesy Dr. Brian Gilger.)

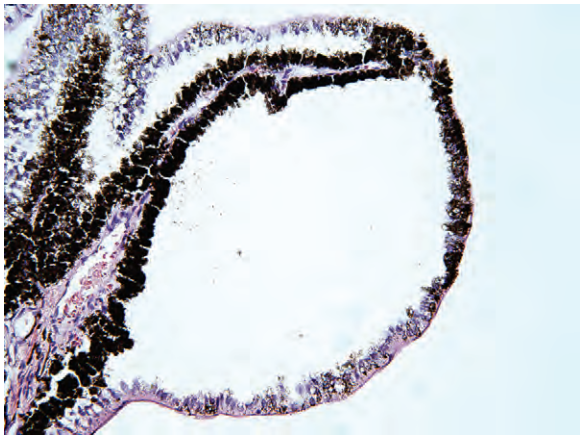


Figure 6-12. Photomicrograph of ciliary body cyst (×10).

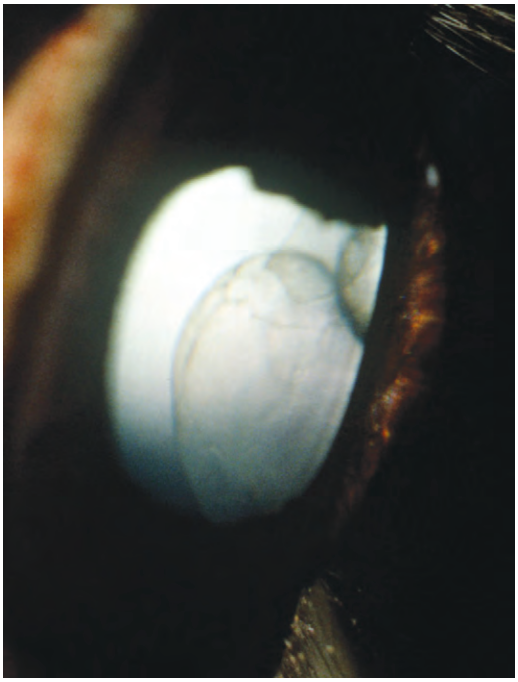


Figure 6-13. Ciliary body cyst visible through pupil.

As with the other anterior uveal cysts discussed, differential diagnoses include inflammatory and neoplastic disease. Although ocular ultrasonography can be used to confirm the diagnosis of ciliary body cyst, the shape, contour, and ability to transilluminate make this differentiation straightforward on the basis of clinical signs alone. These cysts do not routinely cause pain or visual impairment, and treatment is not necessary.

Cysts found within the iris stroma itself are probably not true cysts but represent thin, hypoplastic areas that bulge forward as a result of aqueous pressure differences. This condition is covered in the following section.

IRIS HYPOPLASIA

Historically, dark and bulging areas in the anterior surface of the iris have been interpreted as cysts within the iris stroma.[23] These dark, bulging areas are seen predominately in the dorsal region of eyes with blue irides, although they can be present in the ventral aspect of the iris and in eyes with brown irides. However, in one study, 15 horses with such lesions were examined, and histopathologic examination of lesions was performed for one horse with unilateral signs. The authors of that study concluded that these lesions represent areas of iridal stromal hypoplasia, and that the resulting protrusion was the result of aqueous pressure pushing the relatively weaker portion of iris forward.[24]

The classic clinical picture of iris hypoplasia is a dark area, usually within the dorsal portion of the iris, that bulges forward (Figs. 6-14 and 6-15). Most of these eyes have blue irides, and the condition can be unilateral or bilateral. Age, breed, and sex predispositions do not seem to exist.[24] The affected eyes are not painful, and there is no discernable effect on vision. The dark, bulging areas are most evident when examined in bright light with the pupil miotic. The fact that these protruding areas actually represent thinning of the iris stroma is confirmed by passing a bright, focal beam of light through the pupil and observing the retroillumination of the fundic reflection through the lesion. When the pupil is subsequently dilated, either by the use of mydriatic agents or dark adaptation, the bulging area disappears, taking on a wrinkled appearance.

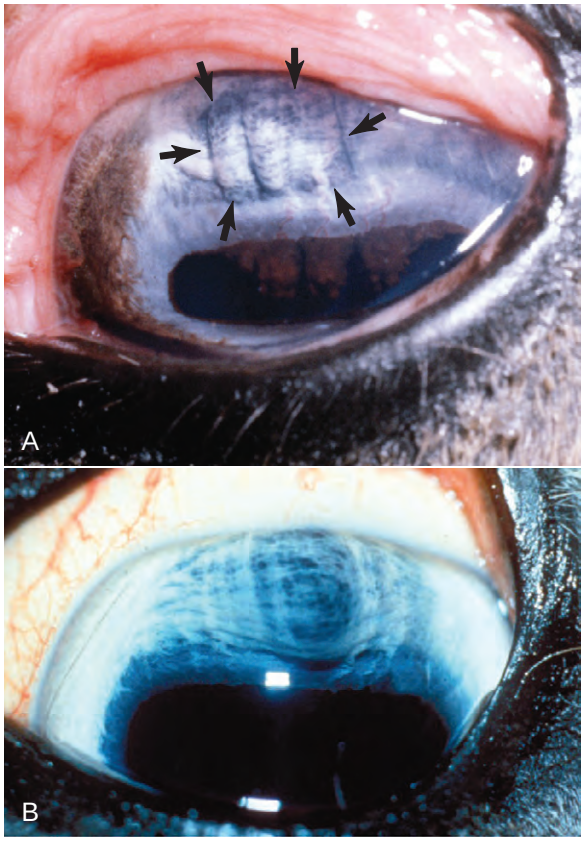


Figure 6-14. **A,** Area of iris hypoplasia *(outlined by arrows)*. **B,** Iris hypoplasia in a pony. (**B,** Courtesy Dr. Mike Davidson.)

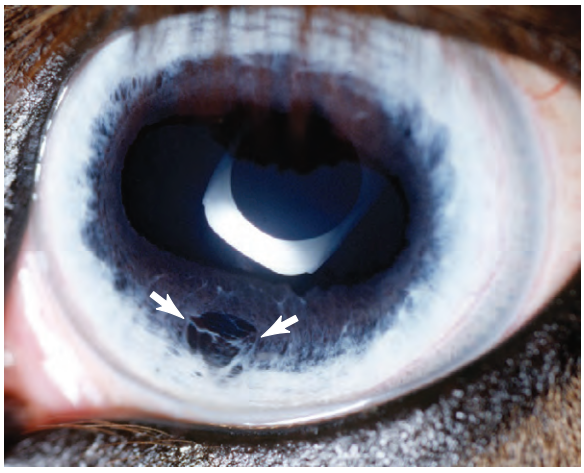


Figure 6-15. Iris hypoplasia with bulging dark area *(between arrows)*.

The most important condition to be ruled out for this clinical presentation is iridal neoplasia, specifically melanoma. Ocular ultrasonography can assist in making this differentiation, but careful examination under conditions of both miosis and mydri-

asis, as described previously, should allow for an accurate diagnosis. It is highly unlikely that a neoplasm or inflammatory cell accumulation would allow for retroillumination of the fundic reflection or would "deflate" under conditions of pupillary dilation. However, should there be confusion after careful ophthalmic examination, ocular ultrasonography would be indicated. Iris hypoplasia does not cause pain or vision impairment, and treatment is not indicated. Unfortunately, there are anecdotal reports suggesting that eyes demonstrating iridal hypoplasia have been removed because the presence of iridal melanoma was suspected.[24]

MEDULLOEPITHELIOMA

Medulloepithelioma of the anterior uvea is infrequently reported in the horse.[25-28] These tumors arise from undifferentiated medullary epithelial cells that line the inner portion of the embryonic optic cup.[25,29] Normally, these cells differentiate into numerous epithelial cell lines in the adult eye, including the posterior iris epithelium, the ciliary body NPE, and the retinal epithelium. In individuals with this tumor, a portion of these cells fail to differentiate. In the horse, medulloepitheliomas most frequently arise from the ciliary body region. On histologic examination, medulloepitheliomas usually demonstrate nonpigmented neuroepithelial cells arranged in tubules and rosettes. They are classified as either teratoid[25] or nonteratoid,[26,27] depending on whether the neoplastic cell population is characterized by relatively homogeneous, undifferentiated primitive neuroepithelium or contains tissues not normally found in the eye, such as cartilage, muscle, and brain tissue.[30]

Medulloepitheliomas are most frequently diagnosed in young adult horses presented because of a fleshy mass noted within the pupil[27] or anterior chamber.[26] Although these tumors are thought to grow slowly, they may be associated with other ophthalmic changes if they have been allowed to become large before presentation. Such changes would include corneal vascularization, corneal edema, corneal fibrosis, anterior uveitis, glaucoma, and buphthalmos (Fig. 6-16).[25]

Differential diagnoses include other intraocular neoplasms, such as melanoma, and cystic changes of the iris or ciliary body. The clinical characteristics of anterior uveal cysts have been described previously. Confirmation that an intraocular mass is solid tissue (as opposed to a cystic structure) and delineation of the specific location of the mass can be readily accomplished with ocular ultrasonography. Distinction between medulloepithelioma and intraocular melanoma is possible on the basis of clinical appearance. Melanomas are usually darkly pigmented and arise from the anterior surface of the iris, whereas medulloepitheliomas are most often fleshy masses apparent within the pupil. Although it is usually not necessary for determining appropriate clinical action, biopsy of a ciliary body medulloepithelioma has been described.[27]

Intraocular medulloepitheliomas are thought to grow slowly, with metastasis being a rare and late event. Extension into the orbit has been described in one horse.[28] The treatment of choice is enucleation or exenteration if there is evidence that scleral integrity has been compromised.

The choroid may be involved with developmental conditions often manifesting as colobomatous lesions of all three fundic layers. These are discussed in Chapter 10, Diseases of the Ocular Posterior Segment.

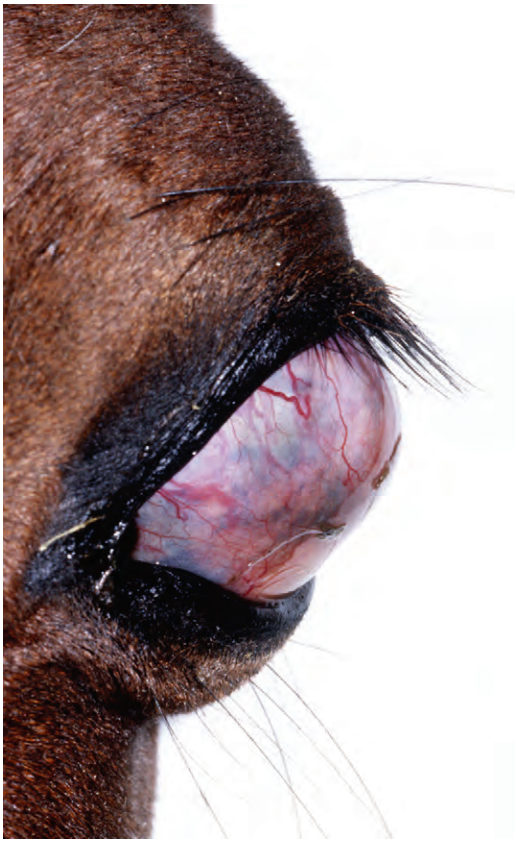


Figure 6-16. Medulloepithelioma causing corneal vascularization, corneal fibrosis, and buphthalmos and completely filling intraocular space. (Photograph courtesy Dr. Carol M. Szymanski.)

ACQUIRED DISEASES

ANTERIOR UVEITIS

Anterior uveitis and its associated complications are the most common causes of blindness in horses worldwide. The prevalence of some manifestation of uveitis in the United States has been estimated to be between 8% and 25%.[7,31] Although acute anterior uveitis must be distinguished from the chronic, recurrent form (ERU), the two conditions share many clinical signs. As the name suggests, ERU is characterized by multiple, recurrent episodes of uveitis, whereas acute uveitis is limited to a single event. Although young adult Draft breeds and Appaloosas are overrepresented in the group of horses with ERU, there is no age, breed, or sex predisposition for acute anterior uveitis. Please see Chapter 8 for more information on the diagnosis and treatment of ERU.

Typical clinical signs associated with acute anterior uveitis are all due to damage of the anterior uvea and subsequent compromise of the blood-aqueous barrier. Box 6-1 summarizes these signs (Figs. 6-17, 6-18, and 6-19). The initial diagnosis of anterior uveitis is based on clinical signs. Because there is an almost endless list of potential causes of anterior uveitis (Box 6-2),[7,17,31-35] a number of laboratory tests have been proposed to augment the complete ophthalmic and physical examination and help determine the underlying cause of a specific episode of acute anterior uveitis (see discussion of systemic diseases in Chapter 13).[17,31] These would include complete

Box 6-1 | Signs Associated With Acute Anterior Uveitis

- Blepharospasm
- Epiphora
- Conjunctival hyperemia
- Episcleral injection
- Diffuse corneal edema
- Corneal vascularization
- Keratic precipitates
- Aqueous flare
- Fibrin clots in anterior chamber
- Hypopyon
- Hyphema
- Change in iris color
- Rubeosis iridis
- Miosis
- Inflammatory deposits on posterior lens capsule
- Hazy appearance to the anterior vitreous

Box 6-2 | Potential Causes of Acute Uveitis

Infectious

- *Leptospira* spp.
- *Brucella* spp.
- *Streptococcus* spp.
- *Escherichia coli*
- *Rhodococcus equi*
- Equine influenza virus
- Equine herpesvirus 1 (EHV-1)
- Equine viral arteritis
- Equine infectious anemia virus
- *Onchocerca* spp.
- *Toxoplasma gondii*
- *Strongylus* spp.
- Corneal disease
- Tooth root abscesses
- Hoof abscesses

Noninfectious

- Idiopathic
- Blunt or penetrating trauma
- Neoplasia
- Phacoclastic

blood count, serum chemistry profiles, serologic tests for specific infectious causes such as leptospirosis, and conjunctival biopsies for detection of *Onchocerca* microfilaria (Fig. 6-20). Although tests for specific infectious agents can assist in ascertaining the underlying cause, the results must be interpreted with caution because horses without uveitis can often have positive test results for many of these agents (see Fig. 6-20).[17]

The common denominator of all the proposed causes of anterior uveitis is damage to the uveal tract. This leads to the release of the mediators of inflammation such as prostaglandins, leukotrienes, and histamines.[21,36] Although the specific roles of the different mediators are still unclear and may vary between species, the overall effects of their release are iris

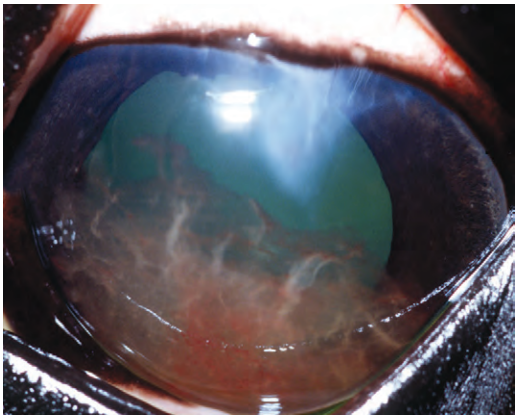


Figure 6-17. Acute episode of anterior uveitis with fibrin clot in anterior chamber. (Photograph courtesy Dr. David J. Maggs.)

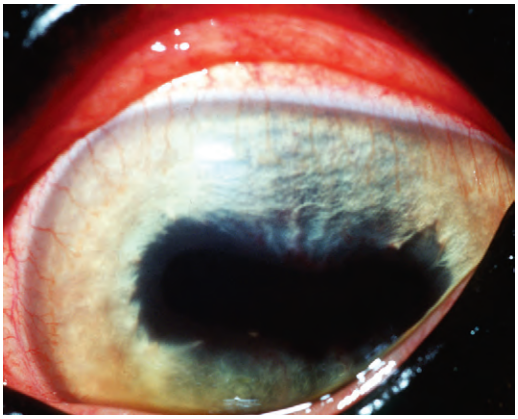


Figure 6-18. Acute episode of anterior uveitis. Note episcleral injection, corneal vascularization, hazy aqueous, and miosis. (Photograph courtesy Dr. David J. Maggs.)

Figure 6-19. Torn corpora nigra caused by blunt trauma. (Photograph courtesy Dr. David J. Maggs.)

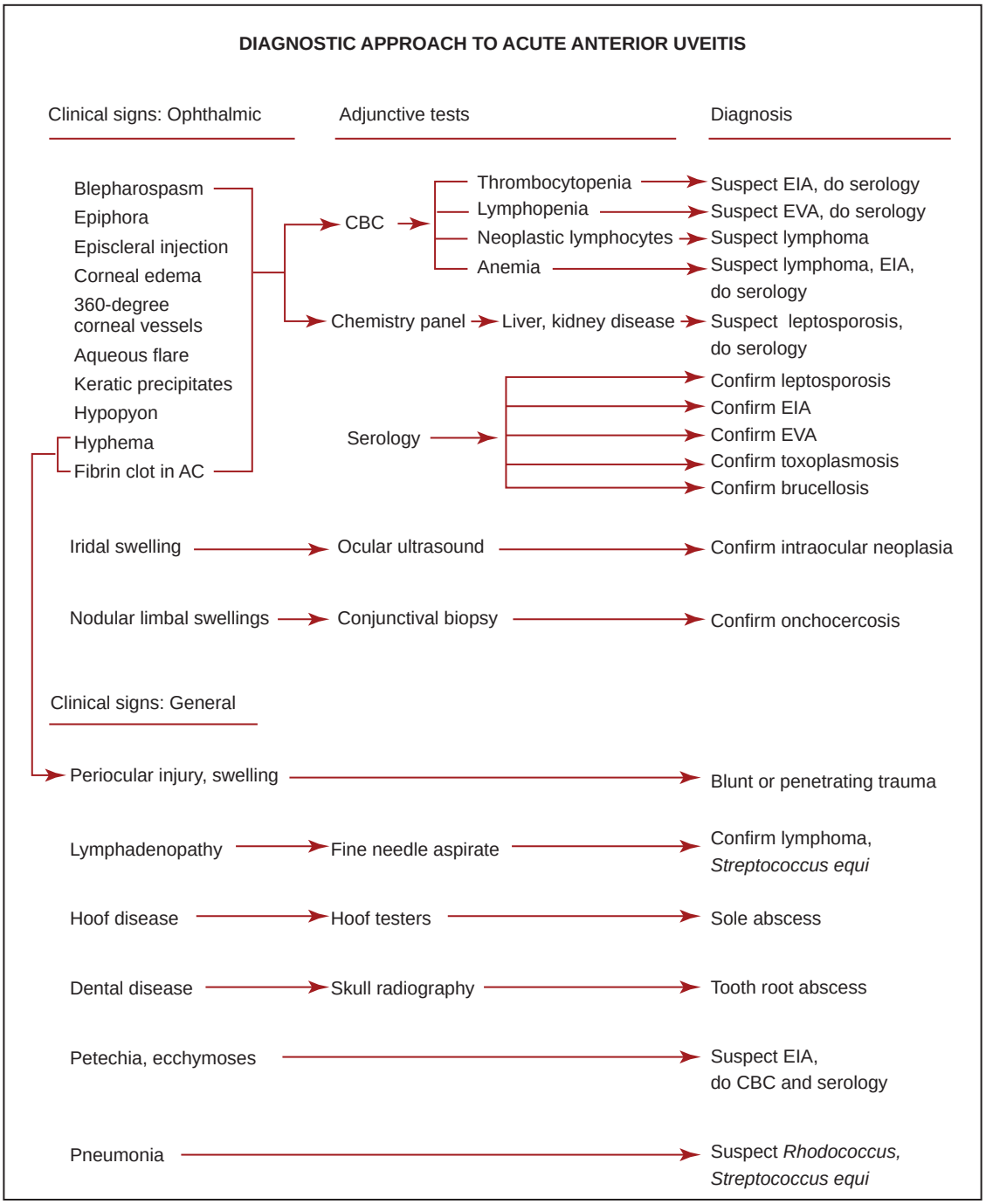


Figure 6-20. Algorithm for the diagnosis of acute uveitis in the horse.

sphincter muscle spasm, ciliary body muscle spasm, increased vascular permeability, and the breakdown of the blood-aqueous barrier. This is followed by leakage of protein, fibrin, and potentially cells into the aqueous, which accounts for the clinical signs most commonly associated with acute anterior uveitis: blepharospasm, epiphora, aqueous flare, fibrin clots in the anterior chamber, and miosis.

If a specific underlying cause can be identified, treatment centers on addressing that cause. Concomitant with treatment of the cause, or if no specific cause is found, the eye is treated symptomatically to reduce pain and minimize the intraocular damage associated with anterior uveitis. A list of common therapeutic agents with rationales for use, usual dosage, and precautions can be found in Table 6-1.[7,17] The initial therapeutic approach for an acute episode of anterior uveitis is aggressive treatment in an attempt to rapidly counteract the inflammation. As the signs of acute uveitis begin to lessen, the frequency of medication can be slowly reduced. However, complete cessation of treatment is not advised until all clinical signs have resolved for at least 1 month. Most horses that are presented with acute uveitis initially respond well to symptomatic treatment. The long-term prognosis can often be problematic because recurrence is common

Table 6-1 | **Medical Therapy for Uveal Diseases**

TOPICAL MEDICATIONS	FREQUENCY	MODE OF ACTION	ADVERSE EFFECTS
Prednisolone acetate, 1%	q1h-bid	Powerful antiinflammatory with excellent penetration	Can compromise ocular surface immunity
Dexamethasone, 0.1%	q1h-bid	Powerful antiinflammatory with excellent penetration	Can compromise ocular surface immunity
Flurbiprofen, 0.03%	q1h-bid	Nonsteroidal with good penetration	May prolong corneal ulcer healing
Diclofenac, 0.1%	q1h-bid	Nonsteroidal with good penetration	May prolong corneal ulcer healing
Cyclosporine A, 0.2%-2%	q1h-bid	Immunosuppressive but poor penetration	
Atropine, 1%	q6h-q48h	Relieves ciliary muscle spasm, provides pain relief, decreases synechia	May decrease gut motility
SYSTEMIC MEDICATIONS	**DOSE**	**MODE OF ACTION**	**ADVERSE EFFECTS**
Flunixin meglumine	0.6 mg/kg IV, IM, PO initially, then 0.26 mg/kg PO	Powerful antiinflammatory	Long-term use can lead to gastric and renal problems
Phenylbutazone	4.4 mg/kg IV or PO q24h, or 1g IV or 1 g PO bid	Antiinflammatory	Long-term use can lead to gastric and renal problems
Aspirin	Mature horses: 2 to 4 240-grain boluses PO or 10-26 mg/kg PO q24h-bid	Antiinflammatory	Long-term use can lead to gastric problems
Dexamethasone	6-10 mg/day PO or 2.6-6 mg IM q24h	Powerful antiinflammatory	Laminitis, must use with caution
Prednisolone	100-300 mg/day IM, PO	Powerful antiinflammatory	Laminitis, must use with caution
Triamcinolone	1-2 mg subconjunctival	Powerful antiinflammatory, 7-10 days' duration of action	Can compromise ocular surface immunity

From References 4 and 14.
bid, Twice a day; *h*, hour; *IM*, intramuscularly; *IV*, intravenously; *PO*, orally; *q*, every.

and each inflammatory episode causes further intraocular damage. Long-term adverse sequelae for uveitis include corneal scarring, cataract formation, glaucoma, and retinal degeneration.

MELANOMA

Although melanoma is relatively rare in horses and is certainly less common than in the dog, the literature contains numerous case reports of equine intraocular melanoma.[37-44] A review of these cases reveals some interesting trends. In older gray horses, cutaneous melanoma is a common finding. Most reported intraocular melanoma cases also occurred in gray or partially gray horses, but most of the horses were young adults, between 5 and 10 years of age. Only one of these horses also had skin lesions, which were described as "inguinal nodules." These nodules were not removed and did not change during the 6-month period during which the horse was followed up and therefore cannot be assumed to be melanomas.[43] Although none of the reported cases documented metastasis, and the neoplasms were generally not judged to be malignant on histopathologic examination, rapid growth within the eye was common. One patient may have had a primary intraocular uveal melanoma extend through the cornea, but the originating tissue of that neoplasm could not be determined.[44] The most common site of origin was the iris, but melanomas arising from the ciliary body were also reported.

The initial clinical appearance of anterior uveal melanomas differs according to whether the ciliary body or the iris is the tissue of origin, how rapidly the neoplasm is growing, and the length of time before a medical evaluation is sought. When a horse with melanoma is presented early in the course of the disease, common clinical signs include focal corneal edema with a dark mass filling the anterior chamber, which is often in contact with the posterior surface of the cornea (Figs. 6-21 and 6-22). Depending on the location and extent of the mass, dyscoria may be present. It should be noted that melanomas in horses with lightly pigmented irises will often appear pink and fleshy (Fig. 6-23).[42] The rest of the cornea in these patients is usually clear, and there is no aqueous flare. Evidence of pain is usually absent. As the neoplasm gets larger, common clinical signs include blindness, blepharospasm, epiphora, buphthalmos, diffuse corneal edema, aqueous flare, and anterior chamber

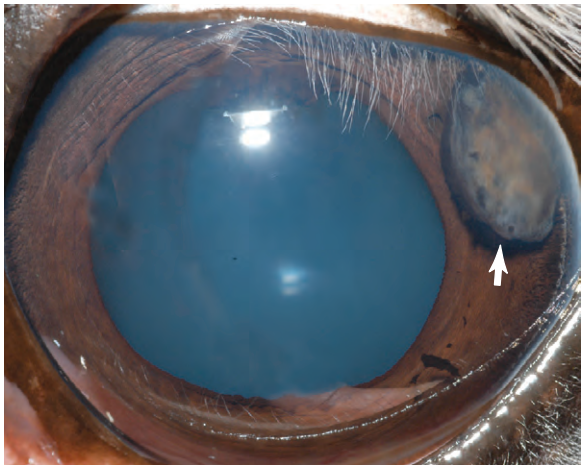


Figure 6-21. Intraocular melanoma *(arrow)* arising from anterior surface of iris, filling the anterior chamber, and in contact with the posterior surface of the cornea.

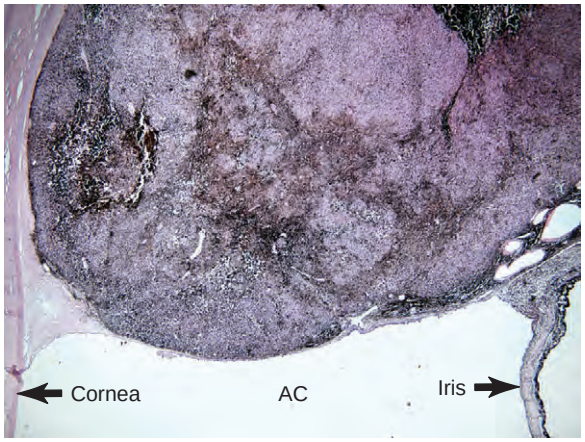


Figure 6-22. Photomicrograph of intraocular melanoma arising from anterior surface of iris, filling the anterior chamber, and in contact with the posterior surface of the cornea (×2).

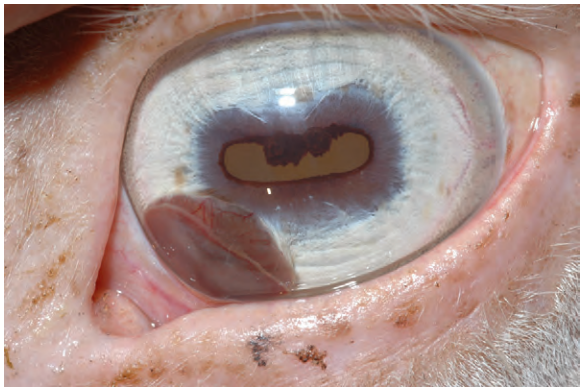


Figure 6-23. Intraocular melanoma in a lightly pigmented horse arising from the anterior face of the iris, filling the anterior chamber, and in contact with the posterior surface of the cornea. (Photograph courtesy Dr. Nicole Scotty Trumble.)

masses that often obliterate any normal architecture and prevent visualization of deeper structures. When structures deep to the iris can be seen, the lens is usually cataractous. If the tissue of origin is the ciliary body, a dark mass may be seen on the posterior surface of the lens, extending into the vitreous cavity.[40]

Differential diagnoses for a mass in the anterior chamber include uveal cyst, iris hypoplasia, or extension of a mass from the posterior segment (Fig. 6-24).[24,38,45] This determination is usually not difficult to make. Cysts of the ciliary body, iris, and corpora nigra are all smooth and oval to spherical. Additionally, cysts can occasionally be transilluminated. This clinical presentation would be contrasted to that of melanoma, which most frequently appears as an irregularly shaped mass arising from the anterior aspect of the iris and filling most if not all of the anterior chamber. On those occasions when there is doubt on the basis of clinical presentation, ocular ultrasonography can be used to differentiate cystic structures from solid masses.[37] As discussed previously, horses with iris hypoplasia usually have either completely blue irides or exhibit heterochromic irides. Although the bulging forward of dark tissue characteristic of iris hypoplasia can mimic a melanoma, a number of characteristics allow for differentiation between the two conditions. These include ability to transilluminate, deflation of the bulging area with mydriasis, and absence of significant enlargement over time.[24] In the case of the tumor extension from the posterior segment, careful examination will reveal a large mass present in the vitreous cavity, making primary intraocular melanoma less likely.[45]

The pathogenesis of melanoma has been debated for years in both human and veterinary medicine.[46-48] Although differences exist in regard to intraocular melanoma among species, many believe that melanomas in general arise from preexisting nevi.[37,40,49] This theory is based in part on the fact that histopathologic examination of anterior uveal melanomas commonly reveals two cell types: (1) plump, spherical cells with abundant melanin granules and (2) smaller, pleomorphic, spindle-shaped cells, which may have a relatively higher nucleus-to-

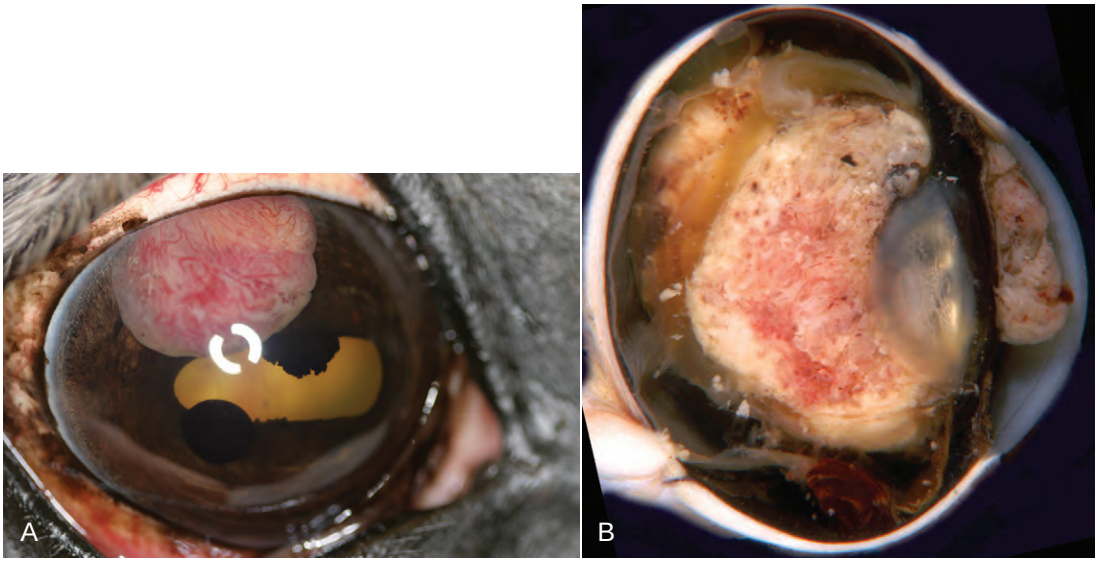


Figure 6-24. **A,** Fleshy mass apparently originating from the iris. **B,** Gross histopathologic section demonstrating anterior chamber mass to be an extension of a neoplasm arising from the posterior segment. (Photograph courtesy Dr. Derek C. Knottenbelt.)

cytoplasm ratio (Fig. 6-25).[37,39,41] Mitotic figures are rare. One theory is that the plump, spherical cells represent a melanocytoma or nevus, which is the precursor of the melanoma portion of the mass represented by the spindle-shaped cells.[37,40,49]

In human medicine, a number of factors have been considered in determining the most appropriate treatment modality for intraocular melanoma. Considerations include whether excision or enucleation is the most efficacious therapy and whether enucleation promotes metastasis.[50-52] Among equine patients, sector iridectomy has been successful in the treatment of intraocular melanoma (Fig. 6-26).[41,42] In one report, a diode laser was used to treat 23 dogs with isolated masses believed to represent iridal melanoma.[53] The results of that study were encouraging in that the dogs were able to maintain comfortable, visual eyes as long as 4 years after treatment. Surgical Nd:YAG laser treatment of uveal melanomas in equine eyes has caused shrinkage of the masses (B. Gilger, personal communication); however, corneal edema and secondary uveitis are common adverse effects of laser therapy (Fig. 6-27). Oral cimetidine (dose 2.5 mg/kg body weight, administered orally [PO] every 8 hours) has been used to shrink nonocular melanomas in horses, but no studies have been done to determine the effect of cimetidine on uveal masses.[54] Generally, intraocular melanoma in horses has been treated by enucleation or exenteration. Success with these procedures has been high, and metastasis has not been reported.[37,40,43,44]

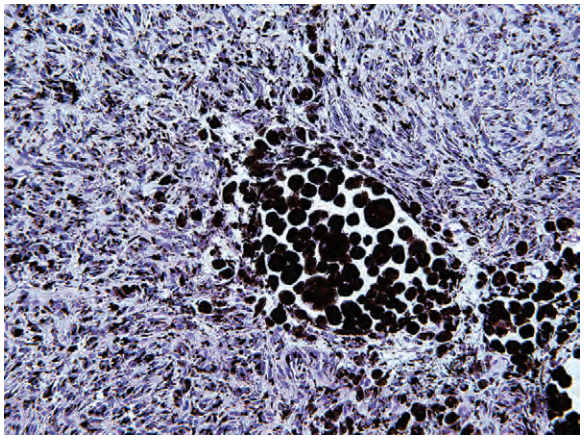


Figure 6-25. Photomicrograph of intraocular melanoma. Note central area of plump, spherical, highly melanotic cells surrounded by pleomorphic, spindle-shaped cells (×10).

LYMPHOMA

Lymphoma is the most common systemic neoplastic disease with an ocular manifestation in the horse.[55,56] Ocular manifestation of lymphoma has been documented in many species, but the specific ophthalmic structure most commonly affected varies among species. In cattle, exophthalmos caused by orbital masses is the most common ocular manifestation of lymphoma,[57] whereas in dogs and cats with systemic lymphoma, anterior uveal involvement is the most common ocular sign.[58,59] In one study of 79 horses with confirmed systemic lymphoma, 21 had ocular lesions. In these horses, eyelid swelling and inflammation were the most common ocular signs (11/21), with anterior uveal involvement being the next most common sign (4/21).[60]

The signs associated with anterior uveal manifestation of systemic lymphoma are nonspecific and include blepharospasm, episcleral injection, corneal edema and vascularization, aqueous flare, hypopyon, hyphema, iridal congestion, and swelling. Frequently these nonspecific signs are accompanied by a history of chronicity and poor response to antiinflammatory medication. In addition, the ophthalmic signs are usually accompanied by nonspecific signs of systemic disease such as fever, respiratory disorders, weight loss, peripheral lymphadenopathy, and anemia.[61,62]

Intraocular lymphoma cannot usually be differentiated from other potential causes of anterior uveitis on the basis of ocular signs alone (see Box 6-2). The diagnosis of systemic lymphoma should be considered in any horse with anterior uveitis, especially when it is accompanied by systemic signs of illness such as fever, weight loss, lethargy, and swollen lymph nodes. The diagnosis of lymphoma can be confirmed by identification of neoplastic lymphocytes from samples of solid tissues such as the spleen, lymph nodes, or skin nodules or by centesis of affected body cavities (thoracic or abdominal). In spite of this, diagnosis can be challenging, and confirmation occurs in less than 60% of cases.[55]

The pathogenesis of systemic equine lymphoma remains obscure. There are currently no known risk factors. Most affected horses are young adults between 4 and 10 years of age. No breed or sex predisposition has been demonstrated.[55]

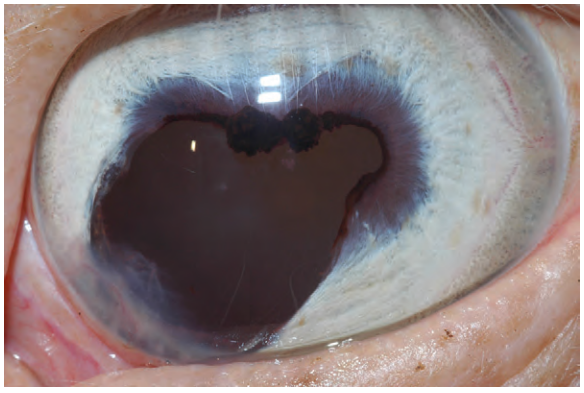


Figure 6-26. Four months after sector iridectomy on patient in Fig. 6-23. (Photograph courtesy Dr. Nicole Scotty Trumble.)

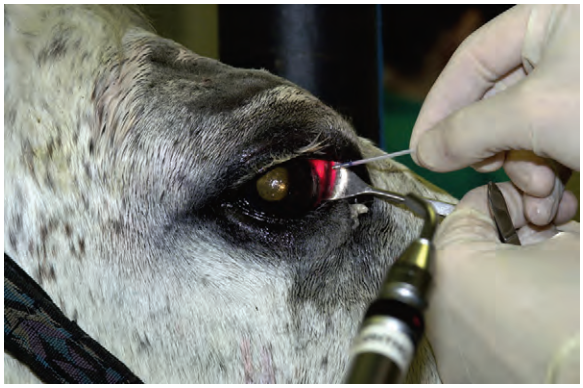


Figure 6-27. Surgical neodymium-yttrium aluminum garnet (Nd:YAG) laser treatment of uveal melanomas in an equine eye. (Photograph courtesy Dr. Brian Gilger.)

The systemic treatment of lymphoma is outlined in equine medicine texts.[55] In general, success rates have been low for systemic lymphoma. The ocular portion of the treatment regimen would be the same as that previously described for anterior uveitis.

Inflammation of the choroid is most frequently seen associated with ERU or systemic disease (see Chapters 8 and 13).

FUTURE RESEARCH

Many of the conditions described in this chapter are classified as developmental with a suspected heritable element. Although in the last 10 years significant advances have been made in the elucidation of the genetic details of canine heritable eye diseases, the same cannot be said for ophthalmic conditions with a suspected heritable component in horses. There are at least a couple of reasons for this. First, test matings in horses are more difficult than in dogs because of the longer gestation period and much smaller progeny number. Second, the suspected inherited ocular diseases in horses are frequently not blinding (especially those involving the uveal tract), so the motivation to eliminate these conditions is not as great as it is for dogs.

Another area in which great improvements have been made over the last 10 years is the use of imaging techniques in the diagnosis of ocular disease. Specifically, ocular ultrasonography has become increasingly useful in the diagnosis of intraocular conditions. Of particular benefit is the development of high-resolution, high-frequency probes that allow for ever-increasing detail in the evaluation of intraocular structures, particularly anterior uveal structures. The use of infrared digital photography has been recently reported for examining the anterior uvea. Conversion of a standard digital camera to one that is sensitive to infrared light is relatively inexpensive and straightforward and enhances the ability to examine the iris through a diseased and opacified cornea (Fig. 6-28).[63] As the detail and resolution of imaging techniques continue to improve, diagnoses can be made earlier, allowing for intervention sooner in the course of disease.

As noted earlier, medical laser technology has become a valuable addition to the treatment options for eye disease. In the future, it is anticipated that lasers will be even better at targeting specific diseased intraocular tissues and sparing adjacent normal tissue.

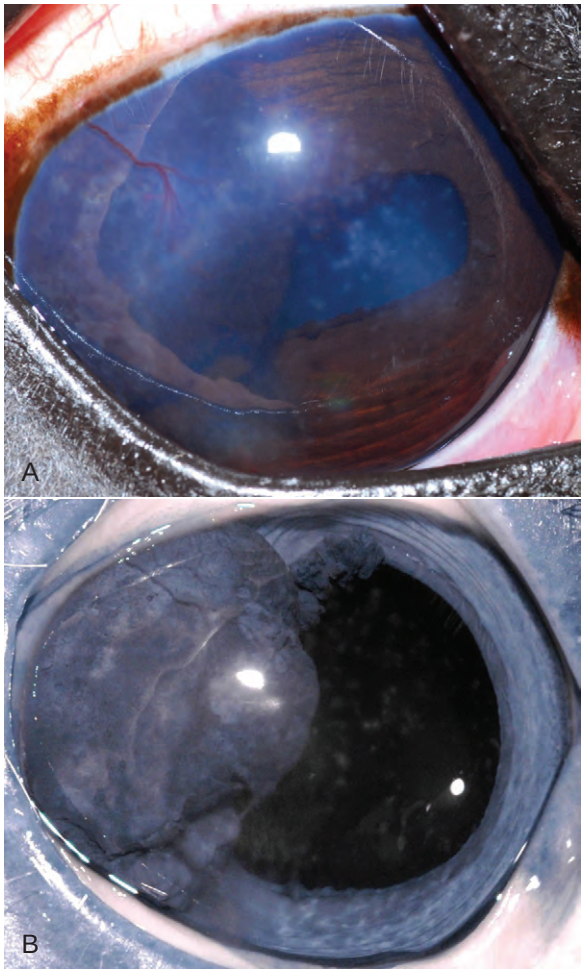


Figure 6-28. **A,** Iris melanoma detail partially obscured by corneal vascularization and fibrosis as seen with normal photography. **B,** Iris melanoma detail enhanced by the use of infrared digital imaging. (Photographs courtesy Dr. Richard J. McMullen, Jr.)

References

1. Samuelson DA: Ophthalmic anatomy. In Gelatt KN, editor: Veterinary ophthalmology, ed 4, Ames, IA, 2007, Blackwell Publishing, pp 37–148.
2. Miller TL, et al: Description of ciliary body anatomy and identification of sites for transscleral cyclophotocoagulation in the equine eye, Vet Ophthalmol 4:183–190, 2001.
3. Gum GG, Gelatt KN, Esson DW: Physiology of the eye. In Gelatt KN, editor: Veterinary ophthalmology, ed 4, Ames, IA, 2007, Blackwell Publishing, pp 149–182.
4. Rubin LF: The horse fundus. In Atlas of veterinary ophthalmoscopy, Philadelphia, 1974, Lea and Febiger, pp 289–325.
5. Matthews AG, Crispin SM, Parker J: The equine fundus. II. Normal anatomical variants and colobomata, Equine Vet J Suppl 22:50–54, 1990.
6. Gelatt KN: Ophthalmoscopic studies in the normal and diseased ocular fundi of horses, J Am Anim Hosp Assoc 7:158–163, 1971.
7. Gilger BC: Equine recurrent uveitis. In Robinson NE, editor: Current therapy in equine medicine 5, Philadelphia, 2003, Saunders, pp 468–473.
8. Eriksson K: Hereditary aniridia with secondary cataract in horses, Nord Vet Med 7:773–779, 1955.
9. Joyce JR: Aniridia in a quarterhorse, Equine Vet J Suppl 2:21–22, 1983.
10. Joyce JR, et al: Iridial hypoplasia (aniridia) accompanied by limbic dermoids and cataracts in a group of related quarterhorses, Equine Vet J Suppl 10:26–28, 1990.
11. Ueda Y: Aniridia in a thoroughbred horse, Equine Vet J Suppl 10:29, 1990.
12. Irby NL, Aguirre GD: Congenital aniridia in a pony, J Am Vet Med Assoc 186:281–283, 1985.
13. Ramsey DT, Ewart SL, Render JA, et al: Congenital ocular abnormalities of Rocky Mountain horses, Vet Ophthalmol 2:47–59, 1999.
14. Barnett KC, et al: Buphthalmos in a thoroughbred foal, Equine Vet J 20:132–135, 1988.

15. Cook CS: Ocular embryology and congenital malformations. In Gelatt KN, editor: Veterinary ophthalmology, ed 4, Ames, IA, 2007, Blackwell Publishing, pp 3–36.
16. Crispin SM: Developmental anomalies and abnormalities of the equine iris, Vet Ophthalmol 3:93–98, 2000.
17. Brooks DE, Matthews AG: Equine ophthalmology. In Gelatt KN, editor: Veterinary ophthalmology, ed 4, Ames, IA, 2007, Blackwell Publishing, pp 1165–1274.
18. Swanson HL, et al: A case of Peters' anomaly in a Springer spaniel, J Comp Pathol 125:326–330, 2001.
19. Gilger BC, et al: Neodymium:yttrium-aluminum-garnet laser treatment of cystic granula iridica in horses: eight cases (1988–1996), J Am Vet Med Assoc 211:341–343, 1997.
20. Gemensky-Metzler AJ, Wilkie DA, Cook CS: The use of semiconductor diode laser for deflation and coagulation of anterior uveal cysts in dogs, cats, and horses: a report of 20 cases, Vet Ophthalmol 7:360–368, 2004.
21. Collins BK, Moore CP: Diseases and surgery of the canine anterior uvea. In Gelatt KN, editor: Veterinary ophthalmology, ed 3, Philadelphia, 1999, Lippincott Williams & Wilkins, pp 755–795.
22. Dziezyc J, Samuelson DA, Merideth R: Ciliary cysts in three ponies, Equine Vet J Suppl 10:22–25, 1990.
23. Rubin LF: Cysts of the equine iris, J Am Vet Med Assoc 149:151–154, 1966.
24. Buyukmihci NC, MacMillan A, Scagliotti RH: Evaluation of zones of iris hypoplasia in horses and ponies, J Am Vet Med Assoc 200:940–942, 1992.
25. Szymanski CM: Malignant teratoid medulloepithelioma in a horse, J Am Vet Med Assoc 190:301–302, 1987.
26. Bistner SI: Medullo-epithelioma of the iris and ciliary body in a horse, Cornell Vet 64:88–95, 1974.
27. Riis RC, Scherlie PH, Rebhun WC: Intraocular medulloepithelioma in a horse, Equine Vet J Suppl 10:66–68, 1990.
28. Blodi FC, Ramsey FK: Ocular tumors in domestic animals, Am J Ophthalmol 64:627–633, 1967.
29. Peiffer RL, et al: Fundamentals of veterinary ophthalmic pathology. In Gelatt KN, editor: Veterinary ophthalmology, ed 3, Philadelphia, 1999, Lippincott Williams & Wilkins, pp 355–425.
30. Broughton WL, Zimmerman LE: A clinicopathologic study of 56 cases of intraocular medulloepitheliomas, Am J Ophthalmol 85:407–418, 1978.
31. Schwink KL: Equine uveitis, Vet Clin North Am Equine Pract Ophthalmol 8:557–574, 1992.
32. Blogg JR, et al: Blindness caused by *Rhodococcus equi* infection in a foal, Equine Vet J Suppl 2:25–26, 1983.
33. Faber NA, et al: Detection of *Leptospira* spp. in the aqueous humor of horses with naturally acquired recurrent uveitis, J Clin Microbiol 38:2731–2733, 2000.
34. Grahn BH, Cullen CL: Equine phacoclastic uveitis: the clinical manifestations, light microscopic findings, and therapy of 7 cases, Can Vet J 41:376–382, 2000.
35. Maggs DJ: Ocular manifestations of equine herpesviruses. In Robinson NE, editor: Current therapy in equine medicine 5, Philadelphia, 2003, Saunders, pp 473–476.
36. Millichamp NJ, Dziezyc J: Mediators of ocular inflammation, Prog Comp Vet Ophthalmol 1:41, 1991.
37. Davidson HJ, et al: Anterior uveal melanoma with secondary keratitis, cataract and glaucoma in a horse, J Am Vet Med Assoc 199:1049–1050, 1991.
38. Barnett KC, Platt H: Intraocular melanomata in the horse, Equine Vet J Suppl 10:76–82, 1990.
39. Matthews AG, Barry DR: Bilateral melanoma of the iris in a horse, Equine Vet J 19:358–360, 1987.
40. Murphy J, Young S: Intraocular melanoma in a horse, Vet Pathol 16:539–542, 1979.
41. Latimer CA, Wyman M: Sector iridectomy in the management of iris melanoma in a horse, Equine Vet J Suppl 2:101–104, 1983.
42. Scotty NC, Barrie KB, Brooks DE, et al: Surgical management of a progressive iris melanocytoma in a Mustang, Vet Ophthalmol 11:75–80, 2008.
43. Neumann SM: Intraocular melanoma in a horse, Mod Vet Pract 66:559–560, 1985.
44. Ramadan RO: Primary ocular melanoma in a young horse, Equine Vet J 7:49–50, 1975.
45. Knottenbelt DC, Hetzel U, Roberts V: Primary intraocular primitive neuroectodermal tumor (retinoblastoma) causing unilateral blindness in a gelding, Vet Ophthalmol 10:348–356, 2007.
46. Albert DM: Ocular melanoma: a challenge to visual science, Invest Ophthalmol Vis Sci 23:550–579, 1982.
47. Lerner AB, Cage GW: Melanomas in horses, Yale J Biol Med 46:646–649, 1973.
48. Wilcock BP, Peiffer RL: Morphology and behavior of primary ocular melanomas in 91 dogs, Vet Pathol 23:418–424, 1986.
49. Yanoff M, Fine MS: Ocular melanotic tumors. In Ganoff M, Fine MS, editors: Ocular pathology, Hagerstown, Md, 1975, Harper & Row, pp 619–683.
50. Reese AB, Jones IS, Cooper WC: Surgery for tumors of the iris and ciliary body, Am J Ophthalmol 66:173–184, 1968.
51. Niederkorn JY: Enucleation in consort with immunologic impairment promotes metastasis of intraocular melanomas in mice, Invest Ophthalmol Vis Sci 25:1080–1086, 1984.
52. Zimmerman LE, McLean IW: An evaluation of enucleation in the management of uveal melanomas, Am J Ophthalmol 87:741–760, 1979.
53. Cook CS, Wilkie DA: Treatment of presumed iris melanoma in dogs by diode laser photocoagulation: 23 cases, Vet Ophthalmol 2:217–225, 1999.
54. Goetz TE, et al: Cimetidine for treatment of melanomas in three horses, J Am Vet Med Assoc 196:449–452, 1990.
55. Schneider DA: Lymphoproliferative and myeloproliferative disorders. In Robinson NE, editor: Current therapy in equine medicine, ed 5, Philadelphia, 2003, Saunders, pp 359–362.
56. Cullen CL, Webb AA: Ocular manifestation of systemic disease. Part 3: The horse. In Gelatt KN, editor: Veterinary ophthalmology, ed 4, Ames, IA, 2007, Blackwell Publishing, pp 1588–1616.
57. Rebhun WC: Orbital lymphosarcoma in cattle, J Am Vet Med Assoc 180:149–152, 1982.
58. Krohne SG, et al: Prevalence of ocular involvement in dogs with multicentric lymphoma: prospective evaluation of 94 cases, Vet Comp Ophthalmol 4:127–135, 1994.
59. Corcoran KA, Peiffer RL, Koch SA: Histopathologic features of feline ocular lymphosarcoma: 49 cases (1978-1992), Vet Comp Ophthalmol 5:35–41, 1995.
60. Rebhun WC, Del Piero F: Ocular lesions in horses with lymphosarcoma: 21 cases (1977-1997), J Am Vet Med Assoc 212:852–854, 1998.
61. Rebhun WC, Bertone A: Equine lymphosarcoma, J Am Vet Med Assoc 184:720–721, 1984.
62. Germann SE, Richter M, Schwarzwald CC, et al: Ocular and multicentric lymphoma in a young racehorse, Vet Ophthalmol 11(Suppl 1):51–56, 2008.
63. McMullen RJ, Clode AB, Gilger BC: Infrared digital imaging of the equine anterior segment, Vet Ophthalmol 12:125–131, 2009.

Chapter 7

Diseases and Surgery of the Lens

Carmen M.H. Colitz
Richard J. McMullen, Jr.

Diseases of the lens in horses are not common but when present and significant, render the animal devalued, dangerous for some uses, and predisposed to self-injury. This may possibly lead to euthanasia because of the horse's inability to work or produce. The most common lens disease in all species is cataract—opacity of the lens and/or its capsule. Cataracts can occur congenitally or be acquired postnatally. It is estimated that cataracts are present in 5% to 7% of all horses with otherwise normal eyes.[1] These range from incipient opacities to larger visually disturbing cataracts. Other less common lens diseases include abnormal shape and abnormal position of the lens. Diagnosis and treatment of these diseases of the lens will be described in detail in this chapter.

CLINICAL ANATOMY AND PHYSIOLOGY

The crystalline lens is the second most important refractive structure of the eye. Its role is to focus incoming light onto the area centralis. The lens is unique insofar as it is transparent, devoid of innervation and vascular structures, yet it grows throughout embryologic development and continues until the death of the horse. Lens embryology, anatomy, physiology, and function differ little between terrestrial species.[2] Lens epithelial cells (LECs) line the anterior aspect of the lens in a monolayer and perform the majority of the metabolic functions for this structure (Fig. 7-1). They transport solutes between the lens and the aqueous humor, are important for enzymatic activity, secrete capsular material, and their metabolism maintains lens transparency.[3] Any imbalance in enzymatic activity or lens metabolism due to DNA or protein damage to the LEC can lead to cataractogenesis.[3]

The remainder of the lens is made up of terminally differentiating and differentiated lens fiber cells. The process of terminal differentiation begins in the equatorial (or lens bow) region (see Fig. 7-1) that entails elongation, loss of cellular structures, posttranslational modification of proteins, and gradual migration into the cortex. During this migration, they lose their nuclei through an apoptosis-like mechanism.[4] Losing cellular structures ensures the clarity of the lens by removing potentially light-scattering elements from the incoming light pathway. The region immediately inside the area of organelle loss is called the *organelle-free zone* (OFZ)[5] and begins in the peripheral adult nucleus.

Clinically, there are three major regions that are important: the nucleus, the cortex, and the lens capsule. Beginning from the middle towards the outside, the nucleus is the oldest section of the lens. There are three subdivisions of the nucleus, based on the age of the animal (see Fig. 7-1). The innermost nucleus is the embryonic nucleus that is formed from primary lens fibers at the earliest time of lens development. The region that then surrounds the embryonic nucleus is the fetal nucleus. These are the first secondary lens fibers, and they form until the animal is born, so at birth, the lens is only made up of the embryonic and fetal nuclei surrounded by the lens capsule. The lens capsule is continually produced by the anterior lens epithelial cells throughout development and postnatal life. Postnatally, the secondary lens fibers create the cortical region and begin to form the future adult nucleus. In a young adult horse (approximately 5 to 7 years of age), the lens will have an obvious area between the lens capsule and the outermost nucleus that is the cortical region. The cortical region is composed of the newest cells that are continually being moved

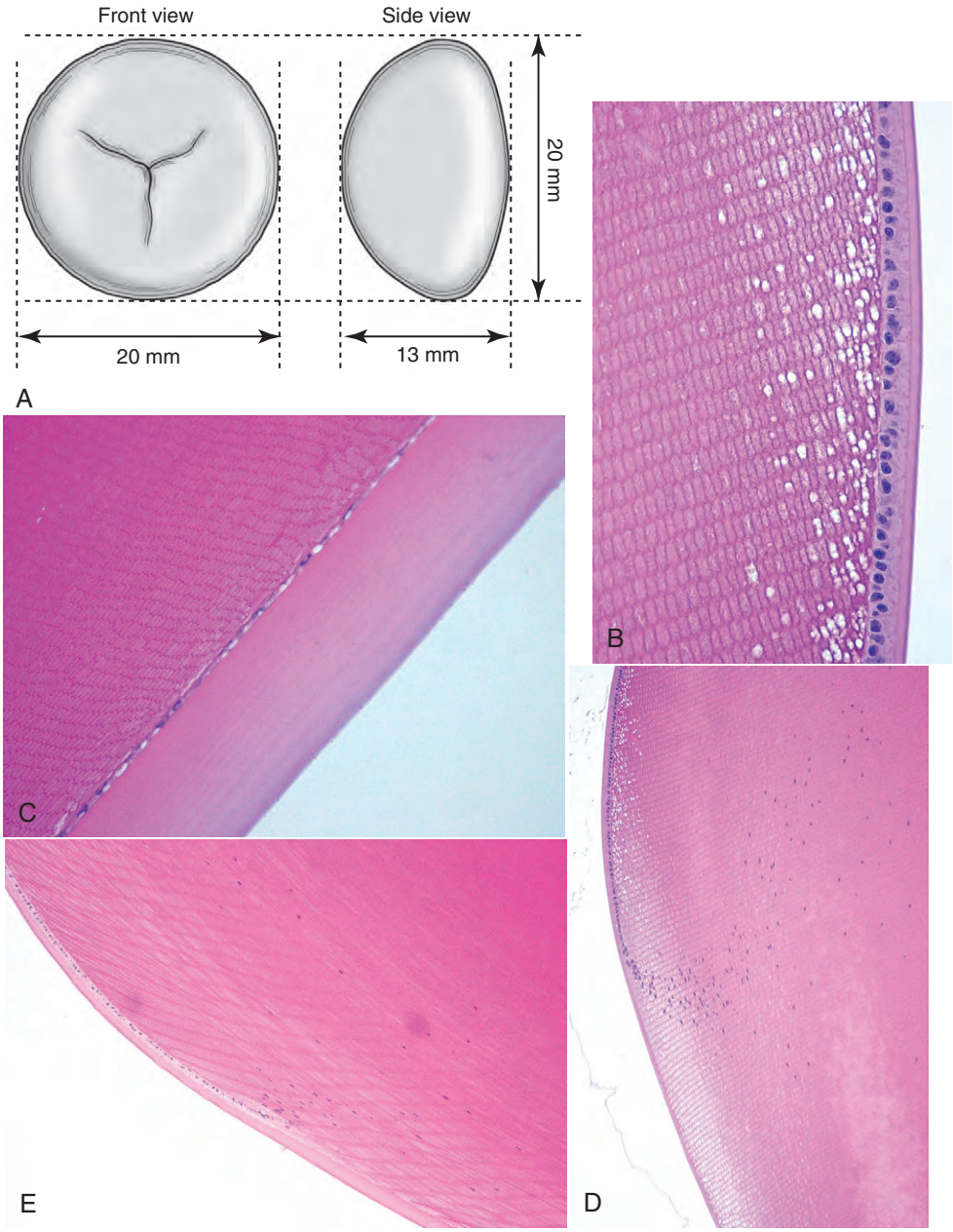


Figure 7-1. **A,** Schematic cross-section of the adult equine lens. **B,** Photomicrograph of the anterior lens capsule from a 2-day-old Thoroughbred foal.[137] Note the prominent lens epithelial cells and thin anterior capsule compared with **C** (H&E ×400). **C,** Photomicrograph of the anterior lens capsule from a 10-year-old Quarter Horse (QH) gelding (H&E ×400). **D,** Photomicrograph of the lens bow in the foal from **B** (H&E ×100). **E,** Photomicrograph of the lens bow from the QH gelding in **C**. (H&E ×100).

inward; therefore, any random elongating cortical fiber cell is surrounded on the inner aspect by an older fiber cell, on each side by similar-aged fiber cells, and at its outer aspect by a newer fiber cell. At approximately 15 to 20 years of age, the entire nucleus is more obvious owing to the layers of cells that have been compressed over time and begin to refract light. This is termed *nuclear sclerosis* and is a typical aging change in all eyes (Fig. 7-2).

ECONOMIC IMPACT OF LENS DISEASE ON THE EQUINE INDUSTRY

The impact of lens disease on the equine industry has not been critically evaluated, but if the estimate of 8% incidence of equine recurrent uveitis (ERU) in all horses holds true, then it is safe to estimate that all of those horses have some cataract formation. The cataract may not be clinically relevant if it is small, but any opacity of the lens could possibly diminish the horse's capacity to work, diminishing its ability to create income for the owner.

CONGENITAL DISEASES

Ocular abnormalities of the neonatal foal may be congenital, inherited, or acquired. Congenital defects may be due to genetic causes/inheritance, toxins, nutritional imbalance, ionizing radiation, or other idiopathic causes.[6,7] Cataracts are the most common congenital abnormality present in foals, with a 33.6% to 35.3% incidence in cases of congenital ocular defects.[7,8]

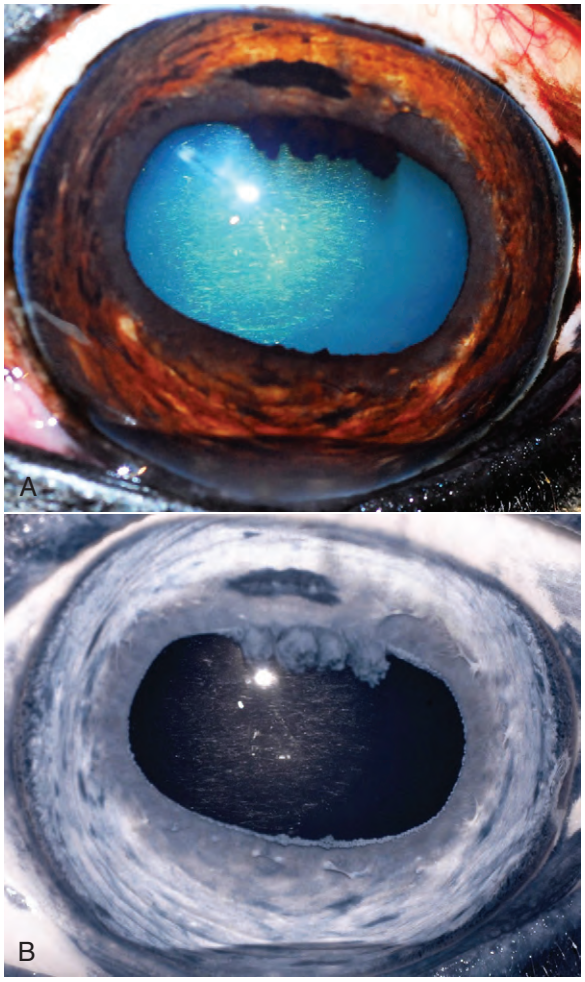


Figure 7-2. A, Nuclear sclerosis in a middle-aged Quarter Horse gelding. **B,** Infrared. Note that the lens changes appear as gray "scratches" within the otherwise jet black pupil.

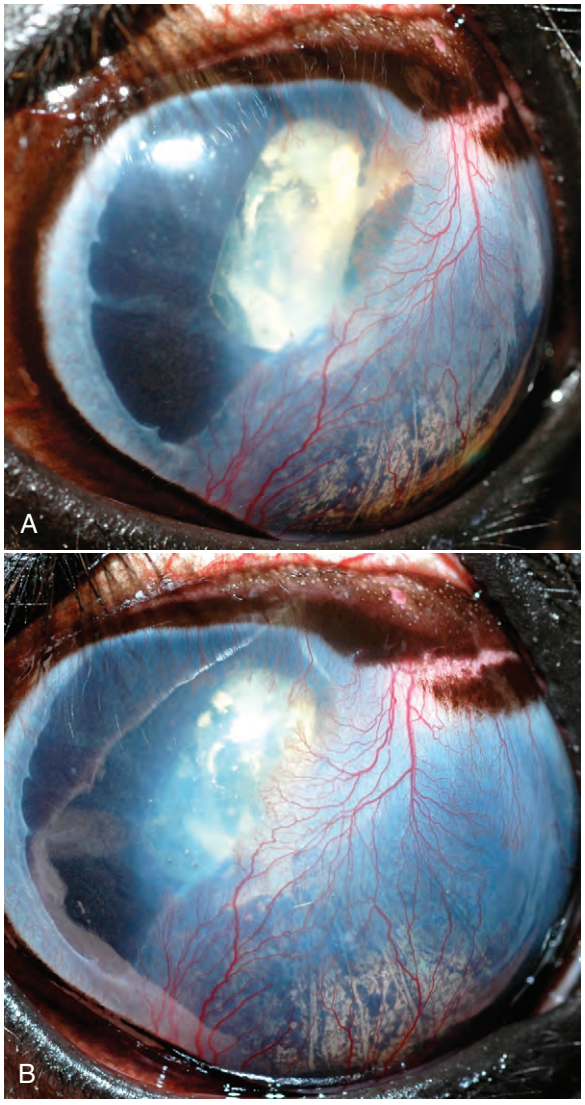


Figure 7-3. A, Temporal view of anterior segment dysgenesis in a young Thoroughbred yearling. **B,** Axial view of the same eye as in **A.**

Other lens anomalies include spherophakia, lenticonus, and coloboma.

CONGENITAL CATARACTS

Congenital cataracts are the largest group of developmental lens opacities in horses. Inherited congenital cataracts have been documented in Thoroughbreds, Quarter Horses, and Morgans.[9-11] Rocky Mountain horses can also develop congenital nuclear cataracts but have concurrent multiple anterior segment anomalies.[12] It is sometimes possible to estimate the time a cataract originated and also determine whether it will progress. Nuclear cataracts involving the embryonic or fetal nuclei do not progress and usually become smaller relative to the rest of the lens as the animal ages. Perinuclear cataracts, by nature of when the cortex begins to develop relative to the date of birth, occur just after the animal is born. The nucleus and the inner nuclei are usually clear. This type of cataract or nuclear cataracts are inherited in the Morgan horse.[9] Cataracts are often seen in equine eyes with other anomalies like microphthalmia and anterior segment dysgenesis (Fig. 7-3). They are present in Rocky Mountain Spotted horses with multiple ocular anomalies.[13,14] Congenital cataracts can occur with other anomalies such as persistent pupillary membranes and aniridia.[15,16]

PRIMARY APHAKIA, MICROPHAKIA, AND COLOBOMA

Primary aphakia and microphakia (Fig. 7-4) are extremely rare and occur with other anomalies in the eye, including coloboma (Fig. 7-5) due to inadequate insertion of zonules at the lens equator.[17,18] In cases of presumed aphakia or microphakia without other ocular anomalies, it is possible that the lens developed a cataract in utero, and it was resorbed prior to birth or soon after.

ECTOPIA LENTIS

Ectopia lentis, also rare, occurs when the lens vesicle fails to enter the optic cup, and the lens attempts to form in the anterior chamber. In one case, the lens was also microphakic and sphe-

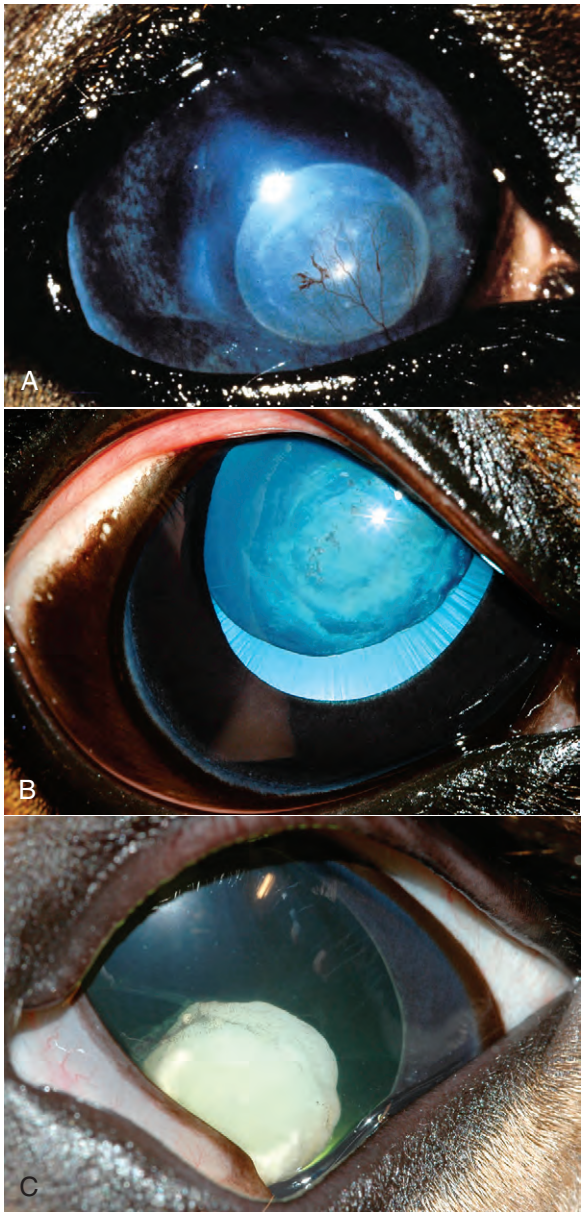


Figure 7-4. **A,** Anterior lens luxation, mild corneal edema and keratitis, and microphthalmia in a foal. **B,** Lens resorption (possible microphthalmia) in a 4-day-old Thoroughbred foal. **C,** Left eye from foal in Fig. 7-3, *B* with further lens resorption and cataract density. Note lack of zonular attachment. (**A** Courtesy Dr. David Wilkie. **B** and **C** Courtesy Dr. Ricardo Stoppini.)

rophakic.[18] Congenitally displaced lenses are often abnormal in shape (spherophakia) and smaller than normal (microphakia). The early contact between the optic vesicle and the surface ectoderm, and its subsequent appropriate changes, result in a normally positioned, normally shaped, transparent lens. If anything changes any of these steps, the lens will be abnormal in position, shape, and opacity. The most severe anomaly occurs when this initial contact does not separate appropriately; this results in anterior segment dysgenesis, anterior lenticonus, and anterior capsular cataracts.[14,19] Anterior segment dysgenesis often occurs with microphthalmia.[17,20-22]

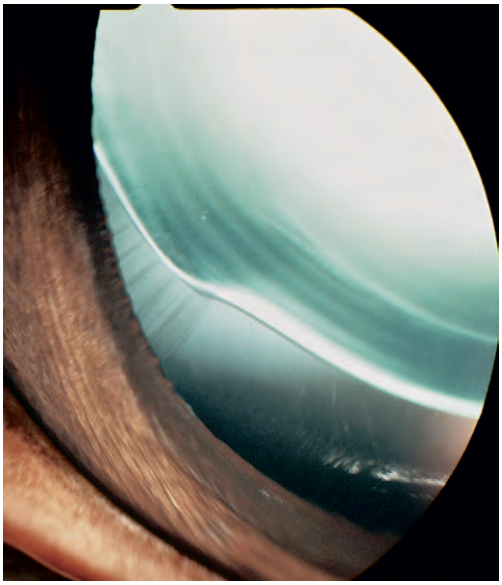


Figure 7-5. Ventral lens coloboma in a young Warmblood stallion. Note the notch along the ventral lens equator just beyond the last visible lens zonules.

LENTIGLOBUS AND LENTICONUS

Lentiglobus is also a malformation of the lens and occurs when the anterior or posterior aspect of the lens is prominent and spheroid in shape. This is in contrast to lenticonus, which is a conical projection of the anterior or posterior aspect of the lens. Both conditions are rare.

CONGENITAL ANOMALIES THAT MAY BE ASSOCIATED WITH CATARACTS

Examples of congenital anomalies that may be associated with cataracts include persistent pupillary membranes, persistent hyaloid artery, persistent hyperplastic primary vitreous/persistent hyperplastic tunica vasculosa lentis (PHPV/PHTVL [Fig. 7-6]), posterior lenticonus, microphakia, microphthalmos, and lens coloboma. The hyaloid artery system is typically resorbed in the first few weeks postnatally. However, complete regression of the hyaloid system, including its remnants, occurs by 6 to 9 months of age in horses.[23]

Persistent pupillary membranes (PPMs) are often seen in clinically normal horses. One study including 169 neonatal Thoroughbred foals found PPMs in 28% of left eyes and 25% of right eyes; 23% of the foals had bilateral involvement.[24] However, PPMs that arise from the iris collarette and attach to the anterior lens capsule are rare.[16] The same study of neonatal foals found the hyaloid artery or its remnants present in 83% of left eyes and 87.5% of right eyes; 80% were bilateral.[24] One horse in this survey had bilateral capsular cataracts related to the hyaloid remnant.[24] In a survey of Thoroughbred racehorses in Australia, one horse from a total of 204 was found to have a hyaloid remnant.[25] PHPV/PHTVL (see Fig. 7-6) has not been described in the equine literature. Mittendorf's dot, the anterior attachment of the hyaloid artery to the posterior lens pole, has been documented and can occur in a triradiate configuration.[16] Bergmeister's papillae, a remnant of the hyaloid artery seen protruding from the optic nerve head, is rare in horses.

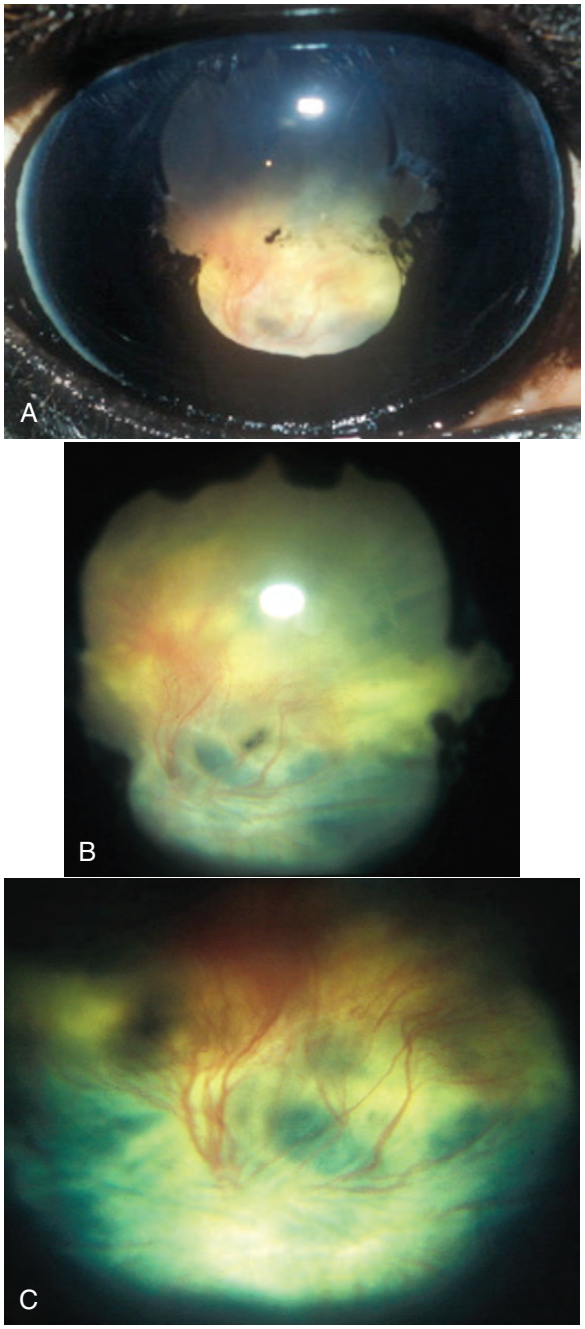


Figure 7-6. **A,** Persistent hyperplastic primary vitreous/persistent hyperplastic tunica vasculosa lentis (PHPV/PHTVL) in a young Warmblood mare. Note the narrow, vertically oval pupil with multifocal posterior synechiae and anterior lens capsule pigment deposition. The retrolental blood vessels and white posterior capsular opacities are slightly out of focus but can be more clearly seen in **B** and **C.**

ACQUIRED DISEASES

Acquired diseases of the lens in mature horses that will be discussed in this section include subluxation, luxation, puncture or laceration, expansion, rupture, and opacity of the lens or lens capsule (cataract). Although several of the lesions discussed in the following section may also be encountered in foals, they are most commonly identified during ophthalmic examination

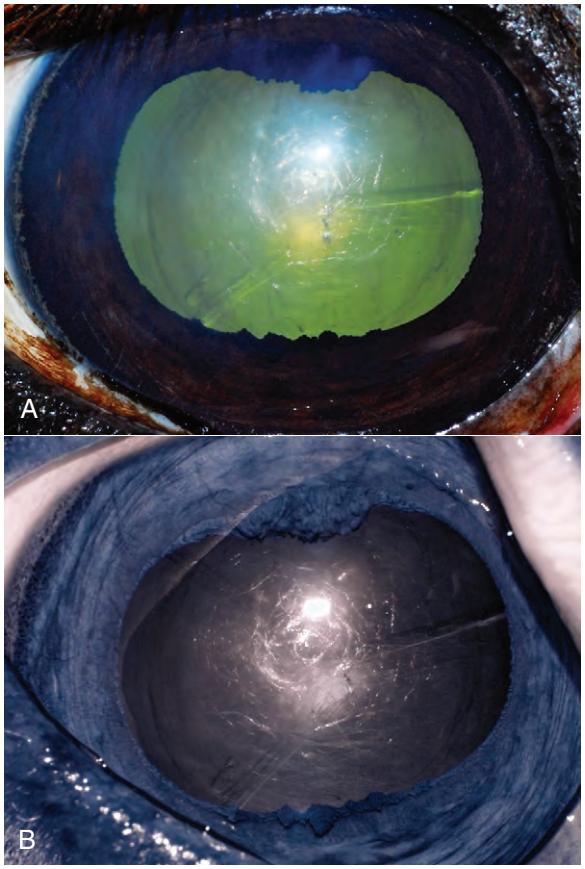


Figure 7-7. **A,** Senile cataract in a geriatric Quarter Horse gelding. A circular zone of discontinuity can be seen at the junction between the lens nucleus and the lens cortex. **B,** Infrared digital image provides an enhanced view of the cataract.

of the adult horse. There is a recent description of lens opacities, with representative photographs providing an extensive classification system based on etiology.[1] Most cataracts in horses develop secondary to intraocular disease such as uveitis (ERU and other forms of anterior and/or posterior uveitis), retinal detachment, neoplasia, coup-contrecoup or whiplash injury to the globe, advanced age, or metabolic diseases or toxins.[1,26] Senile cataracts (Fig. 7-7) can be frequently encountered in horses older than 18 years of age and may interfere with vision.[1] Many geriatric horse lenses show increased nuclear delineation, or nuclear sclerosis (see Fig. 7-2), which may be associated with the development of senile cataracts. Occasionally, increased brunescence (Fig. 7-8) of the lens nucleus can be seen in such instances.[1]

CATARACTS

As in other animal species and humans, cataract development is a common sequela of uveitis (Fig. 7-9) and trauma (Fig. 7-10). The rate of cataract progression is dependent upon the underlying cause. ERU and other forms of uveitis are associated with an accelerated rate of cataract progression, and it is still generally accepted that inflammation of the anterior uvea (e.g., ERU) is the most common cause of acquired cataracts in horses.[1,10,16,27-44]

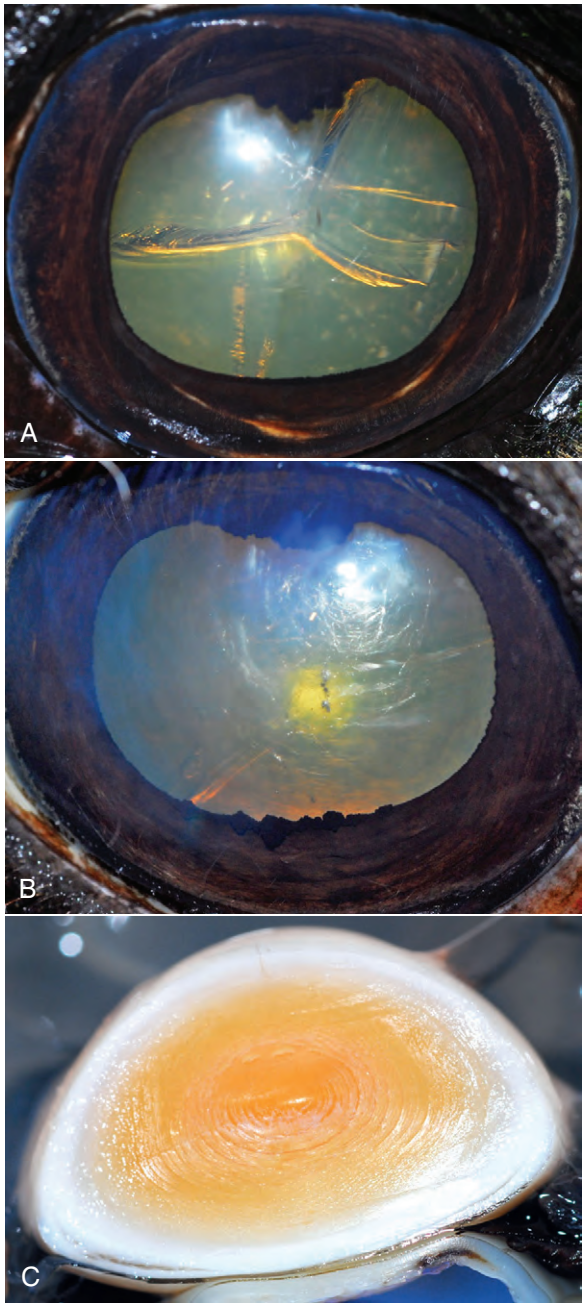


Figure 7-8. A, Brunescence (increased yellow discoloration) of the lens occurs as a normal part of aging. **B,** Central, nuclear brunescence associated with a senile cataract in an aging Quarter Horse. **C,** Gross pathologic section of a lens from a 22-year-old Quarter Horse gelding (not the same eye as in **B**). Note how the brunescence is most intense within the nucleus.

CLINICAL APPEARANCE

The classification of adult cataracts can follow several different schemas. Briefly, cataracts can be described by their age of onset (congenital, juvenile, or senile/geriatric), cause (e.g., hereditary, secondary to uveitis, trauma, toxin, nutritional, or metabolic disease), or location within the lens (anterior polar, anterior subcapsular, anterior cortical, lamellar/perinuclear, equatorial, peripheral cortical, posterior cortical, posterior subcapsular, or posterior polar [Figs. 7-11 to 7-18]). Several characteristics of a cataract, including location, density, size of a

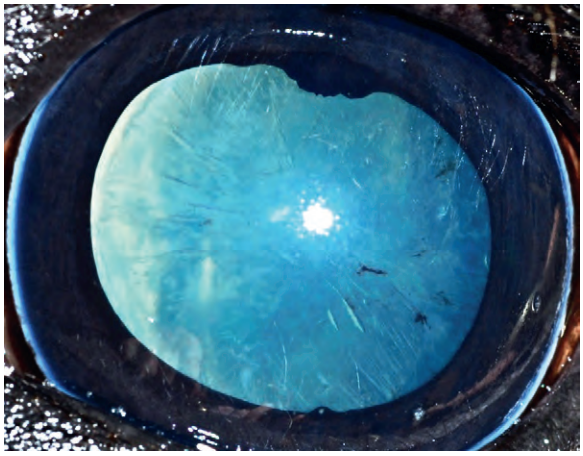


Figure 7-9. Diffuse, immature, anterior and posterior cortical cataract associated with equine recurrent uveitis in a 7-year-old Rocky Mountain horse mare.

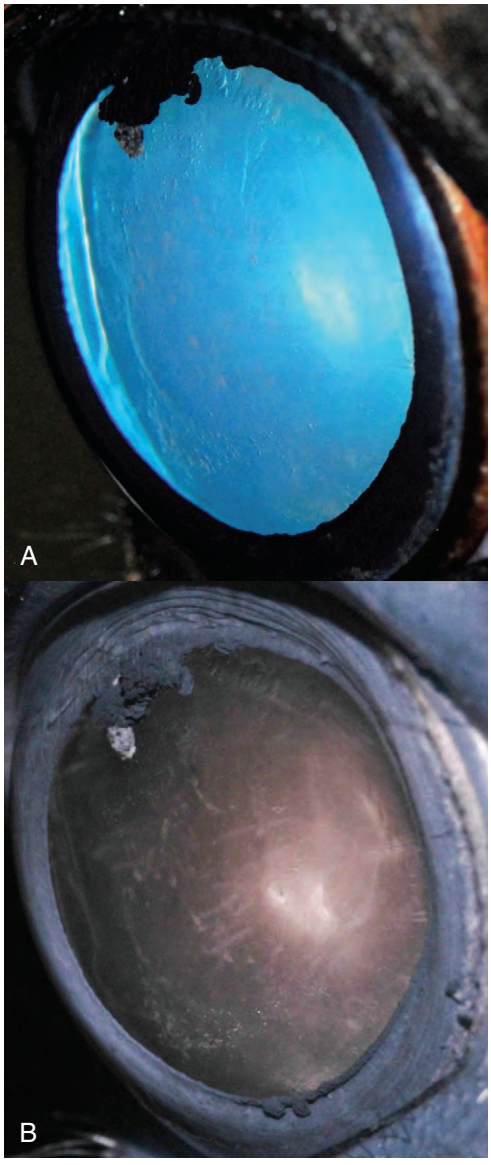


Figure 7-10. A, Diffuse, immature, anterior and posterior cortical and nuclear cataract that developed following blunt force trauma in an 11-year-old Quarter Horse gelding. **B,** Infrared. The view of the cataract is enhanced.

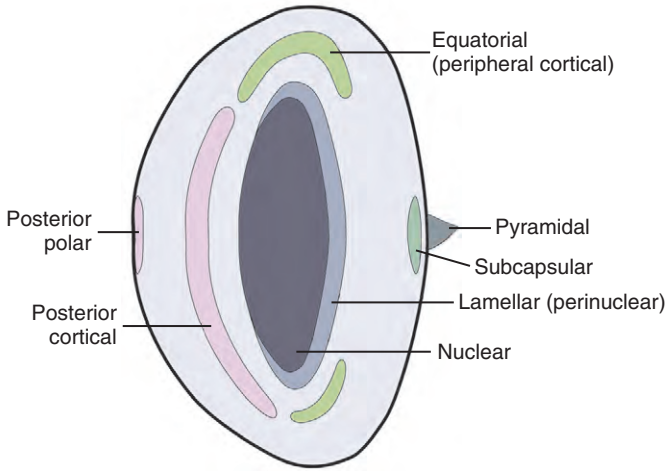


Figure 7-11. Classification scheme for cataracts according to their location within the lens.

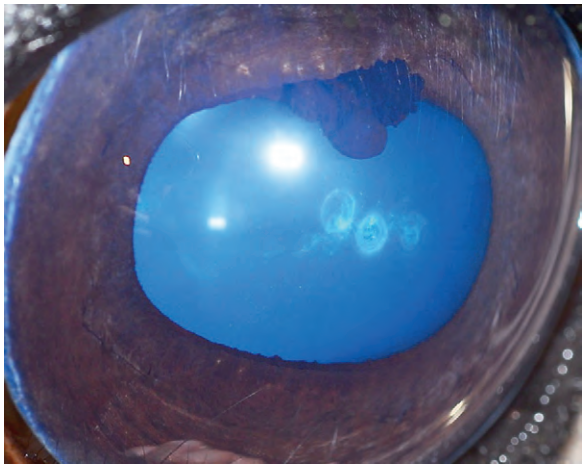


Figure 7-12. Focal, incipient, anterior polar cataract.

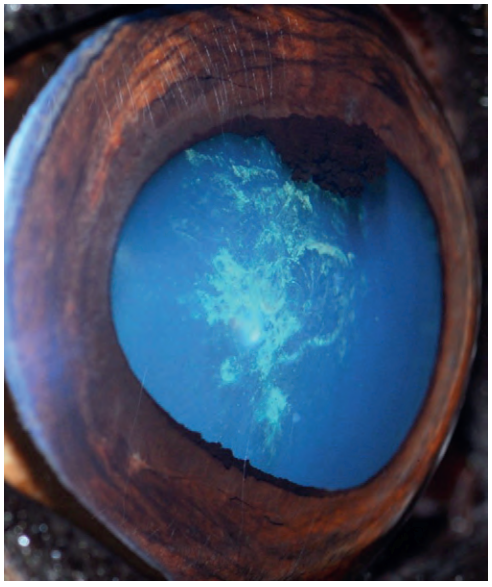


Figure 7-13. Diffuse, incipient, anterior subcapsular cataract in the right eye of a 19-year-old Morgan gelding.

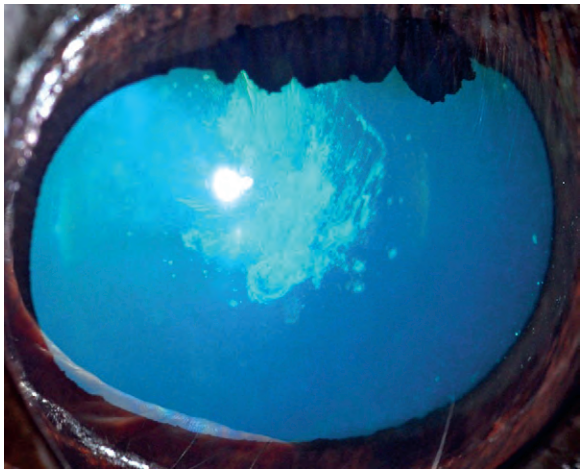


Figure 7-14. Focal, incipient, anterior cortical cataract in the left eye of a 12-year-old Thoroughbred gelding.

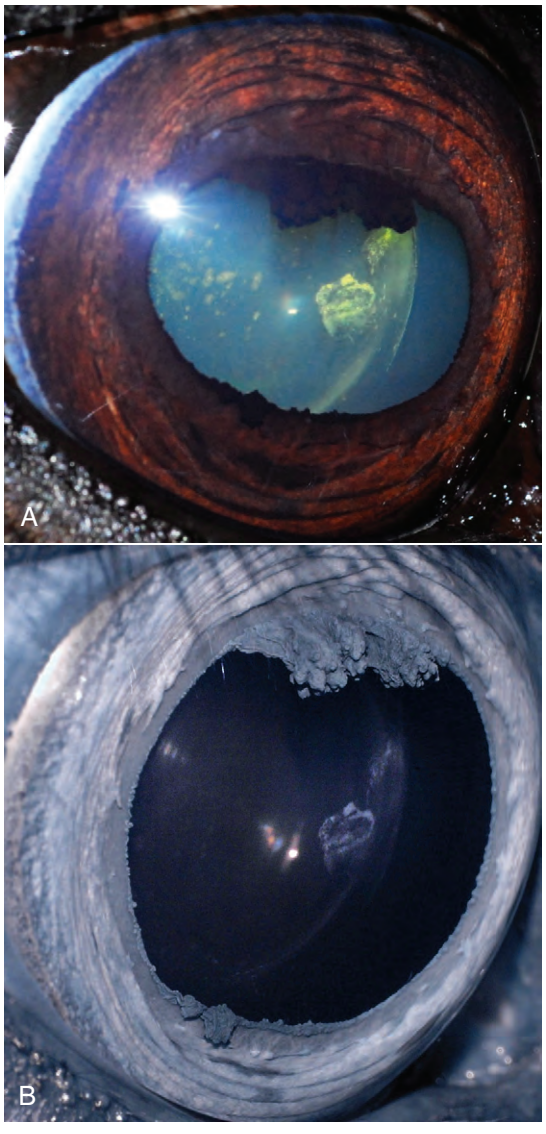


Figure 7-15. A, Lamellar (perinuclear) cataract with a small, focal, anterior cortical cataract in the right eye of a 19-year-old Percheron mare. This clinical presentation can be easily mistaken for subluxation of the lens if careful examination is not performed. **B,** Infrared. Note abrupt transition from a slight gray color (cataractous area of the lens) to jet black, which represents the clear cortical aspect of the lens.

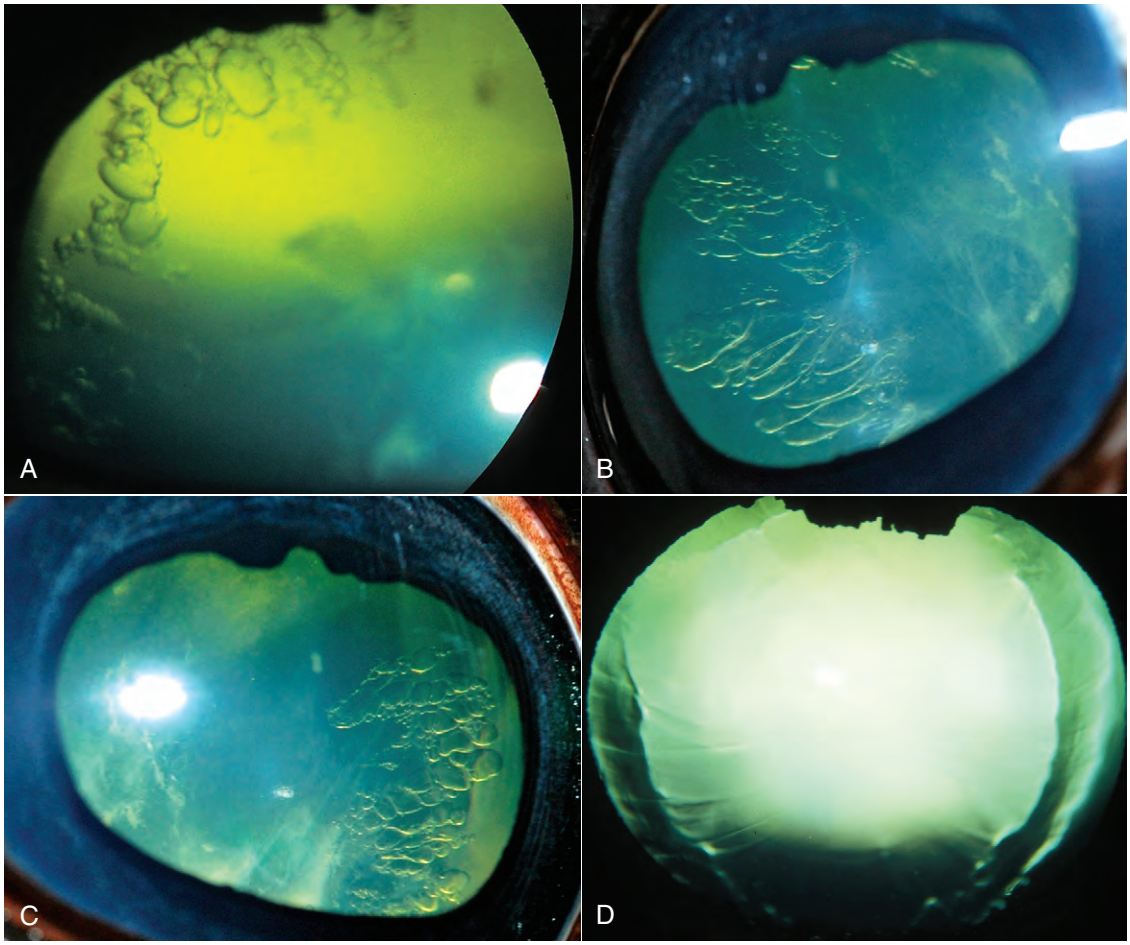


Figure 7-16. **A,** Vesicles within the peripheral equatorial cortex associated with early equine recurrent uveitis (ERU) in a 7-year-old Warmblood mare. **B** and **C,** Vesicles within the peripheral equator of the lens associated with early ERU. **D,** Equatorial cortical cataract in a young Warmblood gelding. This type of cataract can be readily missed if the pupil is not dilated.

focal cataract, and blockage of the fundic reflex, determine its effect on vision.[10,45]

COMMON DIFFERENTIAL DIAGNOSES

Acquired cataracts in horses are often caused by uveitis (Fig. 7-19) or trauma (Fig. 7-20).* Juvenile cataracts, common in many canine breeds, are uncommon in horses.[10,47,48] Cystic lesions associated with the anterior lens capsule and/or anterior subcapsular cortex (Fig. 7-21) are being identified more frequently; they appear to precede anterior uveitis and are independent of ocular trauma.[10,16,35] Senile cataracts significant enough to interfere with vision are also uncommon in horses.[49] Nuclear sclerosis is a relatively common finding among aged horses, but vision remains clinically unaffected.[35,50]

Lens suture lines (Y sutures) can be visualized in most foals and adult horses during routine ophthalmic examination, and it is important to differentiate these opacities from cataracts.[6,7,50,51] In a group of 144 foals ranging in age from 5 days to 19.5 weeks (mean age 9.4 weeks), lens sutures were visible in 137 animals.[6]

TREATMENT

Historically, horses with cataracts associated with ERU were not considered appropriate candidates for cataract surgery. Concurrent pathologic ocular changes in the eye and the high rate of postoperative complications resulted in very low surgical success rates.[45,52] However, horses with well-controlled uveitis should be considered reasonable candidates for cataract surgery to restore vision.[32,53-55]

LENS LUXATION

Lens luxation or subluxation may be caused by congenital anomalies of the zonules, chronic uveitis, or glaucoma and may be exacerbated by trauma.† A luxated lens will usually become cataractous, with focal or diffuse opacification appearing immediately or weeks following a traumatic incident as a result of the disruption in the protein exchange between the aqueous humor and the lens.[41,57,58]

*References 26-29, 32, 34, 36, 37, 39-43, and 46-48.

†References 36, 37, 41, 43, 46, and 56.

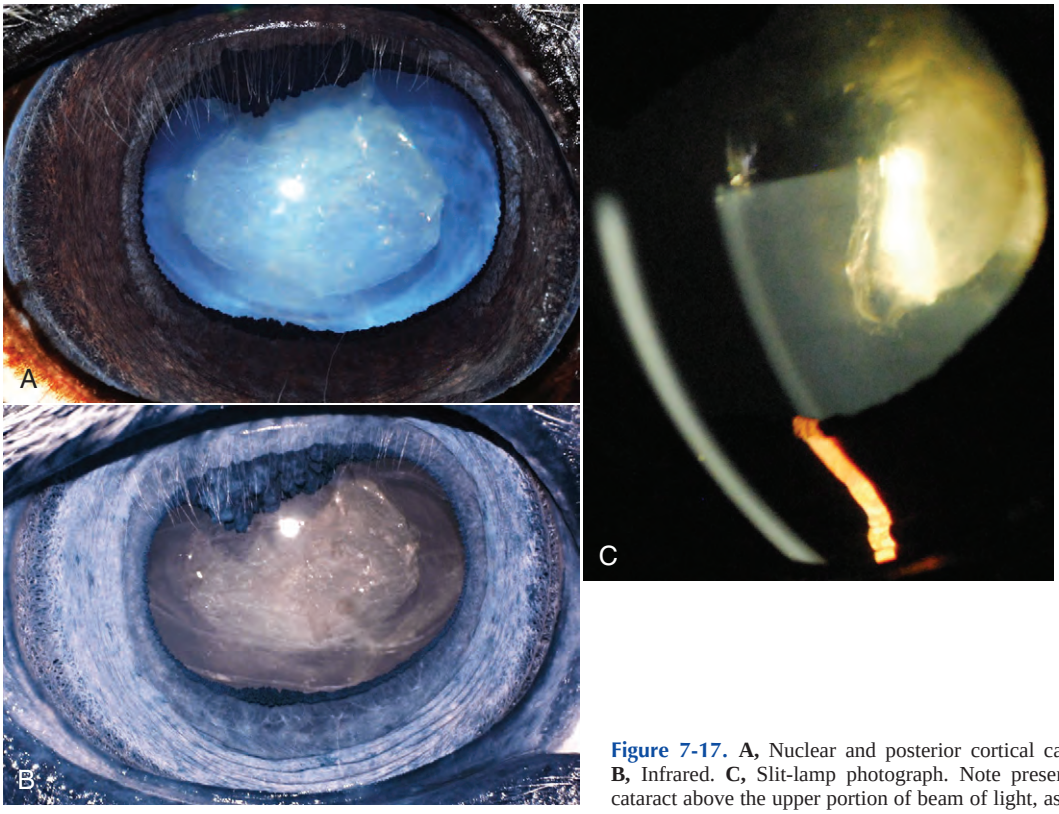


Figure 7-17. **A,** Nuclear and posterior cortical cataract in a 12-year-old Pony gelding. **B,** Infrared. **C,** Slit-lamp photograph. Note presence of a small focal anterior cortical cataract above the upper portion of beam of light, associated with the anterior lens capsule.

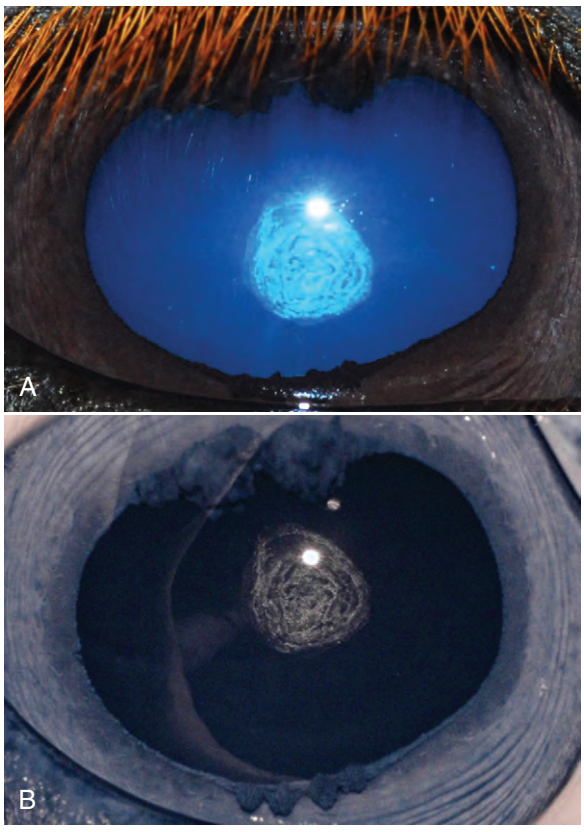


Figure 7-18. **A,** Focal, axial, posterior cortical cataract. **B,** Infrared. Axial location of this axial posterior cortical cataract is demonstrated.

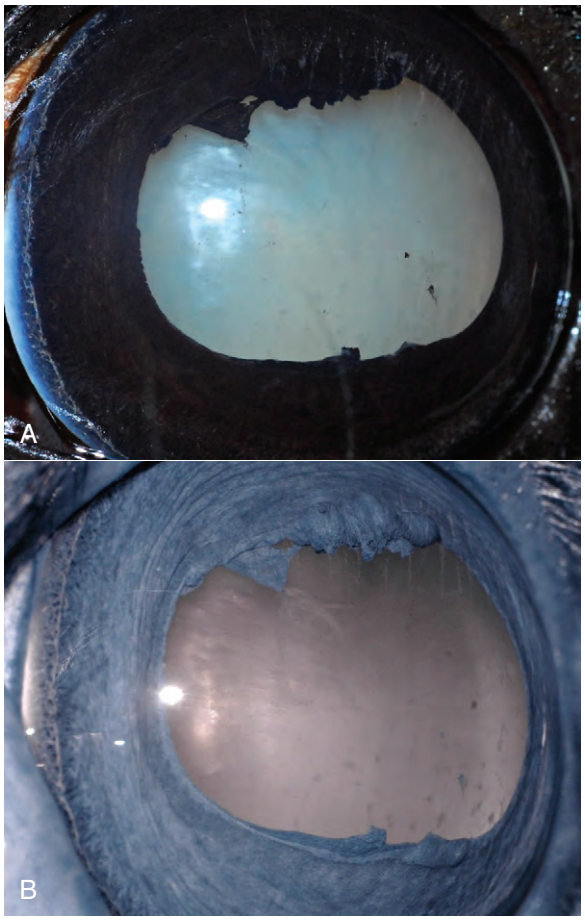


Figure 7-19. **A,** Complete mature cataract associated with chronic equine recurrent uveitis. **B,** Infrared. Note bluish-gray color of the pupil, consistent with cataractous changes, or opacifications, of the lens.[136]

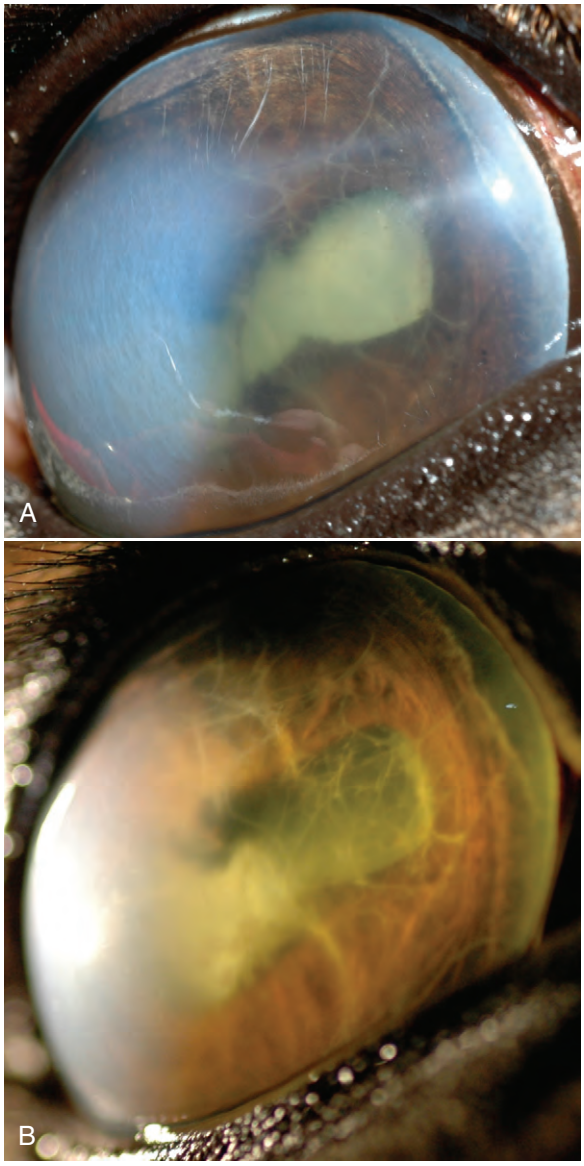


Figure 7-20. **A,** Mature cataract developed as a result of significant blunt force trauma. Also note the medial corneal edema and fibrin accumulation in the anterior chamber. **B,** Tangential lighting allows direct visualization of the temporal iris disinsertion.

CLINICAL APPEARANCE

Lens luxation and subluxation are rare in horses.[55] A subluxated lens is one that has partially broken free from its zonular attachments, but the lens remains within its normal position behind the iris and within the patellar fossa (Fig. 7-22). Slight displacement of the lens, however, allows the edge of the lens to be visible within the pupil, producing the appearance of an aphakic crescent (Fig. 7-23). Complete luxation manifests as displacement of the lens into either the anterior chamber (i.e., anterior lens luxation [Fig. 7-24]) or into the vitreous body (i.e., posterior lens luxation [Fig. 7-25]).[13]

Because of the lack of physical contact between the posterior iris surface and the anterior surface of the lens in cases of either subluxation or luxation of the lens, iridal instability manifests as a slight vibration of the iris (iridodonesis) that can be

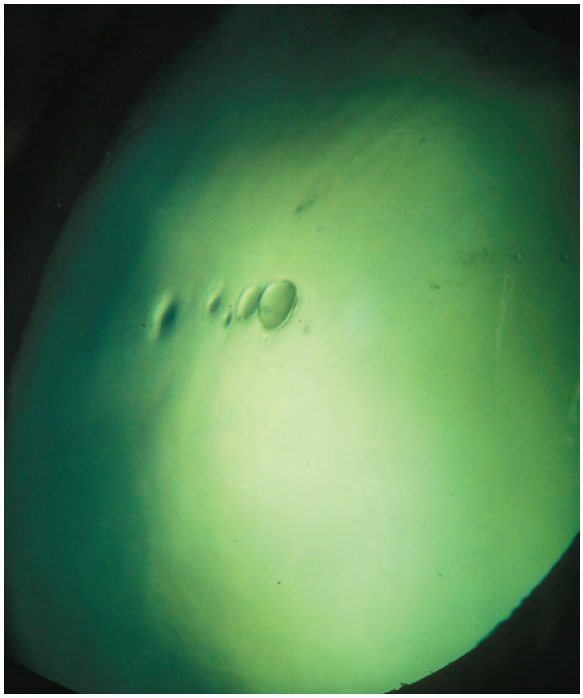


Figure 7-21. Multiple small anterior subcapsular cysts.

visualized during ophthalmic examination. Although primary (hereditary) lens luxation has not been documented in the adult horse, there are reports of congenital bilateral lens subluxation in an Arab cross foal[59] and subluxation and cataract formation associated with the multiple congenital ocular anomalies syndrome described in Rocky Mountain Spotted horses.[13] The prognosis for vision and globe retention is dependent upon the nature and severity of the primary ocular disease.[55,60]

COMMON DIFFERENTIAL DIAGNOSES

It is imperative that the primary underlying condition be identified when a horse with either a lens subluxation or luxation is being evaluated.

A rare, presumably congenital anomaly that must be differentiated from a lens subluxation is a lens coloboma (Fig. 7-26).[18] Faulty lens zonular formation, and therefore lack of insertion at the lens equator, results in an area where the lens equator is not stabilized and held in its normal position. This results in a focal flattened area or notch in the peripheral lens equator, associated with the missing zonules. An aphakic crescent can usually be identified (Fig. 7-27), but signs of ocular inflammation (e.g., aqueous flare, miosis) are not generally associated with lens colobomas and should be differentiated from a subluxation of the lens secondary to anterior uveitis or glaucoma (Fig. 7-28).

TREATMENT

A lens that is partially (subluxation) or completely displaced into the vitreous body (posterior lens luxation) may not require surgical intervention as long as the eye remains comfortable and the inflammation associated with the primary insult can be controlled with topical and systemic antiinflammatory medications. The horse should be continually monitored for signs of discomfort, corneal discoloration, blepharospasm, epiphora,

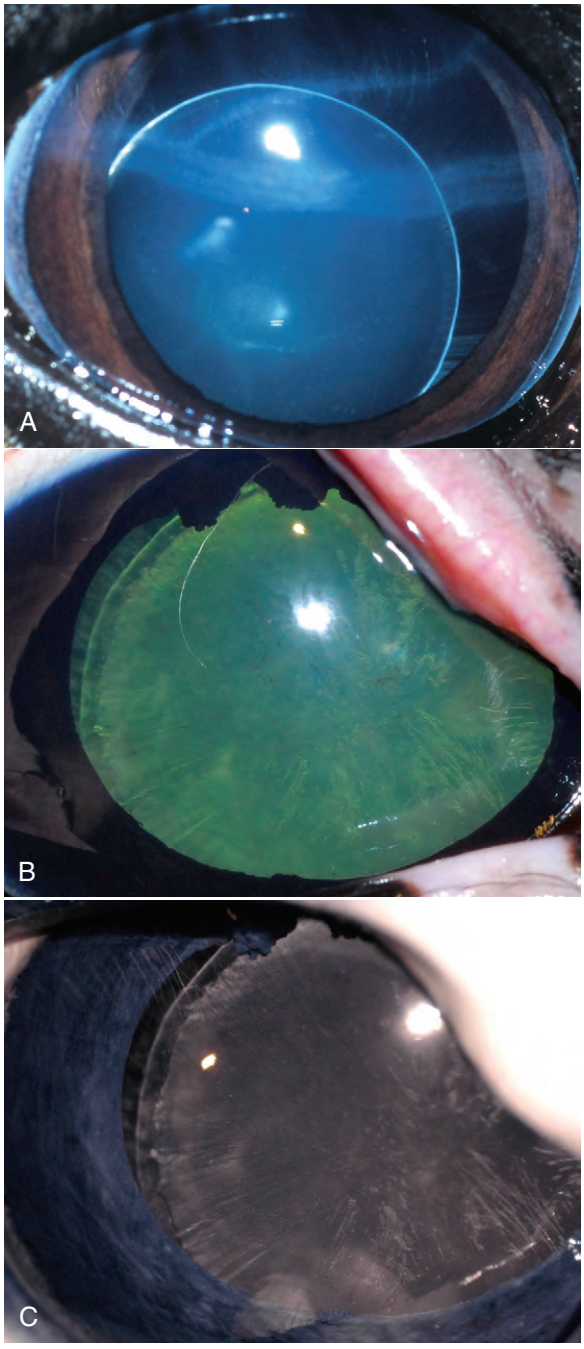


Figure 7-22. **A,** Lens subluxation associated with primary glaucoma in a 12-year-old Icelandic Pony mare. **B,** Early lens subluxation associated with chronic equine recurrent uveitis. Note refractile edge of lens just axial to temporal edge of pupil. **C,** Infrared. Space between pupil and edge of lens is more readily identified.

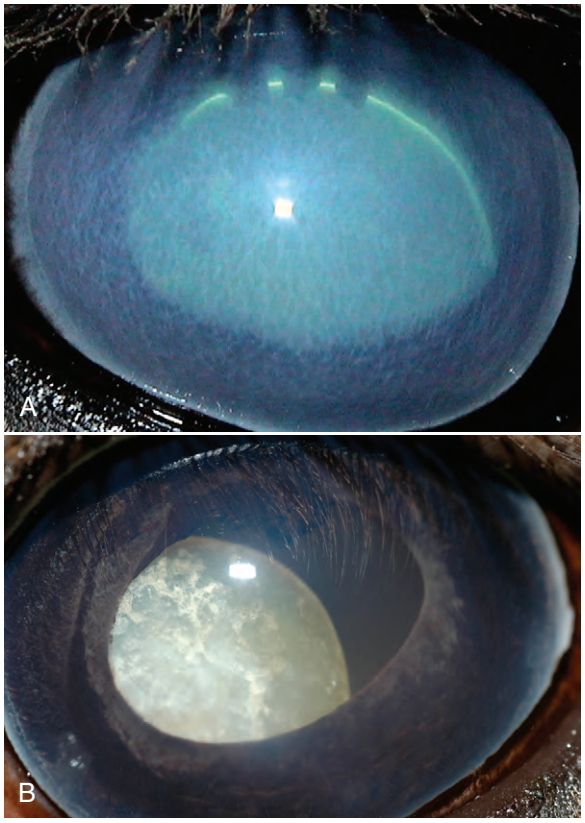


Figure 7-23. **A,** Superior subluxation associated with chronic equine recurrent uveitis and secondary glaucoma. Although the cornea is diffusely edematous, the edge of the lens is readily identified during direct retroillumination. **B,** Subluxation and mature cataract in a young Warmblood gelding. Note large aphakic crescent within temporal aspect of pupil.

and corneal edema, which may indicate inflammation, glaucoma, or anterior lens luxation.

Intracapsular lens extraction has historically been recommended in cases of lens luxation in an attempt to preserve vision.[9,10,61,62] Recent retrospective long-term evaluation in such cases has revealed that surgical intervention is coupled with an extremely poor prognosis for both retention of vision and the globe.[60] However, prior to surgical intervention being considered, an attempt should be made to determine the underlying cause for the displacement. Because extensive uveal tissue damage may be incurred as a result of the underlying uveitis or trauma precluding lens luxation, phthisis bulbi or blindness associated with retinal degeneration may result, especially in cases involving posterior lens luxation.[55,63] As an alternative to lens removal in uncomfortable blind eyes with secondary lens luxation, enucleation or evisceration with insertion of intrascleral silicone prosthesis may be considered.[64-68]

LENS CAPSULE RUPTURE

Blunt and penetrating ocular trauma is relatively common in the horse, and lens capsule rupture may be incurred as a result. Lens capsule ruptures are usually associated with rupture, laceration, or puncture of the cornea or sclera. Uveal or retinal tissue exposure as well as herniated lens material may develop leading to severe uveitis or blindness.[9,61,69]

CLINICAL APPEARANCE

Any penetrating ocular injury has the potential to cause damage to the lens capsule, and corneal lacerations are relatively common in the horse.[46,70-73] Thorough evaluation of the lens capsule is required following any case involving penetrating or perforating corneal injuries. The inherent nature of such injuries often make it difficult, if not impossible, to adequately

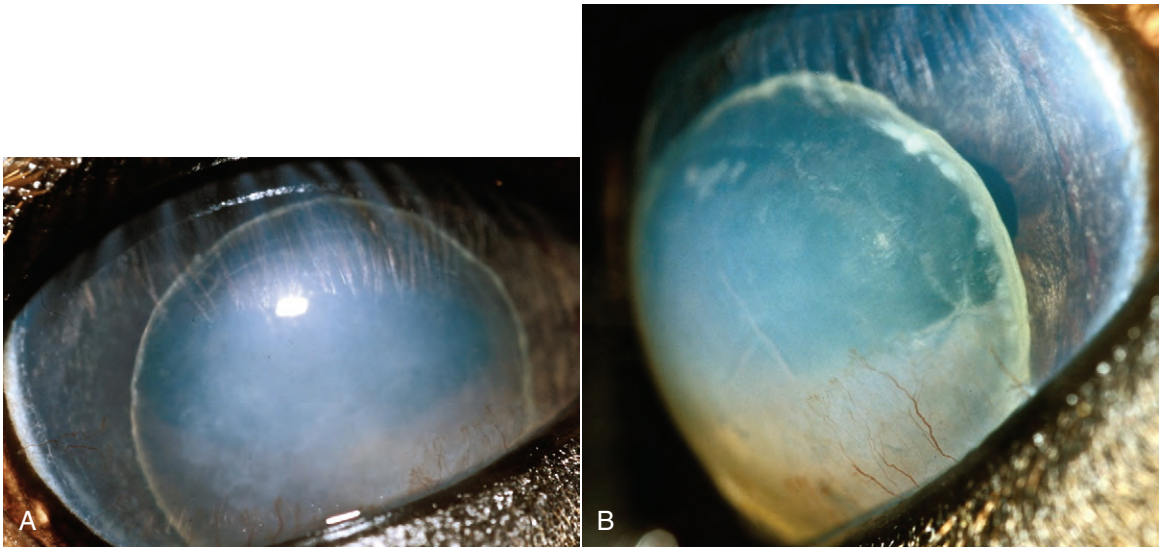


Figure 7-24. **A,** Anterior lens luxation in an 18-year-old Warmblood gelding. Note mild, diffuse corneal edema, inferior corneal vascularization, and immature cataract. **B,** Immature cataract and corneal vascularization are more readily appreciated in this oblique view of the anteriorly luxated lens. Note edge of pupil just beyond the temporal edge of the lens.

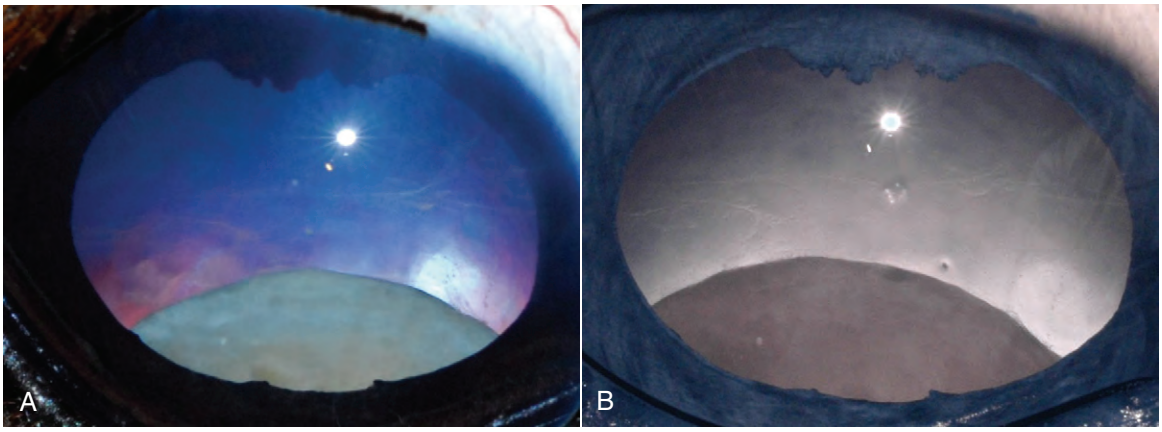


Figure 7-25. **A,** Posterior lens luxation in a 16-year-old Quarter Horse gelding. **B,** Infrared. Superior aspect of the posteriorly luxated lens is readily identified as a bluish-gray half moon within the inferior pupil.

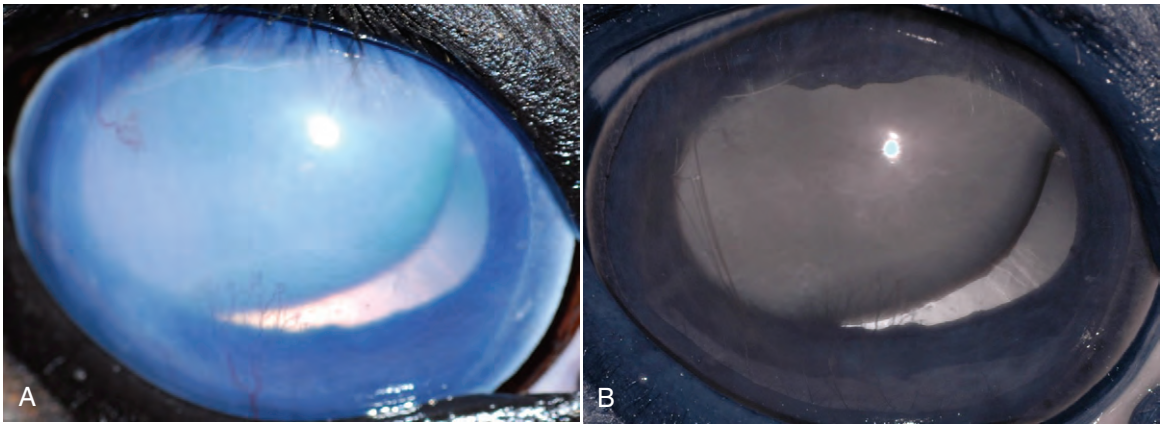


Figure 7-26. **A,** Medial lens coloboma as seen during direct retroillumination through a diffusely edematous cornea. Note superficial corneal vascularization associated with chronic keratitis. **B,** Infrared. View of lens is enhanced. Note zonular attachments along inferior edge of lens. There is a flat spot in the lens between the 2 and 4 o'clock positions and a notch (not completely visible in this image) in the lens between 2 and 3 o'clock.

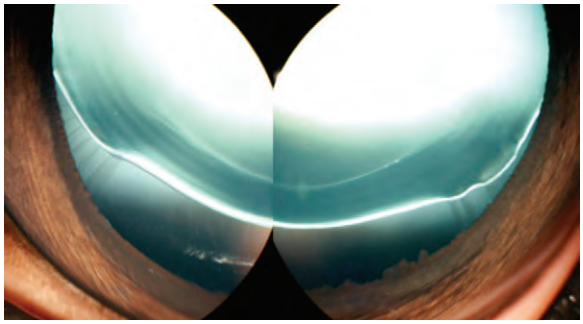


Figure 7-27. This photomontage demonstrates a lens coloboma in a young Warmblood stallion. Note lack of zonular attachments along the inferior border of the lens. Distinct notches in the inferior lens can be seen at the 4 and 8 o'clock positions and represent a transition from an area of zonular attachment to an area devoid of those attachments.

Figure 7-28. Medial lens subluxation in a horse with chronic equine recurrent uveitis and secondary glaucoma. Note multiple focal posterior synechiae, complete mature cataract, and vitreal adhesions along medial lens border.

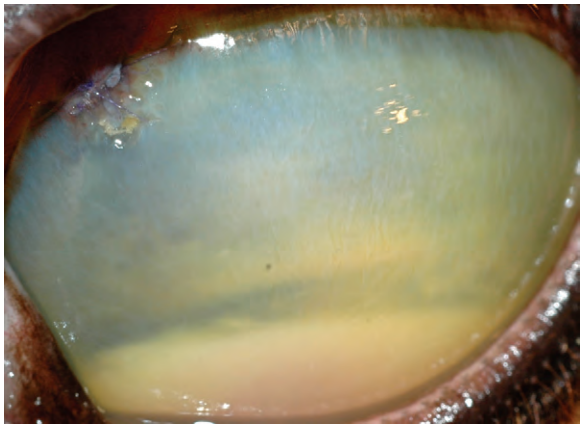


Figure 7-29. Severe endophthalmitis that developed approximately 3 weeks post phacoemulsification. This eye did not receive an intraocular lens.

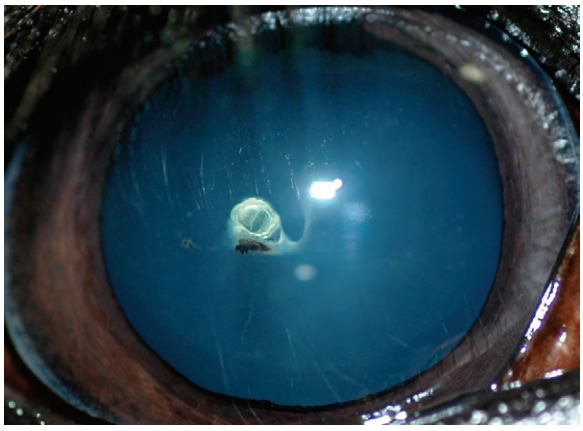


Figure 7-30. Small focal subepithelial anterior lens capsule cyst. Pigment deposition inferior to the cyst is suggestive of a previous rupture of the cyst, resulting in a bout of lens-induced uveitis.

evaluate the lens capsule simply using direct ophthalmoscopy or slit-lamp biomicroscopy. Ocular ultrasonography, or if available, high-resolution ocular ultrasonography, should be performed to increase the probability of identifying a disruption of the anterior lens capsule.[14,74-77]

In severe cases, the anterior chamber may be collapsed, uveal prolapse may be present, and lens material may be extruding from the lens capsule or corneal wound. Even in cases without full-thickness corneal defects, signs of anterior uveitis will usually be present and include fibrin formation, hyphema, and miosis, making examination of the lens nearly impossible. Clinical evaluation of the lens can be facilitated by removal of the intraocular fibrin, irrigating the anterior chamber, and dilating the pupil with dilute (1:10,000) intracameral epinephrine, with the horse in lateral recumbency under general anesthesia prior to surgical correction of the corneal defect.[55] It is important to have the animal paralyzed or to have performed a retrobulbar block in order to fully manipulate the globe and minimize tension from the extraocular muscles when performing these procedures.

COMMON DIFFERENTIAL DIAGNOSES

Chronic and insidious intraocular inflammation may torment a horse following a penetrating ocular injury. Endophthalmitis may be caused by intraocular sequestration of bacterial or fungal organisms, deposition of foreign material such as plant debris, the release of lens proteins, and/or an unrelenting inflammatory response to these insults (Fig. 7-29). Thorough ocular examination, aerobic and anaerobic bacterial and fungal culture and sensitivity of corneal scrapings and intraocular fluids, as well as ocular ultrasonography are necessary to help identify the underlying cause of the ocular inflammation prior to deciding which medical or surgical approach is most appropriate.

Anterior subepithelial cysts (Fig. 7-30) are an additional poorly characterized ocular disease that appears to involve the anterior subcapsular epithelium and/or subepithelial anterior cortex. They should be considered when confronted with a case of recurrent anterior uveitis or ocular trauma with anterior lens involvement. Although very little information exists on this presumably congenital abnormality, it is being identified with increasing frequency (Fig. 7-31). Usually, horses will present with a history and/or clinical signs of chronic recurrent uveitis (i.e., blepharospasm, epiphora, and miosis with mild aqueous flare) that are associated with active and quiescent periods of inflammation. Generally, these lesions respond rapidly to topical and systemic antiinflammatory medications and topical mydriatics, with signs subsiding within 1 or 2 weeks. As with chronic recurrent uveitis, however, they tend to go through a vaguely

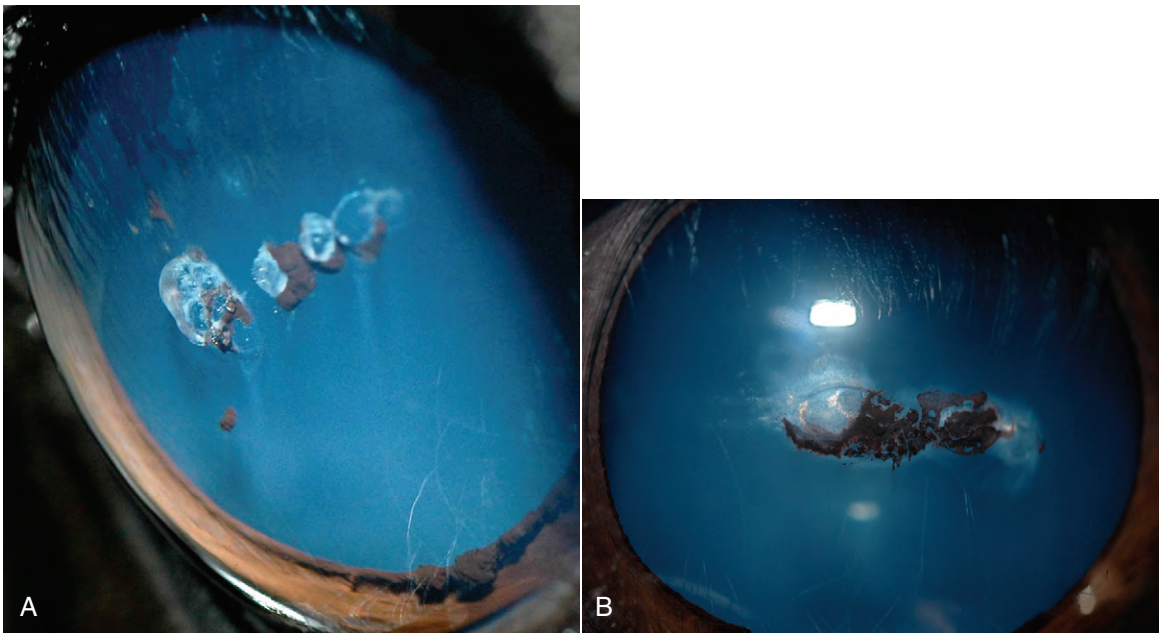


Figure 7-31. **A,** Multiple subepithelial anterior lens capsule cysts with significant vesicle formation and associated pigment deposition. **B,** Contralateral eye to the one depicted in **A.** Note pigment deposition associated with axial anterior lens capsule and anterior cortical opacification. There is a distinct rim of fibrosis within the anterior lens capsule (hemicircle superior to the pigment deposition in the left side of the image) that represents the base of a previously ruptured cyst.

predictable period of quiescence prior to additional phases of acute inflammation. With the exception of pigment deposition surrounding the cystic lesion on the anterior lens capsule, the iris itself does not usually show signs of chronic inflammation (i.e., corpora nigra degeneration, iridal hyperpigmentation). Cases that prove more resistant to tradition medical therapy alone may benefit from surgical implantation of a suprachoroidal cyclosporine implant[78,79] for long-term suppression of inflammation or lens extraction with intraocular lens implantation if the lesion is large enough that it is also affecting vision.[10,16]

TREATMENT

Surgical lens removal is the treatment of choice in dogs following capsule rupture and should be performed at the same time as surgical correction of the corneoscleral injuries.[66,69,80] Although little information pertaining to this manifestation of lens disease in the horse has been published, phacoemulsification following acute anterior lens capsule rupture has been successfully performed.[81] Prognosis for vision is poor following blunt trauma, because it can result in cataract development, lens capsule rupture, and staphylomas at the limbus[66] and subsequent retinal detachment. Evisceration with intrascleral silicone prosthesis or enucleation may be indicated.[62,64,67,68]

EVALUATION AND TREATMENT OF CATARACTS

EVALUATION OF THE EQUINE PATIENT WITH CATARACTS

An ophthalmic examination should be a routine part of any prepurchase or insurance examination and should be conducted during the initial physical examination on all newborn foals.[26,62,83] Prompt and complete pupillary light responses (PLRs) and a blink response to bright light (dazzle) are generally indicative of adequate retinal function.[62] A focal light source such as a penlight or Finnoff transilluminator generally allows for identification of diffuse or focal axial cataracts (Fig. 7-32), but complete evaluation of the lens requires pharmacologic mydriasis.[61] Two doses of topical 1% tropicamide, 0.1 to 0.2 mL topically at 5-minute intervals, will generally provide adequate mydriasis of the equine pupil to facilitate ophthalmic examination within 15 to 30 minutes. Focal incipient cataracts (Fig. 7-33) do not prevent evaluation of the equine ocular fundus. However, if diffuse cataracts are present, both ocular ultrasonography[14] and electroretinography[84] should be performed (see Chapter 1 for more details) to evaluate retinal integrity and function.[10,55,61]

MEDICAL MANAGEMENT OF CATARACTS

Medical therapy that prevents cataract progression in clinical patients is not available.[85,86] Pharmacologic mydriasis has been used in an attempt to increase the visual potential in horses with focal axial or nuclear cataracts. One percent atropine ointment or solution is applied topically once daily until complete mydriasis is achieved, at which time the frequency of administration is reduced to a frequency necessary to maintain the pupil in a dilated state.[9,26,51] Photophobia may be associated with prolonged mydriasis and commonly manifests as lacrimation and blepharospasm in response to bright light.[55] Horses that develop photophobia as a result of the previously described treatment should have the administration of atropine stopped and should be sheltered from bright light until the effects of atropinization have subsided. The effects can take more than 14 days to subside in the normal equine eye.[87]

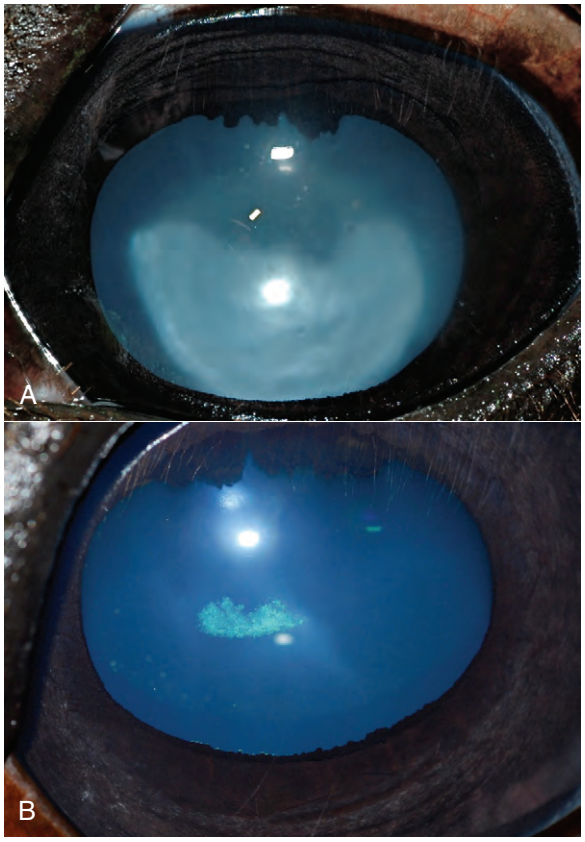


Figure 7-32. **A,** Focal, axial, subcapsular, posterior cortical cataract. **B,** Focal, axial, subcapsular, anterior cortical cataract.

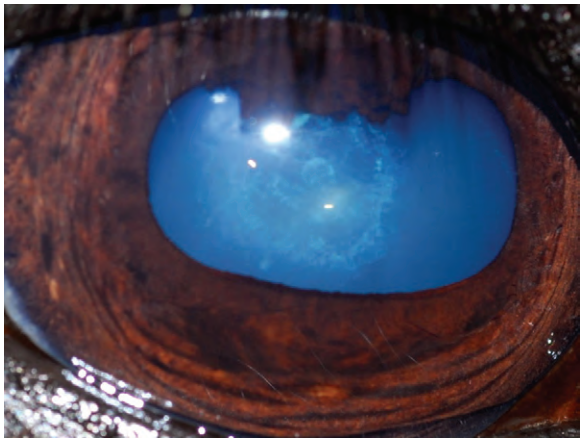


Figure 7-33. Diffuse, anterior subcapsular, incipient anterior cortical cataract.

SELECTION OF PATIENTS FOR CATARACT SURGERY

The decision to treat cataracts in the horse is one wrought with both philosophical and ethical concerns. The question of liability is one that must be addressed, especially in the context of injury to a rider following lens-extraction surgery that leaves the horse with less than optimal vision. Vision in every horse that has had cataract surgery should be considered compromised, even those horses that have received an intraocular lens (IOL) implant. Cataract surgery in horses, as well as the pre- and postoperative treatment periods, represent challenges to the clinician. Both the size of the eye and the animal's mass provide certain obstacles that must first be overcome prior to surgical intervention being considered successful. The horse's potential for return to function must also be considered thoroughly.

Although postoperative vision in the aphakic horse has recently been reported as being functionally normal,[31,47,88-90] aphakia has historically been considered to result in significant visual impairment.[9,10,30,89] Current methods routinely used to evaluate vision in the horse are very crude and consequently provide only a subjective and rudimentary assessment of a horse's ability to see.[31] The aphakic equine globe (Fig. 7-34) has been reported as being markedly hyperopic.[47,89] The average refractive error of the adult equine globe is +9.5 D (n = 14, range +7.5 to +10 D).[47,89,91,92] Despite this marked degree of ametropia and the limited number of cases with long-term follow-up, horses were considered to have no visual difficulties; in some, vision was considered to be as good as it was prior to the development of cataracts.[88,89] A recent report by Fife et al. reported favorable short-term visual results following equine cataract surgery over a 10-year period, but long-term follow-up (1 year or more) was only available for 13 of the eyes originally undergoing phacoemulsification.[31] None of the horses received an IOL implant, nor were they refracted postoperatively. Visual function was assessed using standard diagnostic tests (i.e., PLR, menace, dazzle, and behavioral testing) and relied to a large extent on responses from owners or referring veterinarians.[31] It has been eloquently stated that the perception of vision may be more affected by the limitations of one's ability to accurately evaluate the visual performance of the horse.[93]

The age of the horse at the time of surgery has historically been an important variable associated with a successful outcome following lens extraction in horses. Recently, most of the publications pertaining to equine cataract surgery have represented a wide age range, with cataract surgery in adult horses receiving increasingly more attention.*

The age of the equine patient at the time of surgery may also influence the postoperative success rate.[55] A condition known as *deprivation amblyopia* has been described in children with congenital cataracts and in laboratory animals deprived of early vision.[55,97-100] Vision is decreased in one or both eyes subsequent to central fixation disuse as a result of ocular opacities.[98] The potential for deprivation amblyopia should be considered in foals presenting for cataract surgery. This would dictate that early surgical intervention should be recommended for foals with congenital cataracts.[10,30,98,100] The incidence of deprivation amblyopia has not been ascertained in older foals following extraction of congenital cataracts.[55] Congenital cataracts, if left untreated, may progress to hypermature cataracts as the animal ages, and lens-induced uveitis may develop. The severity and duration of the intraocular inflammation may increase the likelihood of postoperative complications such as ocular hypertension or secondary glaucoma (Fig. 7-35).[10,62]

In the past, it has been suggested that younger foals were more suitable for cataract surgery because their smaller size

*References 31, 53, 63, 88, 89, and 94-96.

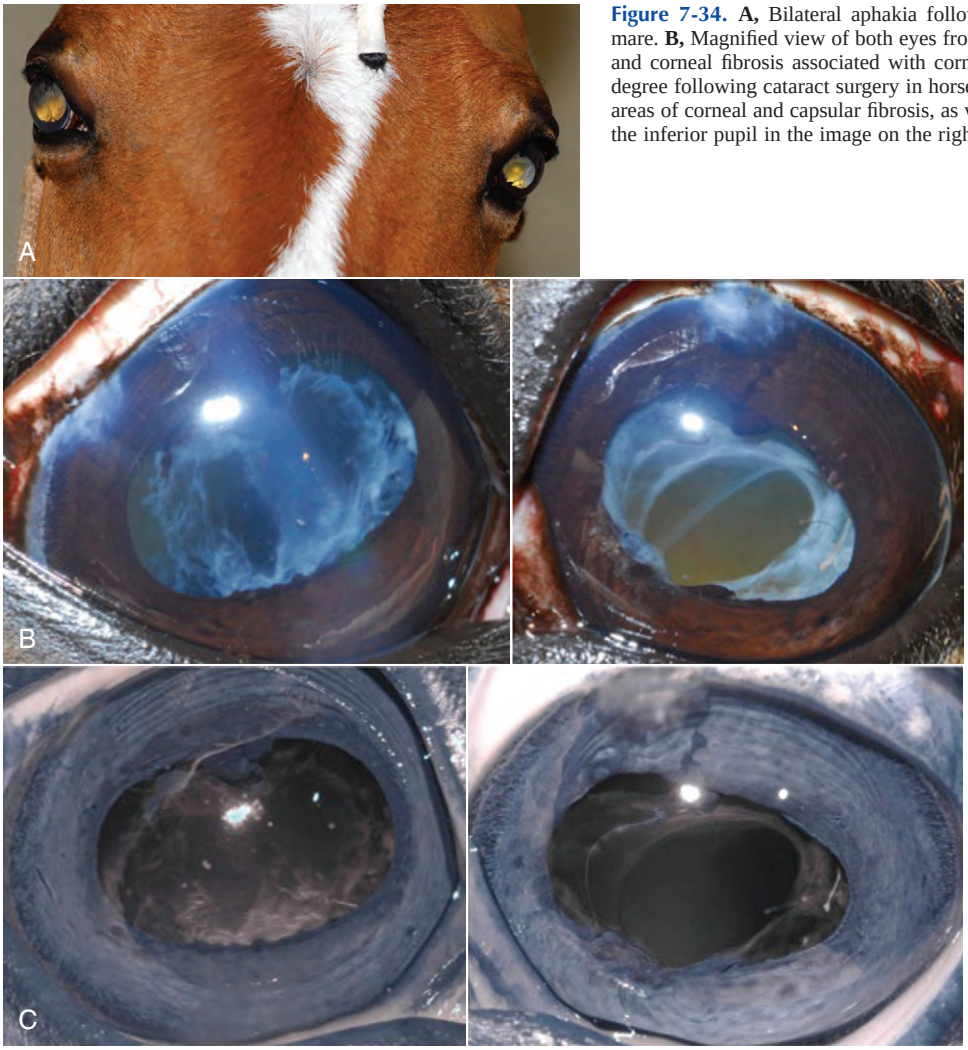


Figure 7-34. **A,** Bilateral aphakia following phacoemulsification in a 13-year-old pony mare. **B,** Magnified view of both eyes from **A.** Note anterior and posterior capsular fibrosis and corneal fibrosis associated with corneal incisions. These are to be expected to some degree following cataract surgery in horses. **C,** Infrared. Enhanced view of the more dense areas of corneal and capsular fibrosis, as well as focal posterior synechiae, especially along the inferior pupil in the image on the right.

made them easier to restrain, thus facilitating postoperative ocular medication. The temperament of the foal should be such that it allows for frequent handling and treatment.[10,48,59,101] Foals that are accustomed to frequent handling and are halter-trained are preferred candidates for cataract surgery, as they are more likely to tolerate postoperative treatments with minimal risk to themselves or the personnel administering the medication.* Previous studies evaluating the results of cataract surgery in foals demonstrated that foals younger than 6 months of age were more likely to have a positive outcome following cataract surgery.[48,101,102] Foals older than 6 months of age were found to be more difficult to medicate topically following surgery and were more likely to have hypermature cataracts. Therefore, the best postoperative prognosis was reserved for halter-trained foals amenable to regular handling and possessing a docile demeanor.[48,88,102] Since then, several reports describing successful cataract surgery in the adult horse have been published.[31,47,63,89,94-96]

*References 10, 30, 48, 59, 66, 88, 90, and 101.

Concomitant systemic problems or additional ocular anomalies may justify postponement or denial of cataract surgery. Foals should have thoracic radiographs taken in addition to routine preoperative blood screening to rule out *Rhodococcus* spp. or other infections.[55-103]

Once it has been determined that a cataract is present, complete examination of the ocular and adnexal structures should be carried out to identify any additional congenital or acquired abnormalities. Foals with complete congenital cataracts associated with blindness are potential candidates for surgery. Careful evaluation of the eyelids, conjunctiva, and cornea should reveal any concomitant congenital or acquired diseases present requiring treatment prior to cataract surgery.[10,48,62] Retinal function can be confirmed with the presence of brisk pupillary light responses (PLRs), a blink response to bright light (dazzle), and an electroretinogram (ERG).[10,62,83,84,104]

Congenital stationary night blindness has been reported in the Appaloosa, Thoroughbred, and Paso Fino breeds.[105-109] Preoperative ERG should be considered mandatory in the aforementioned breeds and is recommended in any potential equine cataract surgery candidate. Other congenital ocular

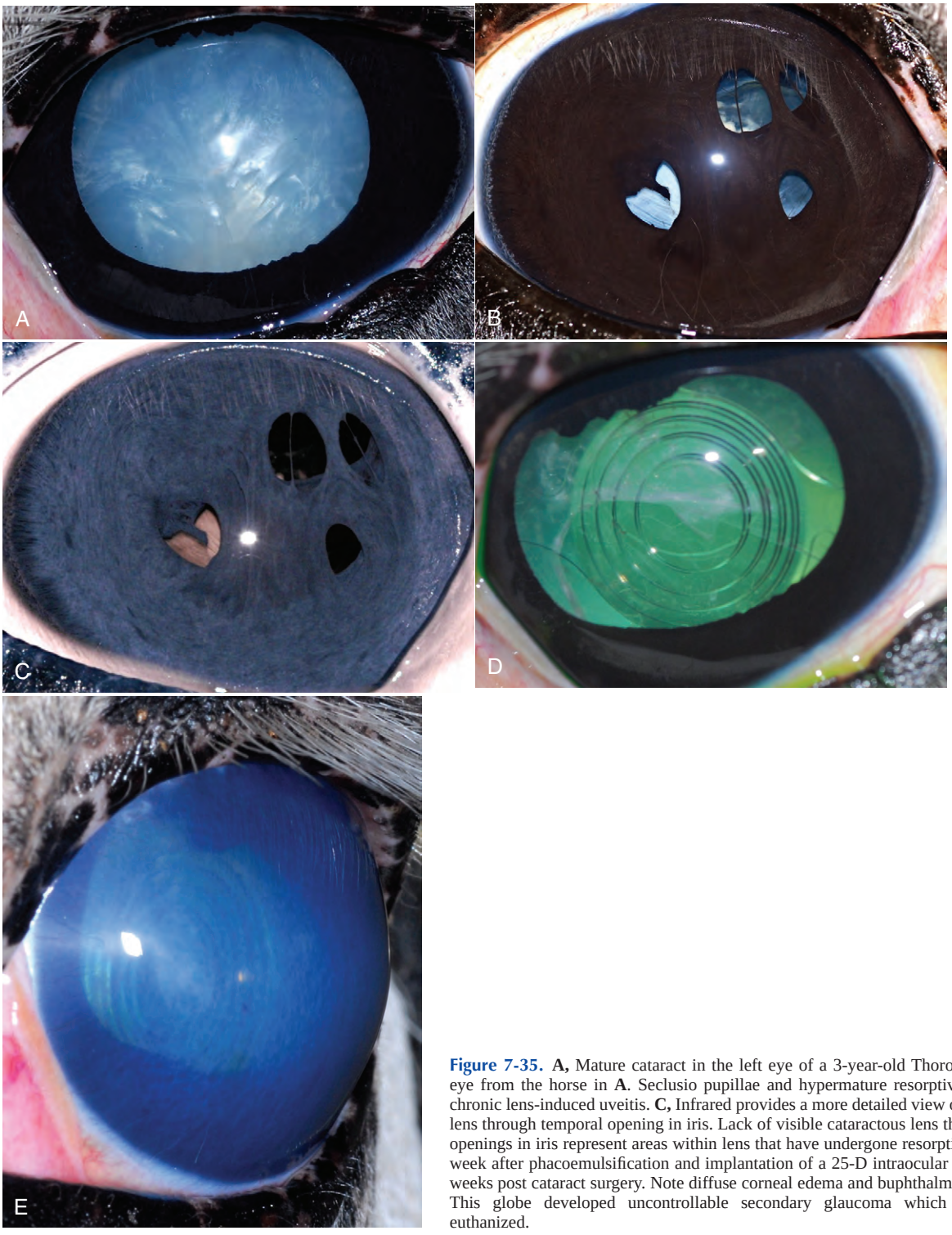


Figure 7-35. A, Mature cataract in the left eye of a 3-year-old Thoroughbred gelding. **B,** Right eye from the horse in **A**. Seclusio pupillae and hypermature resorptive cataract associated with chronic lens-induced uveitis. **C,** Infrared provides a more detailed view of the iris. Note cataractous lens through temporal opening in iris. Lack of visible cataractous lens through other three (medial) openings in iris represent areas within lens that have undergone resorption. **D,** Same eye as in **A** 1 week after phacoemulsification and implantation of a 25-D intraocular lens (IOL). **E,** Same eye 8 weeks post cataract surgery. Note diffuse corneal edema and buphthalmic appearance of the globe. This globe developed uncontrollable secondary glaucoma which led to the horse being euthanized.

anomalies with the potential to cause blindness regardless of the condition of the lens are generally considered a contraindication to cataract surgery. They include retinal detachment and optic nerve hypoplasia.[10,30] Microphthalmia is also considered a contraindication to cataract surgery, but mild cases have undergone lens extraction surgery with favorable results.[10,30,88]

Use of subpalpebral lavage systems allow postoperative medication protocols to be more easily followed because they increase the ease in topical medication application (Fig. 7-36).[110,111] Commercially available subpalpebral lavage kits are available, and as a result, a potential surgical candidate's attitude and demeanor play only a minor role in the preoperative decision-making process.

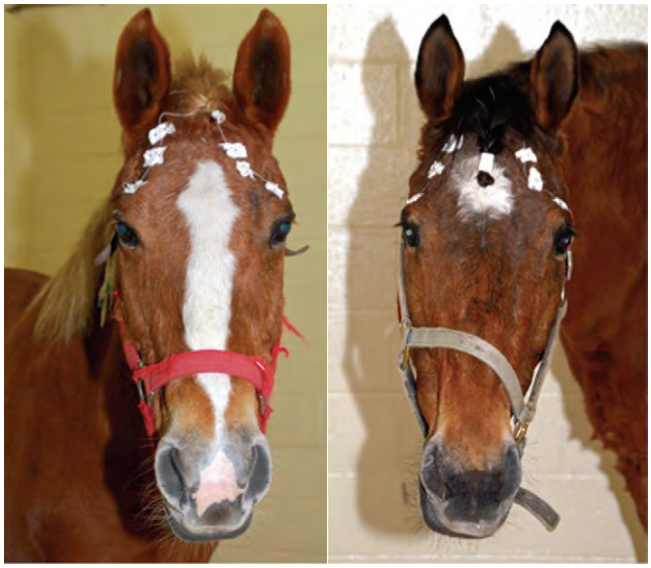


Figure 7-36. Bilateral, superior eyelid subpalpebral lavage systems (SPL) in two horses prior to bilateral phacoemulsification and subsequent intraocular lens implantation. The SPLs greatly facilitate pre- and postoperative ophthalmic medications.

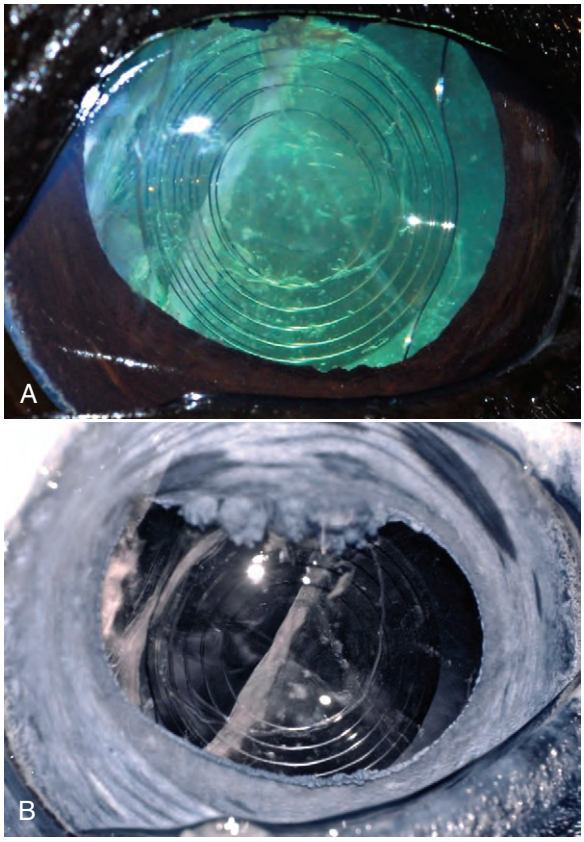


Figure 7-37. A, Postoperative photograph of an 18-D foldable equine intraocular lens (IOL) implant in a 23-year-old Walking Horse gelding. The haptics are in a vertical position because of preexisting posterior and medial capsular tears that prevented horizontal positioning. **B,** Infrared. One of the fibrotic edges of the posterior capsular tear can be seen passing directly behind the IOL optic. Note the white material at the medial aspect of the pupil. This is lens material that had been extruded through a medial equatorial lens capsule tear at some point prior to presentation for cataract surgery evaluation. See Fig. 7-42 for a preoperative view of this horse's cataract.

Much progress has been made over the past few years in the development of an appropriate equine intraocular lens implant (IOL).[63,96,112-114] Although much work remains to be performed before a universal equine IOL can be recommended, our current recommendation is that an IOL should be placed in any equine globe that undergoes lens extraction unless intraoperative complications prevent its insertion (Fig. 7-37). Postoperatively, horses that have received an IOL subjectively appear to have much better vision than aphakic horses, even in horses with a marked myopic refractive error.[96]

Extensive owner education is necessary prior to equine cataract surgery. The owner should be informed that their horse will require prolonged aftercare for at least 3 months postoperatively, even if there are no immediate, short-term, or long-term complications associated with the surgery. Also, owners should be cautioned that vision in the eye(s) undergoing lens extraction, with or without IOL implantation, will not be normal after surgery. It is not possible at this time to make accurate predictions as to how well a horse will see following cataract surgery. Postoperative assessment of vision will rely on reports from the owner, referring veterinarian, and follow-up ophthalmic examinations and visual testing, and should also include ocular ultrasonography and streak retinoscopy.

PRESURGICAL DIAGNOSTIC TESTING

Any horse that is a potential candidate for cataract surgery, regardless of age, should be otherwise healthy and amenable to prolonged medical therapy. Any concurrent health problems and ophthalmic disease or abnormalities should be addressed and treated if necessary prior to scheduling elective cataract surgery.

In foals, special attention should be paid to the respiratory tract. A thorough pulmonary examination including auscultation and thoracic radiographs and ultrasonography are recommended to rule out subclinical or insidious pulmonary diseases.

A complete preoperative evaluation of the potential surgical candidate should be performed and include a complete history (including current and previous medical therapy), physical, and ophthalmic examination. Preanesthetic evaluation should also include a complete blood count (CBC) and serum chemistry profile (Chem) with fibrinogen (Box 7-1).

If the cataracts are determined or suspected to be congenital, the animal should be closely examined for evidence of additional general or ophthalmic congenital defects. Similar precautions should be taken if trauma or uveitis is suspected. In these cases, thorough evaluation of the uveal tract, vitreous, and retina is of prime importance.

A thorough and detailed history should reveal when the owner or handler initially noticed visual deficits and whether they can be associated with any specific time of day. If the animal's vision is more severely affected under normal daylight conditions, cataracts may likely be the reason. However, if vision is adversely affected in poor or dim lighting, retinal degeneration may be responsible. Some foals or horses with visual deficits may be presented to the veterinarian with a history of repeated cuts and abrasions to the face, chest, and forelimbs or may be suspected of having neurologic or gait

Box 7-1 | Preoperative Diagnostic Tests for Equine Cataract Surgery Patients

Ocular examination
Tonometry
Electroretinography (ERG)
Streak retinoscopy
- Perform on contralateral eye if no cataract is present

Ocular ultrasonography
- Axial globe length (AxL)
- Anterior chamber depth (ACD)
- Crystalline lens thickness (CLT)
- Vitreal chamber depth (Vitr)

CBC/serum chemistry/fibrinogen
Subpalpebral lavage system (SPL) placement

abnormalities. In addition to thorough physical and ocular examination, additional diagnostic testing in the form of an ERG is indicated.

A complete ophthalmic examination is an essential part of the preoperative evaluation of the potential cataract surgery candidate. Evaluation of vision is performed as part of this examination and may include observation of the animal in an obstacle course setting, alternately blindfolding each of the eyes in order to observe subtle changes in performance. Standard tests including menace, dazzle, and direct and consensual PLRs should also be done. This should be followed by thorough examination of the orbit and eyelids, the nictitating membrane, conjunctiva, cornea, anterior chamber, iris, lens, and if visualization is possible, the vitreous, retina, and optic disc. Ocular examination is facilitated if performed in a semidark, quiet examination room, stall, or isolated area of the barn. A focal light source, such as a transilluminator or portable handheld slit lamp, is used to perform the examination. Additional instrumentation includes direct ophthalmoscope, head-mounted indirect ophthalmoscope, and condensing lenses (14 D, 20 D and 28 D). For details regarding their use, please refer to Chapter 1. Pupillary light responses, Schirmer tear tests, and intraocular pressure (IOP) measurements with an applanation (Tono-Pen) or rebound (TonoVet) tonometer should be performed prior to the pupils being dilated.

Tropicamide 1%, a short-acting mydriatic agent, is applied topically to facilitate dilation of the pupil, allowing complete evaluation of the lens (grading and staging of the cataract), vitreous, retina, and optic disc. Two-tenths of a milliliter of tropicamide is applied to the cornea via a 1-mL syringe with a 25-gauge needle hub (needle broken off at the tip of the hub) attached. Application may be repeated at 5- to 10-minute intervals, and maximal dilation can be expected after 20 or 30 minutes. One or two applications are typically sufficient.

Various concomitant ocular diseases may be a contraindication for elective lens removal or may increase the risk of intra- or postoperative complications. Examples of diseases that can potentially complicate surgical intervention if not eliminated prior to lens removal are distichiasis, entropion, keratoconjunctivitis sicca, and corneal ulceration. Examples of more serious ocular diseases that may not only complicate surgical intervention, but may also serve as a contraindication include immune-mediated keratitis (Fig. 7-38), ERU (Fig. 7-39), lens subluxation

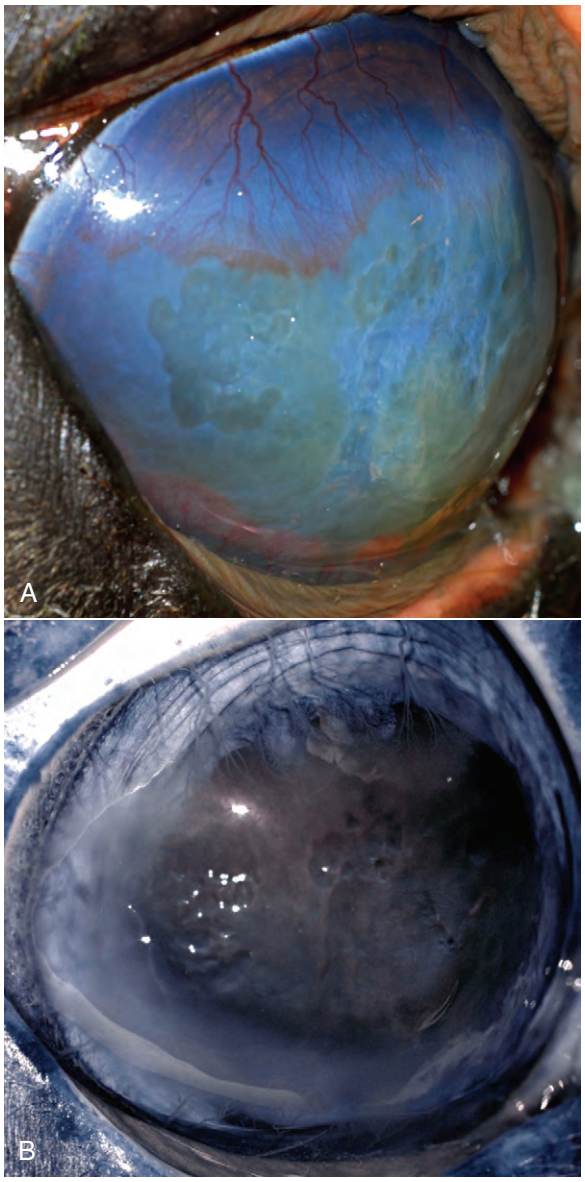


Figure 7-38. A, Chronic immune-mediated keratitis (IMMK). **B,** Infrared. Note thick peripheral corneal vessels. Although the cornea is diffusely edematous, a decent view of the pupil can be obtained using this photographic technique.[134]

with or without vitreal presentation into the anterior chamber (Fig. 7-40), and retinal diseases (retinal degeneration or retinal detachment [Fig. 7-41]). However, advances in the treatment of ERU and improvements in equine phacoemulsification techniques and instrumentation have recently led to favorable results in several cases that would have been previously deemed unsuitable for surgery (Fig. 7-42).[53,63,96,113]

Additional diagnostic testing in the form of an ERG and ocular ultrasonography should be performed as part of every presurgical equine cataract patient workup. Both of these tests reveal information about the posterior segment that cannot be obtained (or may be missed) during routine ophthalmic examination. Cataract formation is a complication associated with ERU, and as a result, concomitant retinal involvement must be

Figure 7-39. Chronic changes associated with equine recurrent uveitis and secondary glaucoma. Note multiple Haab's striae, subluxated cataractous lens, extensive posterior synechiae, and corpora nigra degeneration.

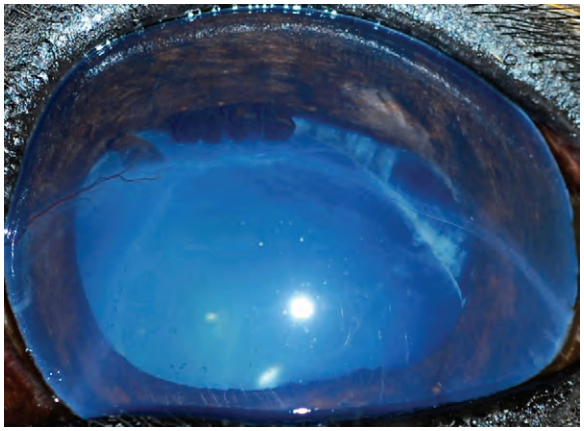


Figure 7-40. Lens subluxation associated with chronic uveitis. Note vitreal presentation within the space between the superior edge of the lens and the margin of the pupil.

ruled out prior to recommending the horse for surgery. Both ERG and ocular ultrasonography are standard preoperative diagnostic tests used routinely in small animal ophthalmology. Both of these procedures can adequately be performed on the standing, sedated horse, so every effort should be made to make them routine procedures in equine ophthalmology as well.[14,84,96,112] Ocular ultrasonography is an important tool used to identify preexisting lens or vitreal abnormalities and to rule out retinal diseases as part of the preoperative cataract patient evaluation.* Additionally, the data generated, collected, and evaluated on the various globe dimensions (i.e., anterior chamber depth [ACD], crystalline lens thickness [CLT], vitreal

*References 14, 75, 77, 96, 102, and 115-117.

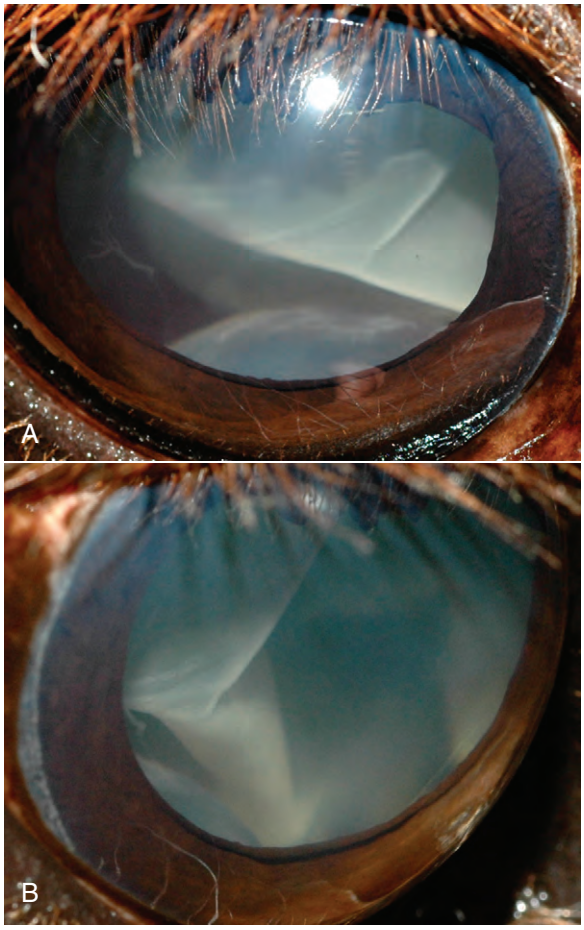


Figure 7-41. **A,** Complete retinal detachment seen as a veil of white material within the pupil. The superior edge of the posteriorly luxated lens can been seen near the inferior margin of the pupil. **B,** Anterior oblique view of the detached retina through the dilated pupil.

chamber depth [Vitr], and axial globe length [AxL]) obtained using this examination technique are invaluable in the quest to develop an appropriate IOL for the horse.[96,112,114]

PREOPERATIVE CARE

The preoperative treatment protocol that has been used to successfully manage equine cataract patients at North Carolina State University is shown in Table 7-1. Placement of a subpalpebral lavage system the day prior to cataract surgery greatly facilitates the application of topical ophthalmic medications.[110,111] Preoperative medical management is extremely important and greatly influences the overall success in equine cataract patients undergoing surgical lens removal and subsequent lens replacement. Preoperative mydriasis is essential to ensure visualization of the lens during phacoemulsification as well as inhibit postoperative adhesions between the iris and anterior lens capsule (posterior synechia) and/or the cornea (anterior synechia). Mydriasis is facilitated with the topical application of 1% atropine sulfate ophthalmic solution. Several ocular diseases (i.e., ERU, uveitis secondary to trauma or severe corneal disease) can lead to the formation of posterior or anterior synechiae that may prevent complete mydriasis.

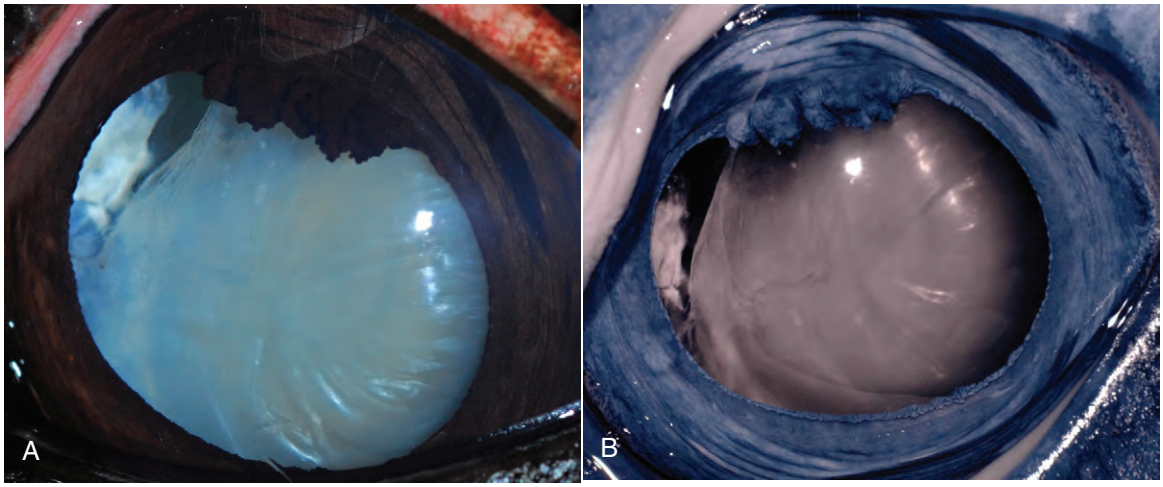


Figure 7-42. A, Mature cataract with a subluxation and equatorial lens capsule rupture at the medial aspect of the lens extending from 8 to 11 o'clock. The bright white material at the medial border of the pupil is extruded lens material. **B,** Infrared. The mature cataract appears bluish-gray within the pupil, and the extruded lens material can be readily observed at the medial aspect of the pupil.

Table 7-1 | **Preoperative Treatment Protocol for Equine Cataract Surgery Patients**

DRUG	DOSE & ROUTE OF ADMINISTRATION	FREQUENCY	DURATION
SYSTEMIC MEDICATIONS			
Penicillin	22,000 IU/kg, IV	q6h	24-48 hours
Gentamicin	6.6 mg/kg, IV	q24h	24-48 hours
Flunixin meglumine	1.1 mg/kg, IV, PO	q12h	10-14 days
	0.55 mg/kg, IV, PO	q12h	10-14 days
Omeprazole	2 mg/kg, PO	q24h	28 days
TOPICAL OPHTHALMIC MEDICATIONS			
Corticosteroids			
Neomycin-polymyxin B sulfates	0.2 mL, SPL	q6h	24 hours before surgery
Dexamethasone		q30min	2 hours before surgery
Antibiotics			
Neomycin-polymyxin B sulfates	0.2 mL, SPL	q6h	24 hours before surgery
Dexamethasone		q30min	2 hours before surgery
Moxifloxacin	0.2 mL, SPL	q2h	24 hours before surgery
Mydriatics			
Atropine sulfate 1%	0.2 mL, SPL	q12h	24 hours before surgery
Nonsteroidal Antiinflammatories (NSAIDs)			
Flurbiprofen	0.2 mL, SPL	q30min	2 hours before surgery

IU, International units; *IV*, intravenous; *kg*, kilogram body weight; *PO*, per os (oral); *SPL*, through subpalpebral lavage catheter.

Secondary infection of the globe following cataract surgery is a well-recognized and devastating complication in this species.[31,47,118] As a consequence, rigid pre- and postoperative antibiotic treatment protocols have been established to minimize the risk of this complication. All horses undergoing cataract surgery at North Carolina State University also receive a 24- to 48-hour course of intravenous antibiotics to minimize the risk of postoperative endophthalmitis.

Topical and systemic antiinflammatory medications are key in preventing or minimizing both pre- and postoperative ocular inflammation (uveitis). Systemic nonsteroidal antiinflammatory medications (NSAIDs) in combination with topical NSAIDs or glucocorticoids are very effective at preventing or controlling ocular inflammation in the horse.

ANESTHESIA

General anesthesia is required for horses having cataract surgery. Following induction, inhalant anesthetics are used for maintenance. The horse is positioned in lateral recumbency with the head elevated with pads, sandbags, and/or inflatable ring-shaped cushions (small, thick innertubes [Fig. 7-43]). It is essential that the head be positioned so that the iris is on a parallel plane with the ground. Any deviation from this parallel plane will result in difficulties in all aspects of the surgical procedure.

To facilitate proper globe position and minimize anterior vitreous presentation, either systemic paralytic muscle relaxants (e.g., atracurium, vecuronium, or pancuronium) or a retro-

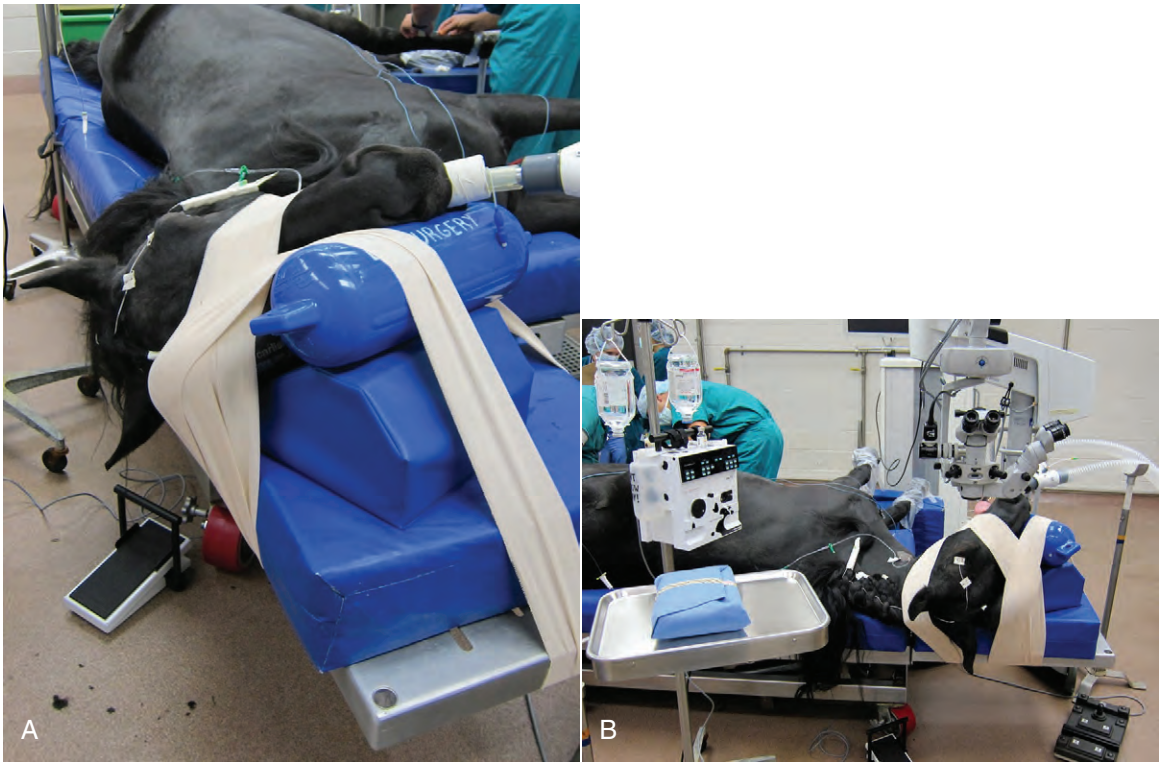


Figure 7-43. **A,** The horse's head is elevated using multiple pads and a small rubber innertube. Elastic tape is used to secure the patient's head to the table. **B,** This view shows the head position in relation to the horse's body, operating microscope, and the necessary surgical equipment to perform phacoemulsification.

bulbar block (see Chapter 1 for a description of this technique) will facilitate a motionless, slightly anteriorly displaced globe during phacoemulsification. Systemic paralyzation or a retrobulbar block also decrease the potential for the oculocardiac reflex and limit forward movement of the posterior lens capsule and vitreous during surgery by decreasing tension on the globe from extraocular muscles.[47]

SURGERY, PREPARATION, DRAPING, AND EQUIPMENT

Clipping of the periocular hair followed by aseptic preparation using 1:50 Betadine solution diluted in sterile saline solution are performed. Types of drapes used at the surgical site are at the discretion of the surgeon. Commonly, three or four Huck towels covered with a complete surgical drape (covering the head and neck with the eye shape cut out) or special adhesive ophthalmic drapes are used (Fig. 7-44). Intraocular instruments are standard for cataract surgery in most species, though some longer instruments have been devised for the larger equine eye. There are many phacoemulsification machines to choose from, including human machines or veterinary-specific machines. The phacoemulsification needles used in horses are typically longer than those used in canine or feline patients. Other newer choices include the phacoemulsification needle tips. These include flared tips as well as Kelman tips with or without a flare. These flared or angled tips are designed to engage the cataract better and emulsify the lens fragments more efficiently than the traditional needles, but there are only a limited number of different needle tips available for use with the equine-specific handpieces.

At present, three different (based on overall and optic dimensions) foldable, equine-specific acrylic IOLs are commercially available (Acrivet [S&V Technologies AG], Hennigsdorf, Germany). The different IOLs can be categorized by dioptric strength as well as total (haptic to haptic length) or optic diameter. The 14-D IOL comes in two sizes, with an optic diameter of 12 mm and a total length of 21 mm, or an optic diameter of 13 mm and a total diameter of 22 mm. These IOLs are generally recommended for implantation in foals following phacoemulsification of congenital cataracts, or in small ponies, respectively. The other IOLs have a dioptric strength of 21 D and 18 D and a total length of 24 mm. These lenses are recommended for implantation in adult horses, with the 18-D IOL being the current IOL of choice.[53,96] Special lens-holding forceps and implantation forceps, specifically designed for the horse, facilitate introduction of the IOL into the capsular bag following phacoemulsification.

SURGICAL TECHNIQUES

Four different surgical techniques have been previously described for the removal of equine cataracts: aspiration, extracapsular lens extraction, intracapsular lens extraction, and phacofragmentation (phacoemulsification) with aspiration.* Of

*References 10, 47, 48, 94, 102, and 119-123.

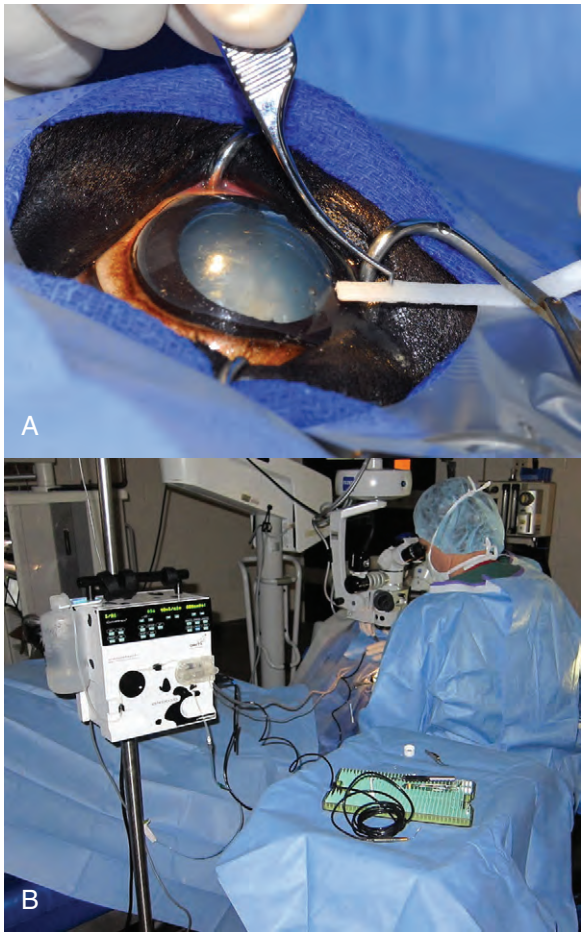


Figure 7-44. A, Head and periocular skin are draped with cloth drapes, and an adhesive aperture drape is used to cover the head and towels, leaving the eye exposed. **B,** Image demonstrates a fully draped horse during phacoemulsification.

these four, only phacoemulsification with aspiration can be recommended for modern routine cataract surgery. Although certain indications for both intra- and extracapsular lens extractions exist, they are infrequently encountered in most species. Clear corneal incisions or limbal-based incisions beneath a conjunctival flap serve as the surgical approach for the techniques listed. In young foals, it is often possible to aspirate the entire lens because of their soft, liquid state, and aspiration with or without phacoemulsification is recommended.

PHACOEMULSIFICATION WITH ASPIRATION

Small-incision phacoemulsification with aspiration utilizing instrumentation specifically modified for the equine eye is the current standard of care for cataract surgery in the horse.*

Following positioning, sterile preparation of the surgical site, and draping of the surgical field, an eyelid speculum is placed to maintain adequate exposure of the globe during surgery. Either a subconjunctival scleral-based incision[94] or a clear corneal incision (CCI) can be made to allow access to the anterior chamber. The choice to use either a scleral-based incision or a CCI is based on surgeon preference. The scleral-based approach has the advantage of positioning the incision farther away from the pupillary margin, reducing the risk of intraoperative iris/corpora nigra prolapse, and is potentially associated with less astigmatism. This type of incision is also covered by conjunctiva following primary closure.[10,94] A disadvantage of the scleral-based incision is hemorrhage that may gain access to the anterior chamber and obstruct the surgeon's view during the procedure. Commonly, a two-step (bilaminar) CCI is made parallel to, and approximately 1 to 2 mm into the clear cornea from the limbus, approximately 2 clock hours medial or lateral to the corpora nigra. An initial 4-mm corneal groove (approximately 90% corneal depth) is made using a #64 microsurgical blade (Beaver blade) followed by penetration of the remaining 10% corneal depth at approximately a 45-degree angle through the center of the initial groove incision using a tapered, beveled keratome (2.8 mm). The advantages of a clear corneal incision are lack of hemorrhage in the surgical field and ease of access to the lens owing to the angle of approach. Disadvantages of the CCI are possible scarring at the incision site (cosmetic) and potential corneal astigmatism induced by creation and closure of the incision. Clear corneal incisions are routinely closed with simple interrupted or continuous suture patterns using absorbable microsurgical suture material (8-0/9-0 polyglactin 910, Vicryl), with or without placement of a small conjunctival hood graft over the incision. A modification to the CCI described is the creation of a trilaminar (three-step) clear corneal incision that is truly self-sealing.[125,126] The initial groove is made as described earlier for the bilaminar CCI and followed by a 2-mm tunnel incision that is initiated at a depth of approximately 50% of the initial incision. The 2-mm tunnel is created by inserting a #64 microsurgical blade through the initial groove incision (depth of approximately 50%) and extending the blade axially, angling slightly toward the corneal endothelial surface. A small amount of viscoelastic material can then be injected through the initial groove and into the 2-mm tunnel to ensure that the correct plane is followed with the beveled keratome for final entry into the anterior chamber. Finally, a beveled keratome is inserted through the initial groove, and tunnel incisions and the remaining deep layers of the cornea are penetrated at an approximately 45-degree angle, allowing access to the anterior chamber (Fig. 7-45).

By performing the CCI in this manner, a proximal hinge is created at the base of the incision, which prevents the incision from leaking. This is especially advantageous in the horse, as it prevents the iris/corpora nigra from migrating to the corneal incision during phacoemulsification of the lens and aspiration of the cortex, as well as during insertion of the IOL following extension of the CCI. This technique allows for a completely formed anterior chamber throughout the surgical procedure and helps decrease the amount of viscoelastic utilized throughout the surgery (Figs. 7-46 and 7-47).

An anterior capsulotomy is performed to provide an opening through which the lens nucleus and cortex can be emulsified and aspirated. The capsulotomy can be performed traditionally as a capsulorhexis or alternatively with the assistance of high-frequency diathermy (Fig. 7-48). A traditional capsulorhexis is performed following penetration of the anterior lens capsule with either the tip of the beveled keratome immediately following penetration of the anterior chamber or multiple interconnecting stab incisions with a small-gauge needle (27-gauge) to

*References 31, 47, 53, 94, 95, 113, and 124.

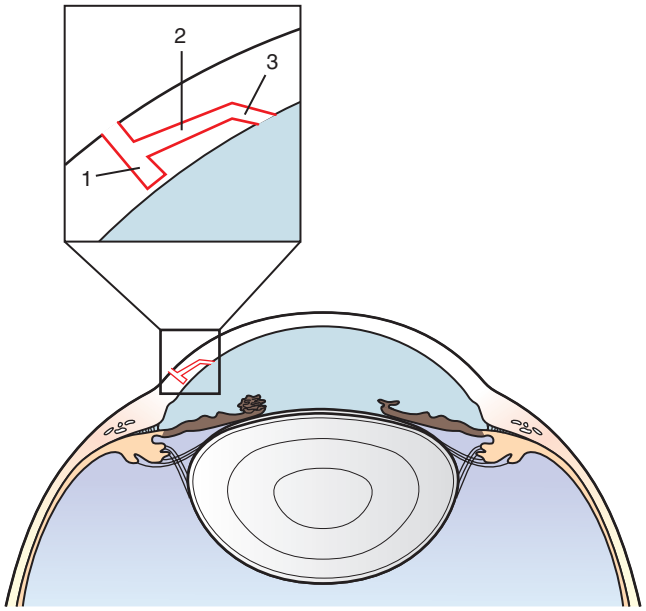


Figure 7-45. Illustration of a trilaminar clear corneal incision (CCI).[126,127] *1,* Initial groove made to a depth of approximately 90% corneal thickness. *2,* Stromal tunnel initiated from the initial groove at a depth of approximately 50%. This tunnel should have length of 2 mm and is angled slightly toward the posterior aspect of the cornea. *3,* Penetration of the posterior cornea (remainder of corneal stroma, Descemet's membrane, and corneal endothelium) is achieved by inserting a beveled keratome through the initial incision *(1)* and stromal tunnel[138] and entering the anterior chamber (AC) at an approximately 45-degree angle. A small amount of viscoelastic can be injected into the stromal tunnel[138] prior to insertion of the keratome to ensure placement into the original tissue plane.

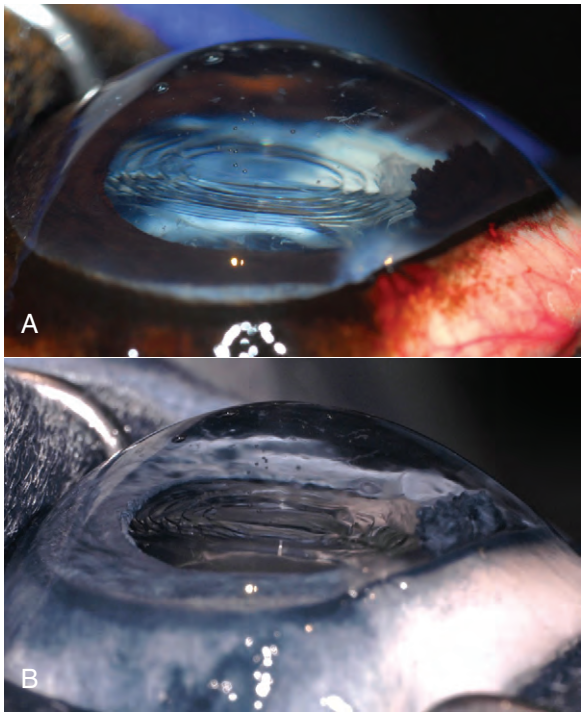


Figure 7-47. A, Same eye as in Fig. 7-42, demonstrating a formed anterior chamber (AC) and immediate postimplantation view of the 18-D foldable equine-specific intraocular lens (IOL) implant. **B,** Infrared. Note formed anterior chamber and IOL position. Small air bubbles suspended in the viscoelastic substance within the AC appear as small, dark, punctate areas in contrast to the lighter iridal background.

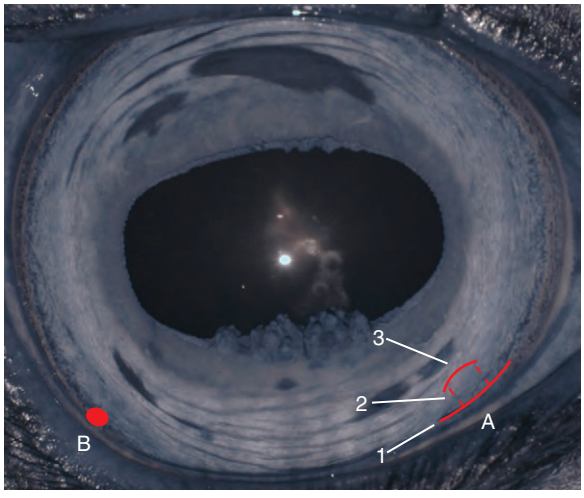


Figure 7-46. Infrared image of an equine globe, demonstrating trilaminar clear corneal incision (CCI) construction and placement of a second incision for a planned two-handed phacoemulsification procedure in the horse. *A,* Suggested position, temporal or medial to the corpora nigra, for construction of a trilaminar CCI (for details see Fig. 7-45). *B,* Placement of a second incision approximately 3 to 4 clock hours away from the CCI. Incision is created using a 20-gauge needle to tunnel through the cornea, beginning just posterior to the limbus. A second instrument, used to assist with phacoemulsification of the lens or manipulation of the intraocular lens (IOL) implant, can be introduced through this incision.

form a small curvilinear opening to allow insertion of Utrata forceps. The circular capsulorhexis is made by grasping the leading edge of the anterior lens capsule flap at the site of the initial incision and tearing the capsule in a clockwise manner, regrasping periodically to prevent radial tears, until the opposite side of the initial incision is reached. Once it has been ensured that the circular capsulotomy is no longer attached to the anterior lens capsule, it is removed from the anterior chamber. The capsulotomy should be approximately 1 mm smaller in diameter than the optic diameter of the IOL that will be inserted following phacoemulsification and aspiration of the lens. Use of a high-frequency diathermy tip to perform the capsulotomy greatly reduces the risk of radial tears and allows for a more accurately sized opening and consistent axial placement of the anterior lens capsule.[53,127]

Phacoemulsification with aspiration is the technique of choice for routine cataract surgery in the horse.[10,31,53,94-96] This technique involves the use of high-frequency ultrasonic vibrations to break down, or emulsify, the lens, with aspiration of the cortex and nucleus through a single needle. Phacoemulsification and aspiration are most commonly performed through a single incision via a single needle which infuses irrigating solution, aspirates, and provides ultrasonic phacoemulsification.[55] Several fluid types have been used to irrigate and maintain the anterior chamber during cataract surgery in the horse.[47,48,120] Balanced saline solution and lactated Ringer's solution, warmed to 37°C (98.6°F) are most commonly used. Heparin, epinephrine, and sodium bicarbonate have also been added to the irriga-

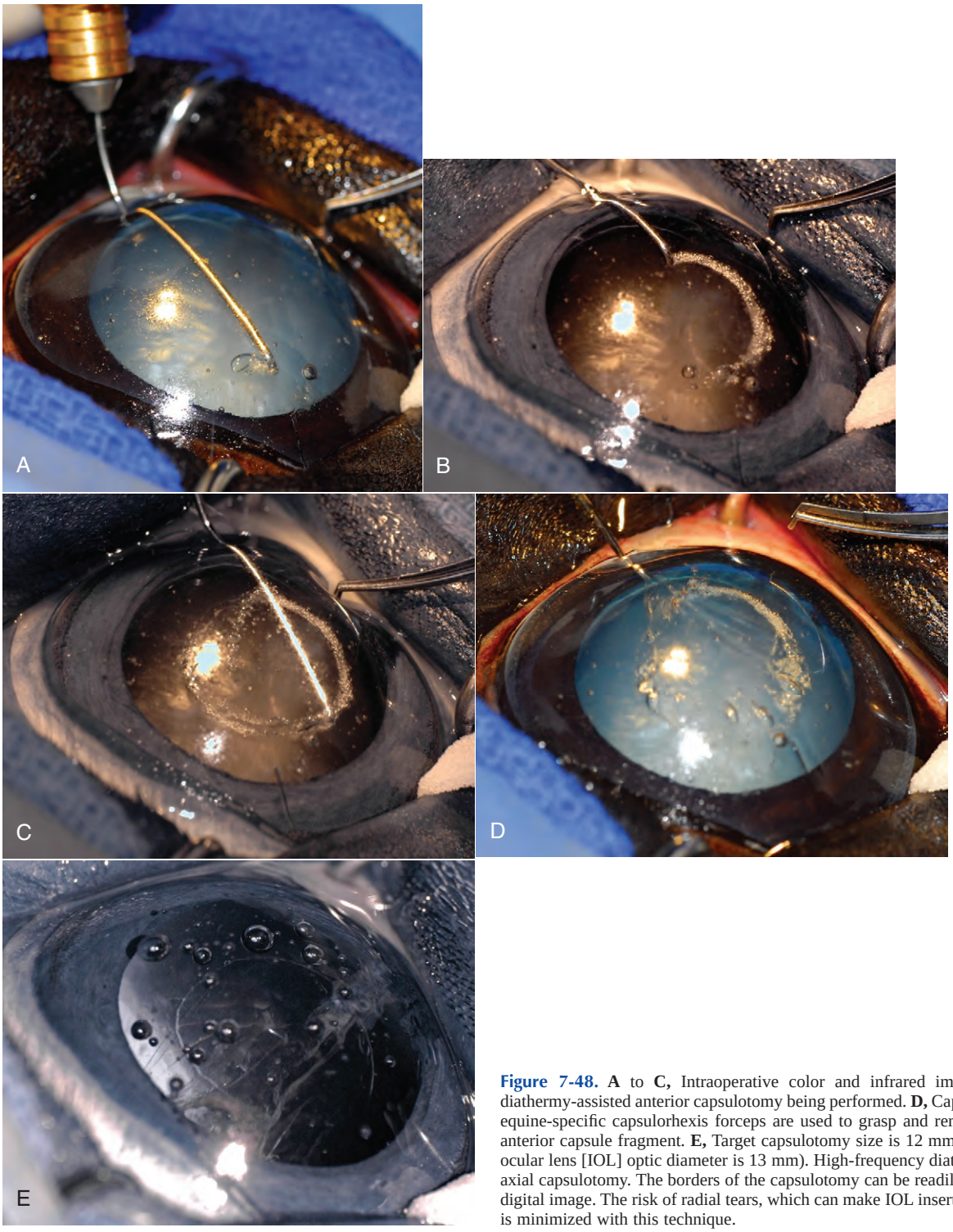


Figure 7-48. A to **C,** Intraoperative color and infrared images of high-frequency[139] diathermy-assisted anterior capsulotomy being performed. **D,** Capsulotomy is complete, and equine-specific capsulorhexis forceps are used to grasp and remove the resulting circular anterior capsule fragment. **E,** Target capsulotomy size is 12 mm in diameter (equine intraocular lens [IOL] optic diameter is 13 mm). High-frequency diathermy allows for a precise axial capsulotomy. The borders of the capsulotomy can be readily identified in this infrared digital image. The risk of radial tears, which can make IOL insertion difficult or impossible, is minimized with this technique.

tion fluids during intraocular surgery in horses.[55] During phacoemulsification, a viscoelastic substance is introduced into the anterior chamber to maintain its shape and protect the corneal endothelium from injury.[128,129] If a single incision or one-handed technique is used, the phacoemulsification needle is introduced through the opening in the anterior lens capsule (Fig. 7-49). The lens cortex and nucleus are emulsified and aspirated, with great care taken to avoid penetrating the posterior lens capsule, which is extremely thin and highly mobile within the globe following removal of the lens material.[55,94] A second stab incision can be made by introducing a 20-gauge needle into the anterior chamber at a point approximately 4 clock hours away from the initial CCI, on the opposite side of the superior corpora nigra (Fig. 7-50). A second instrument

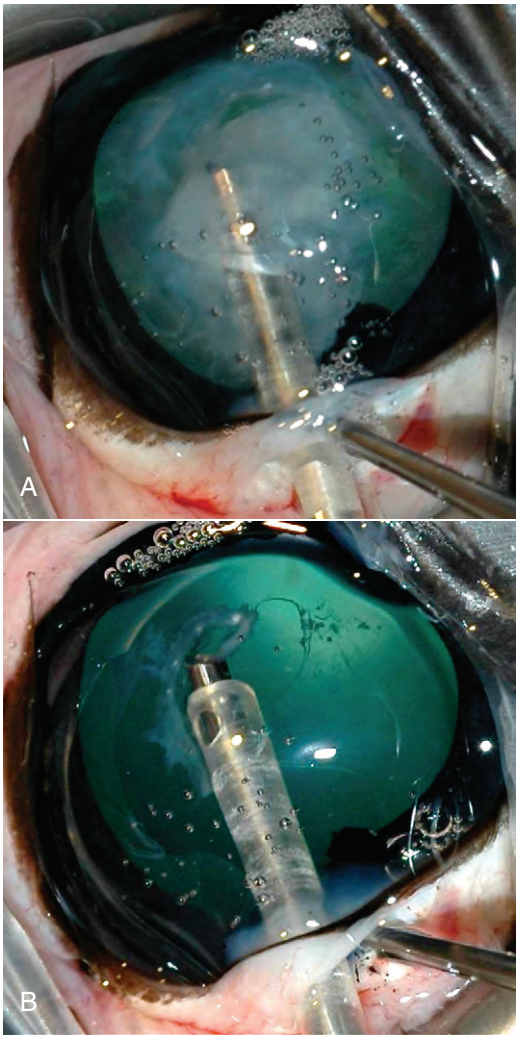


Figure 7-49. **A,** Initiation of the phacoemulsification process. The needle tip is shown just after insertion through the scleral-based tunnel incision. **B,** Final stage of phacoemulsification.

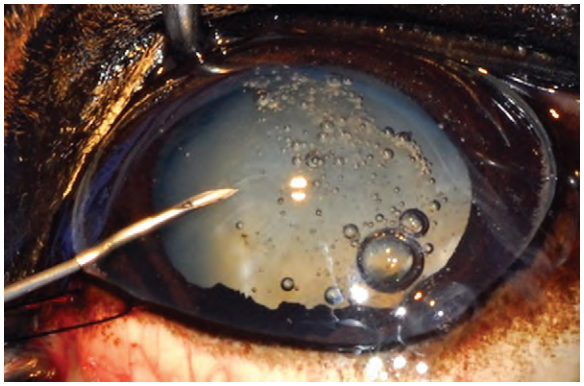


Figure 7-50. A 20-gauge needle is shown creating a second incision at the 2 o'clock position, which provides access to the anterior chamber (AC) for a second instrument. The trilaminar clear corneal incision, illustrated in Fig. 7-45, can be seen at the 10 o'clock position (relative to the globe's normal position).

(e.g., nucleus rotator) can be introduced through this incision and used to assist in phacoemulsification by increasing stabilization and/or manipulating or breaking up the lens (i.e., two-handed phacoemulsification [Fig. 7-51]).

Following emulsification of the cortex and nucleus, the phacoemulsification needle is removed. It is then replaced with an irrigation/aspiration tip (0.5-mm diameter) that is used to remove all remaining lens cortex from the equatorial region of the capsular bag (Fig. 7-52). For complete removal of the peripheral cortex from the lens capsule, a longer equine-specific irrigation/aspiration needle is essential.

Once the cataract has been successfully emulsified and the remaining cortex has been aspirated, the lens capsule and anterior chamber are reinflated with a viscoelastic substance if an IOL is to be implanted into the eye (Fig. 7-53). If preexisting

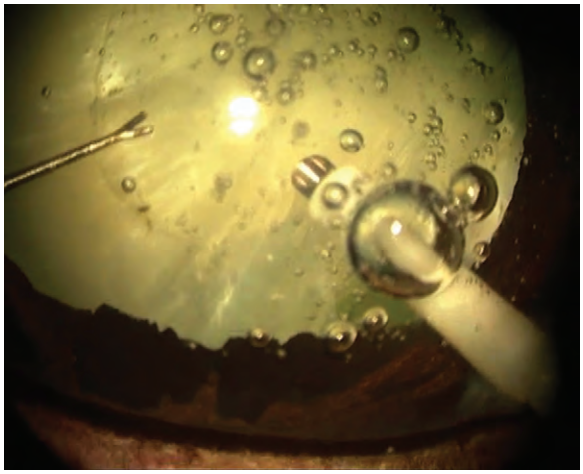


Figure 7-51. Intraoperative digital image demonstrating two-handed phacoemulsification being performed. The phacoemulsification needle is on the right, and an equine-specific nucleus rotator can be seen to the left of the image.

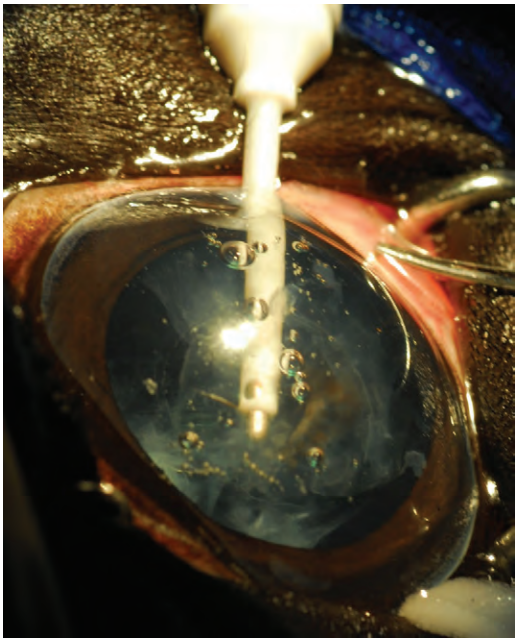


Figure 7-52. Irrigation/aspiration of the lens capsule follows phacoemulsification of the lens nucleus and cortex.

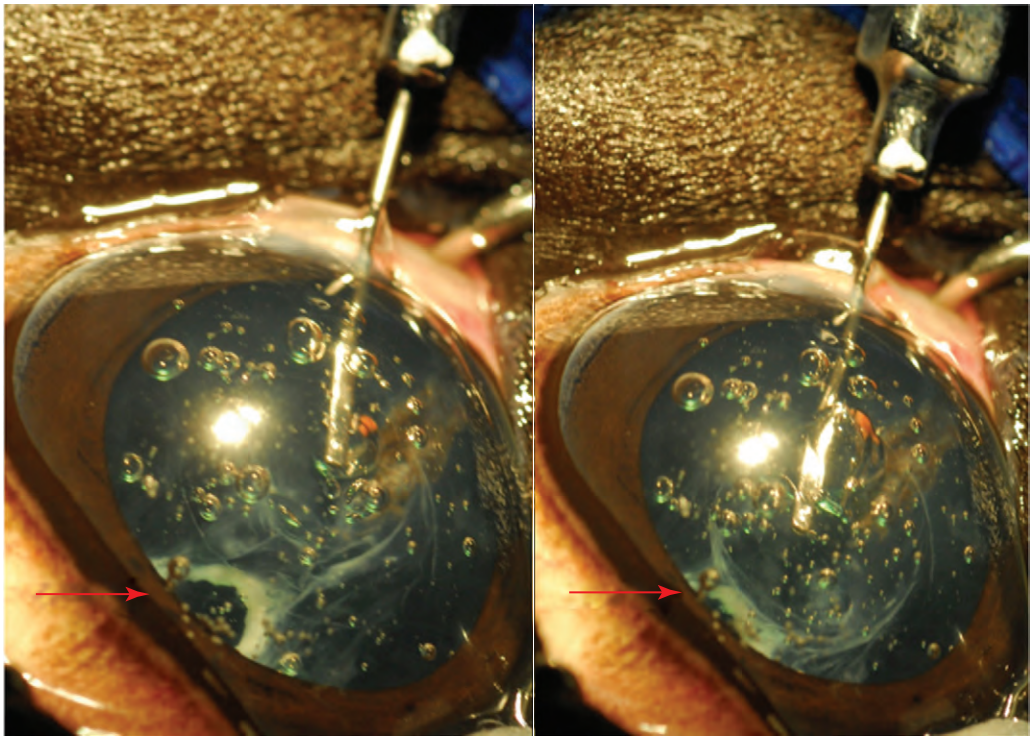


Figure 7-53. Injection of viscoelastic substance into the anterior chamber (AC) and capsular bag following phacoemulsification and irrigation/aspiration to facilitate implantation of an intraocular lens. Note how the area of posterior capsular fibrosis surrounding a rent in the posterior lens capsule *(red arrow)* is being pushed behind the iris by the viscoelastic substance as it is injected.

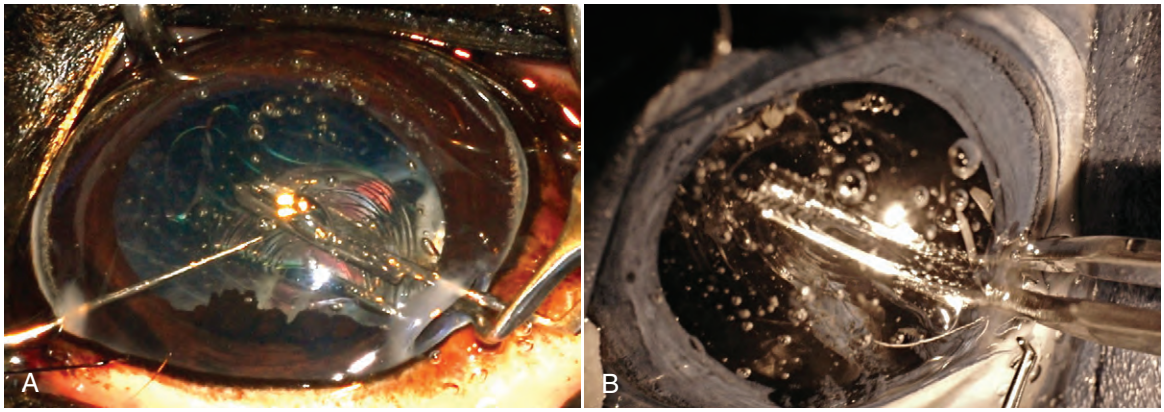


Figure 7-54. A, Manual insertion of a foldable equine-specific 18-D intraocular lens (IOL) through a trilaminar clear corneal incision (CCI). A two-handed technique is being used, with an equine-specific nucleus rotator inserted through the second incision to assist with proper IOL placement. **B,** Infrared. An 18-D IOL is inserted through a trilaminar CCI. A second corneal incision was not necessary in this eye.

or intraoperative complications prevent IOL implantation, the corneal incision(s) are closed using 8-0 or 9-0 polyglactin 910 using the surgeon's preferred suture pattern. If an IOL can be implanted, the CCI is extended to allow for introduction of the lens. Recently, an equine-specific IOL introducer became available (Acrivet), but at the time this chapter was written, the authors had limited experience with the instrument. For manual IOL implantation, lens-folding forceps are used to maintain the lens in a folded position while being introduced into the lens capsule through the extended CCI (Fig. 7-54). A lens rotator inserted through a second incision can be useful in ensuring proper IOL introduction and positioning of the haptics.

The IOL haptics are placed in a horizontal (3 to 9 o'clock) position, as opposed to a vertical (12 to 6 o'clock) position, if possible, to allow for a more aesthetic appearance within the horizontally elongated equine pupil. This also decreases the aphakic area at the temporal and nasal aspects within the pupil. Following introduction and positioning of the IOL, the corneal incision(s) is/are closed using 8-0 to 9-0 polyglactin 910 using the surgeons preferred suture pattern. We do not routinely

remove the viscoelastic from the anterior chamber via irrigation/aspiration in our equine patients. If one chooses to remove the viscoelastic substance, this should be performed prior to final closure of the incision. Once the incision is closed, the globe is reinflated to an IOP of approximately 15 to 20 mm Hg (this is confirmed via applanation or rebound tonometry), and the incision is examined to ensure that a watertight seal has been established.

EXTRACAPSULAR AND INTRACAPSULAR LENS EXTRACTION

Both extracapsular and intracapsular lens extractions require larger incisions than phacoemulsification. Larger incisions increase the risk of complications, including extrusion of the iris and corpora nigra, vitreous herniation, secondary glaucoma and retinal detachment.[60] Lens luxation in horses is rare, and newer phacoemulsification units are powerful enough to emulsify most intact lenses.

POSTOPERATIVE MANAGEMENT

Typical postoperative management of equine cataract patients includes topical and systemic antiinflammatory medications and antibiotics (Table 7-2). If a corneal ulcer is not present, topical corticosteroids are used every 4 to 6 hours. Some surgeons also use topical NSAIDs (e.g., flurbiprofen, diclofenac, nepafenac, bromfenac). All patients receive broad-spectrum antibiotic medications. Systemic use of NSAIDs (flunixin meglumine) is used in all patients at a tapering dose over 2 to 4 weeks. Intravenous antibiotics are typically used perioperatively and continued for 48 hours postoperatively. If a corneal ulcer develops, topical corticosteroids are discontinued, and only topical NSAIDs are used in their place. Newer-generation NSAID drops (i.e., nepafenac and bromfenac) are almost or as effective as topical corticosteroids.

Specific postoperative diagnostic tests should be performed following cataract surgery in all equine patients (Box 7-2). Serial postoperative ophthalmic examinations and tonometry will help the clinician recognize early signs of postoperative complications that may necessitate changes in medical management. Streak retinoscopy and ocular ultrasonography provide important data on the refractive state of the globe and the postoperative IOL position (Fig. 7-55), respectively. These data are extremely important for the development and refinement of equine IOLs, and ocular ultrasonography also allows the clinician to evaluate the posterior segment of the eye in those cases in which postoperative inflammation or infection preclude direct visualization.[14,75,91,96,112]

COMPLICATIONS AND SEQUELAE

POTENTIAL ISSUES PRESENT PRIOR TO SURGERY

Some cataractous lenses can have problems that will complicate the intraoperative procedure as well as increase the incidence of postoperative complications. These include lens capsule rupture, active uncontrolled uveitis, lens instability, posterior or anterior synechia, preexisting lens capsule fibrosis, and vitreal herniation into the anterior chamber. Preoperative identification of any of these findings allows for proper surgical planning.

Box 7-2 | Postoperative Diagnostic Tests for Equine Cataract Surgery Patients

Ocular Examination
Tonometry
Electroretinography (ERG)
- 3 to 6 months postoperatively

Streak retinoscopy
- Perform at each reevaluation

Ocular ultrasonography
- Axial globe length (AxL)
- Postoperative anterior chamber depth (PACD)

Table 7-2 | **Postoperative Treatment Protocol for Equine Cataract Surgery Patients**

DRUG	DOSE & ROUTE OF ADMINISTRATION	FREQUENCY	DURATION
SYSTEMIC MEDICATIONS			
Trimethoprim sulfa (TMS)	20 mg/kg, PO	q12h	10-14 days
Flunixin meglumine	1.1 mg/kg, IV, PO	q12h	10-14 days
	0.55 mg/kg, IV, PO	q12h	10-14 days
Omeprazole	2 mg/kg, PO	q24h	28 days
TOPICAL OPHTHALMIC MEDICATIONS			
Corticosteroids			
Neomycin-polymyxin B sulfates Dexamethasone	0.2 mL, SPL	q6h	Tapering dose over 3-month period
Antibiotics			
Neomycin-polymyxin B sulfates Dexamethasone	0.2 mL, SPL	q6h	Tapering dose over 3-month period 24 hours
Moxifloxacin	0.2 mL, SPL	q4h q6h	24 hours 5-7 days
Mydriatics			
Atropine sulfate 1%	0.2 mL, SPL	q12h, reduce to q24-48h following maximum mydriasis	28 days

IU, International units; *IV*, intravenous; *kg*, kilogram body weight; *PO*, per os (oral); *SPL*, through subpalpebral lavage catheter.

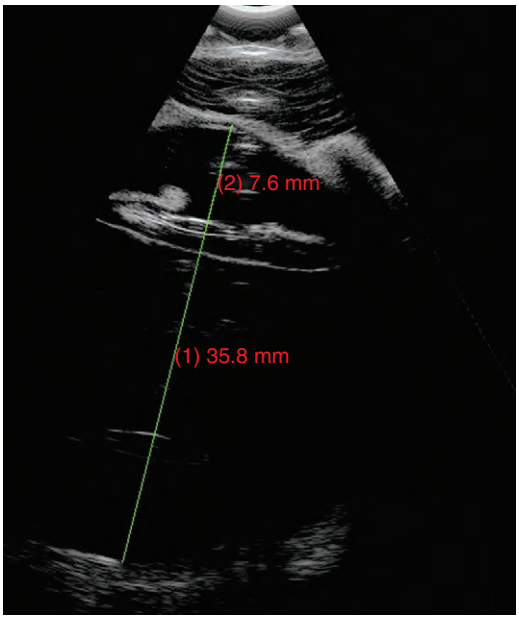


Figure 7-55. Postoperative ocular ultrasound image from a 7-year-old Rocky Mountain horse mare. *1,* Axial globe length (AxL). *2,* Postoperative anterior chamber depth (PACD). The PACD represents the distance of the intraocular lens from the cornea following implantation, and has a significant effect on the postoperative refractive state of the globe.

POTENTIAL ISSUES DURING SURGERY

Intraoperative complications include posterior lens capsule tears, vitreal presentation through the posterior lens capsular tear, and loss of lens material into the vitreous through a lens capsule rupture. Posterior capsular tears can be avoided with careful technique, proper use of viscoelastic material, surgical experience, and patience. If they do occur, cohesive viscoelastic material is used to tamponade the vitreous and avoid its herniation into the lens capsule.[130] Even small posterior capsule tears can enlarge as a result of vitreous bulging anteriorly through the capsular tear.[47] Loss of small fragments of lens material into the vitreous slowly resorb and do not cause excessive inflammation.[131] However, larger fragments of cortical material are very inflammatory, and efforts should be made to remove them from the vitreous using either viscoelastic material to float them anteriorly or using a vitrector.

Other complications include hemorrhage, iris or corpora nigra herniation through the incision, and miosis.[131] Uncontrolled hemorrhage may be difficult to control depending upon where it originates. Some can be stopped by injecting 1 : 10,000 epinephrine at the site of hemorrhage,[132] and viscoelastic material can also be used to stop bleeding. Hemorrhage that has leaked into the vitreous resolves very slowly and predisposes to retinal detachments.

Prolapse of the iris or corpora nigra in horses frequently occurs during cataract surgery. One major cause is injection of an excessive amount of viscoelastic material into the anterior chamber. The viscoelastic material then gains access to the posterior chamber beneath the iris adjacent to the incision, causing the iris and corpora nigra to migrate towards the incision. Iris or corpora nigra prolapse can also occur upon removal of the phacoemulsification needle from the anterior chamber. Careful repositioning of the prolapsed iris is performed, though the iris may be prone to hemorrhage when manipulated.[47] The risk of iris and/or corpora nigra prolapse can be minimized by construction of a trilaminar CCI (see Fig. 7-45).[125,126]

POTENTIAL ISSUES FOLLOWING SURGERY

Postoperative complications include those that occur acutely after surgery and those that occur later. Common postoperative complications that occur immediately or soon after cataract surgery in horses include fibrin formation in the anterior chamber (Fig. 7-56), hyphema, decreased menace response, vitreal prolapse into the anterior chamber, and dislocation of a concurrently implanted cyclosporine implant.[31] Persistent fibrin and contracted blood clots can be dissolved using intracameral tissue plasminogen activator (TPA [Fig. 7-57]). Other complications include corneal edema, postoperative ocular hypertension, and corneal ulceration.[31,47] Use of topical corticosteroids during the postoperative treatment period necessitates close monitoring of any corneal ulcer that develops for signs of fungal keratitis. This should be treated aggressively immediately upon detection.

Complications occurring beyond the immediate postoperative period include chronic uncontrollable uveitis (Fig. 7-58), posterior synechia and resulting dyscoria (Fig. 7-59), or iris bombé, retinal detachment, and endophthalmitis (Fig. 7-60; see Fig. 7-29).[31,47] Endophthalmitis is the most serious sight-threatening complication that can occur in the relative immediate postoperative period. *Streptococcus* spp. and *Staphylococcus* spp. were the most common bacterial organisms cultured in one study.[47] Chronic unrelenting uveitis can occur if ERU was a preexisting condition.[31] Other long-term complications following cataract surgery include fibropupillary membranes and endothelial degeneration resulting in diffuse corneal edema.[131] In foals that had undergone phacoemulsification, the trainers or owners thought the animals had visual impairment at night or in dim light, though their day vision was good.[48] The most common long-term postoperative complication was posterior capsular opacification (Fig. 7-61; see Fig. 7-34).[31,47,48,62] This is also the most common postoperative complication in other species evaluated (i.e., dog, human) after extracapsular cataract surgery.[133-135]

Postoperative hypertension occurred in 9 eyes out of 47, but none of them went on to develop glaucoma in the long term.[31] Only 1 horse in another retrospective study of 36 horses (51 eyes) had glaucoma as a postoperative complication, though 5 horses developed postoperative hypertension that resolved with antiinflammatory and antiglaucoma medications.[47] Glaucoma is not a frequent postoperative complication, and its development may be prevented with aggressive antiinflammatory therapy during the preoperative and postoperative stages. We have had one horse develop postoperative secondary glaucoma following phacoemulsification and subsequent IOL implantation (see Fig. 7-35).

Overall long-term visual outcome reported in the literature is good. However, these studies only involved aphakic horses. Therefore the advent of IOLs in horses will presumably improve postoperative visual function and allow those horses to return to their prior level of performance following surgery.

The study involving foals reported that 10 of 13 eyes had vision 6 months following surgery, though 5 of these had reduced night vision and 3 had severe keratouveitis, leaving them with only light perception.[48] With improved surgical

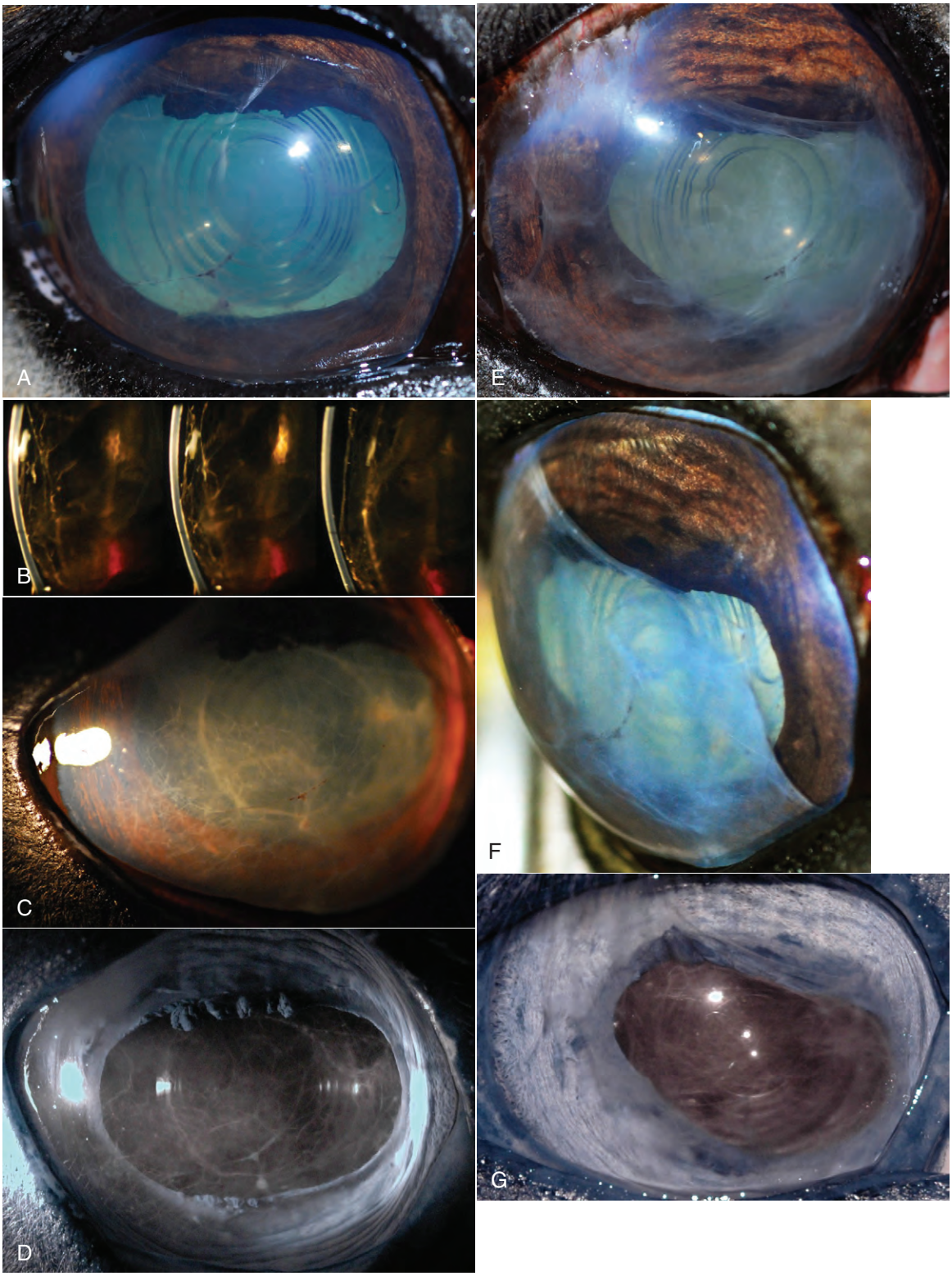


Figure 7-56. **A,** Mild fibrin accumulation in the anterior chamber (AC) during the immediate postoperative period (within 72 hours). Note hazy appearance of AC due to fibrin, as well as focal corneal edema associated with the clear corneal incision (CCI). **B,** Slit-lamp images demonstrating "cobweb-like" appearance of fibrin within the AC. **C,** Tangential lighting highlights accumulation of fibrin within the AC. **D,** Tangential infrared. Note ease with which margins of pupil can be visualized compared to the color image **(C). E** and **F,** Fibrin has been present in the AC for 5 days. Note increase in amount of fibrin within the AC, as well as the effect its presence is having on the pupil. Corneal edema associated with the CCI has become less significant. **G,** Infrared. Effect of fibrin on the pupil is easier to appreciate in infrared.

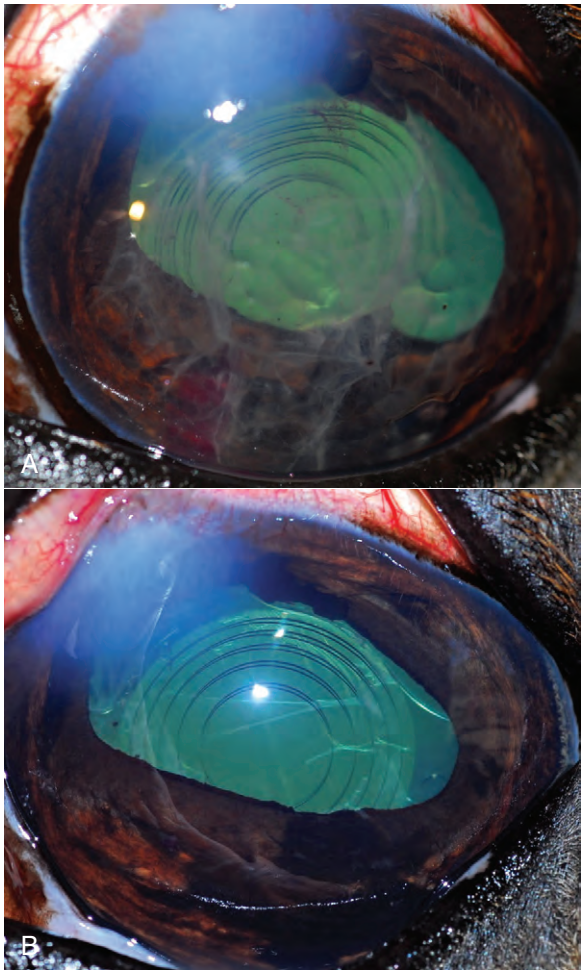


Figure 7-57. A, Moderate intraocular inflammation with fibrin accumulation and hyphema in the anterior chamber (AC) 7 days postoperative. Note focal corneal edema adjacent to site of the clear corneal incision (CCI), the dyscoric pupil resulting from intraoperative iridal prolapse through the CCI, and focal posterior synechia at the 4 o'clock position. **B,** Twenty-four hours following intracameral injection of tissue plasminogen activator (TPA). Note clear anterior chamber and absence of fibrin.

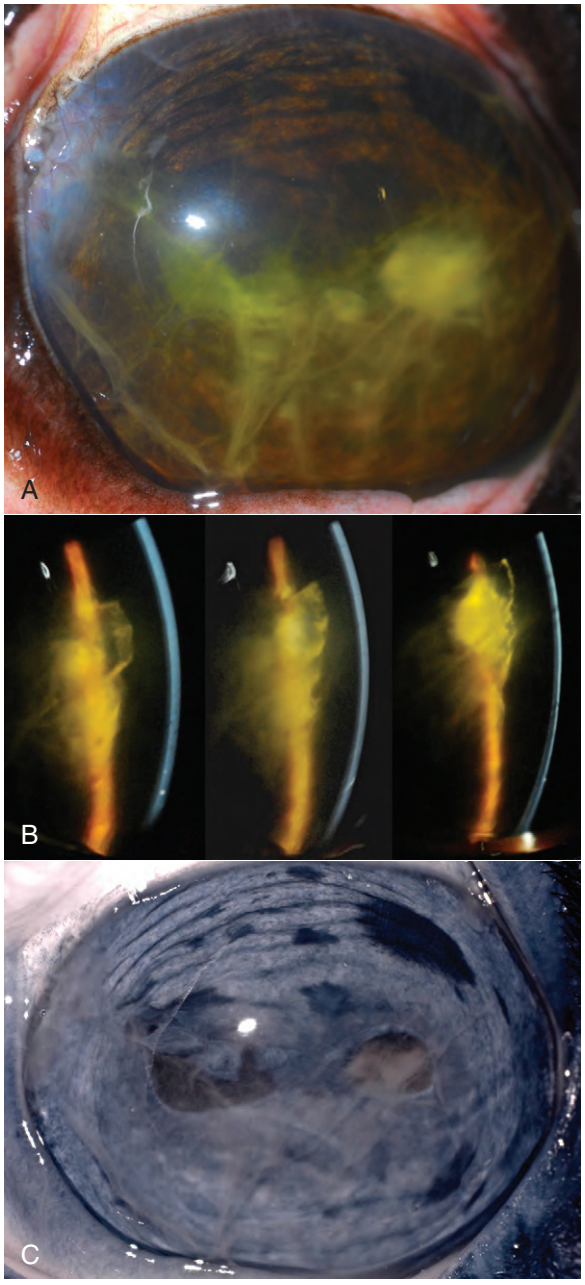


Figure 7-58. A, Severe uncontrollable panuveitis that developed approximately 3 weeks following phacoemulsification and implantation of an 18-D foldable equine-specific intraocular lens. This is the same eye depicted in Fig. 7-42. **B,** Slit-lamp images highlighting the fibrin accumulation within the anterior chamber (AC). Note consolidation of inflammatory debris within the posterior aspect of the AC and relatively clear zone closer to cornea. **C,** Infrared. Clearer view of the anterior iridal surface and pupillary margin. Note that fibrin within the AC is not as readily visible as in the color image **(A),** but infrared image provides an unobstructed view of the focal posterior synechia located at the 6 o'clock position of the pupil.

instruments and techniques and UV-protective and blue-light filtering IOLs, these complications should diminish. More recent studies report that 79% (23 of 29 eyes) had sight at 4 weeks postoperatively; unfortunately, 18 eyes were lost to follow-up after this period.[31] Losing patients to follow-up is very common in equine ophthalmology. A long-term large study would be difficult to perform in horses following cataract surgery but would be incredibly important, especially now with the increasing use of IOLs.

FUTURE RESEARCH ON LENS DISEASE IN HORSES

Much progress has been made regarding the development and validation of an appropriate equine IOL since the first edition of this textbook was published. There are currently three different commercially available foldable equine-specific IOLs that are manufactured and distributed by Acrivet Inc., but substantial data supporting the use of one dioptric strength over another are lacking. Much work remains to be done before a universal equine IOL can be recommended. Ocular ultrasonography should be performed in every horse that presents for evaluation for cataract surgery. Preoperative globe measurements should be obtained and recorded in a standardized manner. Following lens removal and IOL implantation, post-

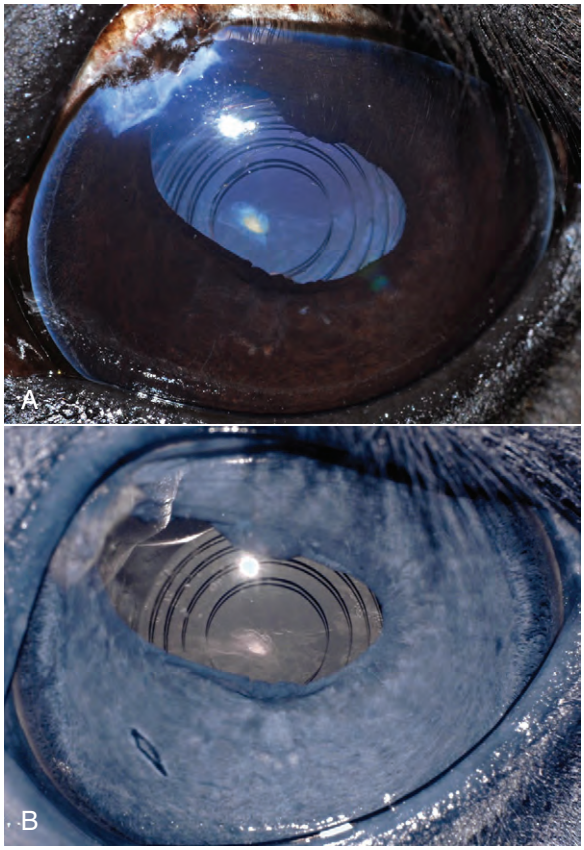


Figure 7-59. **A,** Intraoperative iris prolapse through the clear corneal incision (CCI) resulted in this moderately misshapen pupil (dyscoria). Photograph was taken during the 6-month follow-up. Note small, dense, white opacification within the central area of the intraocular lens optic. This is a small posterior capsular plaque identified during surgery, following removal of the cataractous lens. It has remained unchanged throughout the postoperative follow-up period. **B,** Infrared. Enhanced view of the anterior iris surface, dyscoria, and the small focal posterior-capsular plaque.

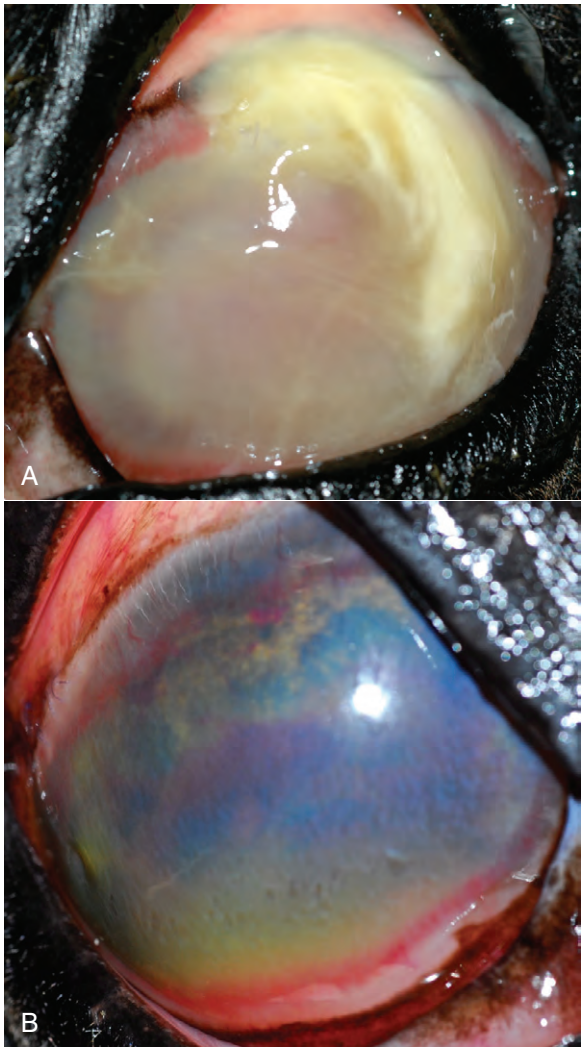


Figure 7-60. **A,** Severe endophthalmitis in a geriatric Quarter Horse following extracapsular lens extraction through a large corneal incision ("open sky" technique). **B,** Endophthalmitis in a 24-year-old Welsh Pony mare that developed between days 14 and 21 following phacoemulsification with subsequent intraocular lens placement.

operative ultrasound data should again be collected. These data can be pooled nationally or even globally, and regression analysis can be performed to help determine the most appropriate dioptric strength for an equine IOL.

Streak retinoscopy is a fairly simple but underutilized diagnostic test that should be used regularly in pre- and postoperative cataract patients. Granted, if a horse presents with bilateral cataracts, it may not be possible to obtain reliable preoperative refractive data. However, in unilateral cataract patients, the refractive state of the contralateral eye can be used to represent the preoperative refractive state of the eye with a cataract. The postoperative refractive state of the eye following IOL implantation, determined by streak retinoscopy, along with the postoperative anterior chamber depth, obtained with ocular ultrasonography, are the only objective means currently available to evaluate the ability of the eye to function visually following lens removal. The more widely used both of these diagnostic tests become, the more the reliability of the data will increase.

Electroretinography, although sporadically utilized as part of the precataract surgery evaluation, is another underused diagnostic test in equine ophthalmology. In order to enhance

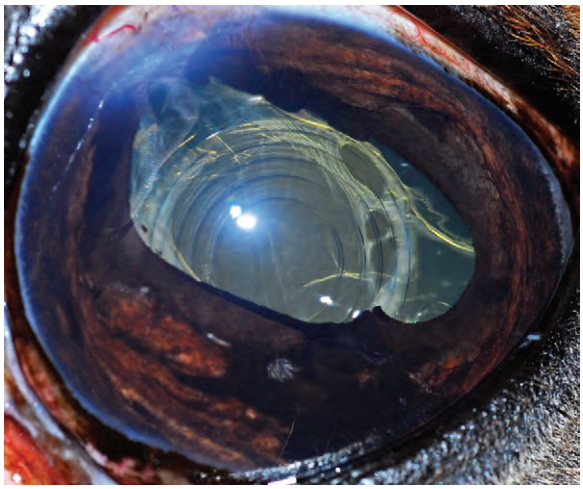


Figure 7-61. Mild posterior capsular opacification (PCO) approximately 1 month following phacoemulsification and implantation of a 25-D foldable equine-specific intraocular lens. Note irregularly shaped (dyscoric) pupil that has resulted from intraoperative iridal prolapse through the clear corneal incision (CCI), and the small focal area of posterior synechia at the 4 o'clock position of the pupillary margin. This is the same eye shown in Fig. 7-59.

our understanding of vision in horses, it is necessary to obtain more detailed information elucidating equine retinal function.

Current existing methods of the clinical evaluation of vision are both crude and inadequate. Efforts are being made to developing simple reproducible methods of visual-field testing that will greatly benefit our ability to assess postoperative evaluation of cataract patients.

Improved surgical technique has continued to improve the success of cataract surgery in horses. The transition from "open sky" lens extractions to small-incision phacoemulsification and aspiration has greatly improved the surgical outcomes in all equine cataract patients. However, there is still much room for improvement with regards to corneal entry incisions to minimize the risk of intraoperative iris prolapse, anterior and posterior capsulotomy techniques, IOL design, appropriate dioptric strength, and insertion techniques. To improve the long-term success of cataract surgery, appropriate and effective postoperative treatment plans need to be further developed.

References

1. Matthews AG: Lens opacities in the horse: a clinical classification, Vet Ophthalmol 3:65–71, 2000.
2. Zucker CS: On the evolution of eyes: would you like it simple or compound? Science 264:742–743, 1994.
3. Paterson CA, Delamere NA: The lens. In Hart WM, editor: Adler's physiology of the eye, ed 9, St. Louis, 1992, Mosby Year Book, pp 348–390.
4. Foley JD, Rosenbaum H, Griep AE: Temporal regulation of VEID-7-amino-4-trifluoromethylcoumarin cleavage activity and caspase-6 correlates with organelle loss during lens development, J Biol Chem 279:32142–32150, 2004.
5. Bassnett S, Mataic D: Chromatin degradation in differentiating fiber cells of the eye lens, J Cell Biol 137:37–49, 1997.
6. Latimer CA, Wyman M, Hamilton J: An ophthalmic survey of the neonatal horse, Equine Vet J (Suppl) 2:9–14, 1983.
7. Roberts SM: Congenital ocular anomalies, Vet Clin North Am Equine Pract 8:459–478, 1992.
8. Priester WA: Congenital ocular defects in cattle, horses, cats, and dogs, J Am Vet Med Assoc 160:1504–1511, 1972.
9. Beech J, Aguirre G, Gross S: Congenital nuclear cataracts in the Morgan horse, J Am Vet Med Assoc 184:1363–1365, 1984.
10. Brooks DE, Matthews AG: Equine ophthalmology. In Gelatt KN, editor: Veterinary ophthalmology, ed 4, Ames, IA, 2007, Blackwell Publishing, pp 1165–1274.
11. Gelatt KN: Congenital and acquired ophthalmic disease in the foal, Anim Eye Res 1–2:15–27, 1993.
12. Ewart SL, Ramsey DT, Xu J, et al: The horse homolog of congenital aniridia conforms to codominant inheritance, J Hered 91:93–98, 2000.
13. Ramsey DT, Ewart SL, Render JA, et al: Congenital ocular abnormalities of Rocky Mountain horses, Vet Ophthalmol 2:47–59, 1999.
14. Scotty NC, Cutler TJ, Brooks DE, et al: Diagnostic ultrasonography of equine lens and posterior segment abnormalities, Vet Ophthalmol 7:127–139, 2004.
15. Erikson R: Hereditary aniridia with secondary cataract in horses, Nord Vet Med 7:773–779, 1955.
16. Matthews AG, Barnett KC: Lens. In Barnett KC, Crispin SM, Lavach JD, et al, editors: Equine ophthalmology: an atlas and text, ed 2, Edinburgh, 2004, Saunders Elsevier, pp 165–182.
17. Baumgartner WA, Storey ES, Paulsen DB: Bilateral intraocular glandular choristomas in a Thoroughbred foal, Vet Ophthalmol 12:106–114, 2009.
18. Gerhards H, Werry H, Deegen E, et al: [Two rare lens abnormalities in horses], Tierarztl Prax 20:282–286, 1992.
19. Cook CS: Ocular embryology and congenital malformations, In Gelatt KN, editor: Veterinary ophthalmology, ed 4, Ames, IA, 2007, Blackwell Publishing, pp 3–36.
20. Lewis D, Kelly D, Sansom J: Congenital microphthalmia and other developmental ocular anomalies in the Doberman, J Small Anim Pract 27:559–566, 1986.
21. Martin C, Leipold H: Aphakia and multiple ocular defects in Saint Bernard puppies, Vet Med Small Anim Clin 69:448–453, 1974.
22. Wilkie DA, Gilger BC: Equine glaucoma, Vet Clin Equine 20:381–391, 2004.
23. Severin GA: Veterinary Ophthalmology, Fort Collins, 1976, Colorado State University.
24. Munroe G: Study of the hyaloid apparatus in the neonatal Thoroughbred foal, Vet Rec 146f:579–584, 2000.
25. Hurn SD, Turner AG: Ophthalmic examination findings of Thoroughbred racehorses in Australia, Vet Ophthalmol 9:95–100, 2006.
26. McLaughlin SA, Whitley RD, Gilger BC: Diagnosis and treatment of lens diseases, Vet Clin North Am Equine Pract 8:575–585, 1992.
27. Angelos J, Oppenheim Y, Rebhun WC, et al: Evaluation of breed as a risk factor for sarcoid and uveitis in horses, Anim Genet 19:417–425, 1988.
28. Bistner S, Shaw D: Uveitis in the horse, Comp Contin Educ Pract Vet 2:S35–S43, 1980.
29. Cook CS, Peiffer RL, Harling DE: Equine recurrent uveitis, Equine Vet J (Suppl) 2:57–60, 1983.
30. Davidson MG: Equine ophthalmology. In Gelatt KN, editor: Veterinary ophthalmology, ed 2, Philadelphia, 1991, Lea & Febiger, pp 576–610.
31. Fife TM, Gemensky-Metzler AJ, Wilkie DA, et al: Clinical features and outcomes of phacoemulsification in 39 horses: a retrospective study (1993–2003), Vet Ophthalmol 9:361–368, 2006.
32. Gilger BC, Wilkie DA, Davidson MG, et al: Use of an intravitreal sustained-release cyclosporine delivery device for treatment of equine recurrent uveitis, Am J Vet Res 62:1892–1896, 2001.
33. Lavach JD: Lens. In Lavach JD, editor: Large animal ophthalmology, St. Louis, 1990, Mosby, pp 185–201.
34. Lavach JD: Pupil, iris, and ciliary body. In Lavach JD, editor: Large animal ophthalmology, St. Louis, 1990, Mosby, pp 150–177.
35. Matthews AG: The lens and cataracts, Vet Clin North Am Equine Pract 20:393–415, vii, 2004.
36. Miller TR, Whitley RD: Equine uveitis, Mod Vet Pract 68:351–357, 1987.
37. Rebhun WC: Diagnosis and treatment of equine uveitis, J Am Vet Med Assoc 175:803–808, 1979.
38. Saunders LZ, Rubin LF: The lens. In Saunders LZ, Rubin LF, editors: Ophthalmic pathology of animals, ed 1, Basel, 1975, S Karger, pp 82–99.
39. Saunders LZ, Rubin LF: Equine recurrent uveitis. In Saunders LZ, Rubin LF, editors: Ophthalmic pathology of animals, ed 1, Basel, 1975, S Karger, pp 78–81.
40. Schwink KL: Equine uveitis, Vet Clin North Am Equine Pract 8:557–574, 1992.
41. Turner LM, Whitley RD, Hager D: Management of ocular trauma in horses. Part II. Orbit, eyelids, uvea, lens, retina, and optic nerve, Mod Vet Pract 67:341–347, 1986.
42. Whitley RD, Gelatt KN: Ocular manifestations of systemic disease. In Gelatt KN, editor: Veterinary ophthalmology, ed 1, Philadelphia, 1981, Lea & Febiger, pp 724–741.
43. Whitley RD, Miller TR, Wilson JH: Therapeutic considerations for equine recurrent uveitis, Equine Pract 15:16–23, 1993.
44. Cullen CL, Webb AA: Ocular manifestations of systemic diseases. Part 3: the horse. In Gelatt KN, editor: Veterinary ophthalmology, ed 4, Ames, IA, 2007, Blackwell, pp 1588–1616.
45. Whitley RD: Cataracts. In Robinson NE, editor: Current therapy in equine medicine, ed 2, Philadelphia, 1987, WB Saunders, pp 456–458.
46. Brooks DE, Wolf ED: Ocular trauma in the horse, Equine Vet J (Suppl) 2:141–146, 1983.
47. Millichamp NJ, Dziezyc J: Cataract phacofragmentation in horses, Vet Ophthalmol 3:157–164, 2000.
48. Whitley RD, Moore CP, Slone DE: Cataract surgery in the horse: a review, Equine Vet J (Suppl) 2:127–134, 1983.
49. Severin GA: Lens. In Severin GA, editor: Severin's veterinary ophthalmology, ed 3, Ft. Collins, 1996, Veterinary Ophthalmology Notes, pp 379–406.
50. Chandler KJ, Billson FM, Mellor DJ: Ophthalmic lesions in 83 geriatric horses and ponies, Vet Rec 153:319–322, 2003.

51. Latimer CA, Wyman M: Neonatal ophthalmology, Vet Clin North Am Equine Pract 1:235–259, 1985.
52. Dziezyc J, Millichamp NJ: Cataracts. In Robinson NE, editor: Current therapy in equine medicine, ed 3, Philadelphia, 1992, WB Saunders, pp 601–602.
53. McMullen RJ, Jr, Utter ME: Current developments in equine cataract surgery, Equine Vet J Suppl 37:38–45, 2010.
54. Gerhards H, Wollanke B, de Boer R: Technique of cataract surgery in horses using phacoemulsification, Tierarztl Prax 31(G):28–35, 2003.
55. Whitley DR: Diseases and surgery of the lens. In Gilger BC, editor: Equine ophthalmology, ed 1, St. Louis, 2005, Elsevier Saunders, pp 269–284.
56. Barros PSM, Feitosa FLF, Alvarengna J: Lens subluxation in a horse, Equine Pract 12:16, 1990.
57. Foley JD, Rosenbaum H, Griep AE: Temporal regulation of VEID-7-amino-4-trifluoromethylcoumarin cleavage activity and caspase-6 correlates with organelle loss during lens development, J Biol Chem 279:32142–32150, 2004.
58. Yanoff M, Fine BS: Ocular pathology. In Yanoff M, Fine BS, editors: Ocular pathology, Hagerstown, 1975, Harper & Row, pp 111–173.
59. Matthews AG, Handscombe MC: Bilateral cataract formation and subluxation of the lenses in a foal: a case report, Equine Vet J (Suppl) 2:23–24, 1983.
60. Brooks DE, Gilger BC, Plummer CE, et al: Complications and visual outcomes associated with surgical correction of lens luxation in the horse, ACVO 40th Annual Conference Chicago, Ill, 2009.
61. Davidson MG, Nelms SR: Diseases of the canine lens and cataract formation. In Gelatt KN, editor: Veterinary ophthalmology, ed 4, Ames, IA, 2007, Blackwell, pp 859–887.
62. Whitley RD, Meek LA: Cataract surgery in horses, Comp Contin Educ Pract Vet 11:1396–1401, 1989.
63. Townsend WM: Intraocular surgery. In Robinson NE, Sprayberry KA, editors: Current therapy in equine medicine, ed 6, St. Louis, 2009, Saunders Elsevier, pp 659–663.
64. Hamor RE, Roberts SM, Severin GA, et al: Ocular cosmetic and prosthetic devices, Vet Clin North Am Equine Pract 8:637–654, 1992.
65. McLaughlin SA: Intraocular silicone prosthesis, Comp Contin Educ Pract Vet 17:945–950, 1995.
66. Lavach JD, Severin GA, Roberts SM: Lacerations of the equine eye: a review of 48 cases, J Am Vet Med Assoc 184:1243–1248, 1984.
67. Meek LA: Intraocular silicone prosthesis in a horse, J Am Vet Med Assoc 193:343–345, 1988.
68. Riggs C, Whitley RD: Intraocular silicone prostheses in a dog and a horse with corneal lacerations, J Am Vet Med Assoc 196:617–619, 1990.
69. Davidson MG, Nasisse MP, Jamieson VE, et al: Traumatic anterior lens capsule disruption, J Am Anim Hosp Assoc 27:410–414, 1991.
70. Brooks DE: Ocular emergencies and trauma. In Auer JA, Stick JA, editors: Equine surgery, ed 3, St. Louis, 2006, Saunders Elsevier, pp 767–774.
71. Capaldo F, Komaromy AM: Ophthalmic emergency, Clin Tech Equine Pract 5:134–144, 2006.
72. Schaer BD: Ophthalmic emergencies in horses, Vet Clin Equine 23:49–65, 2007.
73. Whitley DR, Turner LM: Management of ocular trauma in horses part 1: cornea and sclera, Mod Vet Pract 67:233–238, 1986.
74. Bentley E, Miller PE, Diehl KA: Use of high-resolution ultrasound as a diagnostic tool in veterinary ophthalmology, J Am Vet Med Assoc 223:1617–1622, 2003.
75. Cronau M. [High resolution ultrasound in equine ophthalmology-Thesis]. Clinic for Equine Surgery and Internal Medicine, Munich, 2004, Ludwig-Maximilians-University, pp 1–136.
76. Rampazzo A, Eule C, Speier S, et al: Scleral rupture in dogs, cats, and horses, Vet Ophthalmol 9:149–155, 2006.
77. Wilkie DA, Gemensky-Metzler AJ, Colitz CM, et al: Canine cataracts, diabetes mellitus and spontaneous lens capsule rupture: a retrospective study of 18 dogs, Vet Ophthalmol 9:328–334, 2006.
78. Gilger BC, Miller-Michau T: Equine recurrent uveitis: new methods of management, Vet Clin Equine 20:417–427, 2004.
79. Gilger BC, Salmon JH, Wilkie DA, et al: A novel bioerodible deep scleral lamellar cyclosporine implant for uveitis, Invest Ophthalmol Vis Sci 47:2596–2605, 2006.
80. Hooper PL, Rao NA, Smith RE: Cataract extraction in uveitis patients, Surv Ophthalmol 35:120–144, 1990.
81. Grahn BH, Cullen CL: Equine phacoclastic uveitis: the clinical manifestations, light microscopic findings, and therapy of 7 cases, Can Vet J 41:376–382, 2000.
82. McLaughlin SA, Ramsey DT, Lindley DM, et al: Intraocular silicone prosthesis implantation in eyes of dogs and a cat with intraocular neoplasia: nine cases (1983–1994), J Am Vet Med Assoc 207:1441–1443, 1995.
83. Lavach JD: Examination. In Lavach JD, editor: Large animal ophthalmology, St. Louis, 1990, Mosby, pp 29–41.
84. Komaromy AM, Andrew SE, Sapp HL, Jr, et al: Flash electroretinography in standing horses using the DTL microfiber electrode, Vet Ophthalmol 6:27–33, 2003.
85. Barden CA, Chandler HL, Lu P, et al: Effect of grape polyphenols on oxidative stress in canine lens epithelial cells, Am J Vet Res 69:94–100, 2008.
86. Williams DL: Oxidation, antioxidants and cataract formation: a literature review, Vet Ophthalmol 9:292–298, 2006.
87. Davis JL, Stewart T, Brazik E, et al: The effect of topical administration of atropine sulfate on the normal equine pupil: influence of age, breed and gender, Vet Ophthalmol 6:329–332, 2003.
88. Dziezyc J, Millichamp NJ, Keller CB: Use of phacofragmentation for cataract removal in horses: 12 cases (1985–1989), J Am Vet Med Assoc 198:1774–1778, 1991.
89. Farrall H, Handscombe MC: Follow-up report of a case of surgical aphakia with an analysis of equine visual function, Equine Vet J Suppl 91–93, 1990.
90. Whitley RD, Meek LA, Millichamp NJ, et al: Cataract surgery in the horse: a review of six cases, Equine Vet J Suppl 85–90, 1990.
91. Stuhr CM, Abrams G, Bullimore M, et al: The normal refractive state of the equine (Abstract), Vet Ophthalmol 2:255–266, 1999.
92. McMullen RJ, Jr: Refractive state of the aphakic equine eye, Personal communication, 2009.
93. Holladay JT: Proper method for calculating average visual acuity, J Refract Surg 13:388–391, 1997.
94. Brooks DE: Phacoemulsification cataract surgery in the horse, Clin Tech Equine Pract 4:11–20, 2005.
95. Hardman C, McIlnay TR, Dugan SJ: Phacofragmentation for morgagnian cataract in a horse, Vet Ophthalmol 4:221–225, 2001.
96. McMullen RJ, Jr, Davidson MG, Campbell NB, et al: In vitro and in vivo evaluation of a 30 D and 25 D equine intraocular lens implants, Am J Vet Res 70:In press, 2010.
97. Birch EE, Stager DR: Prevalence of good visual acuity following surgery for congenital unilateral cataract, Arch Ophthalmol 106:40–43, 1988.
98. Crewther SG, Crewther DP, Mitchell DO: The effects of short-term occlusion therapy on reversal of the anatomical and physiological effects of monocular deprivation in the lateral geniculate nucleus and visual cortex of kittens, Exp Brain Res 51:206–216, 1983.
99. Robb RM, Mayer DL, Moore BD: Results of early treatment of unilateral cataracts, J Pediatr Ophthalmol Strabismus 24:178–181, 1988.
100. Tytla ME, Lewis TL, Maurer D, et al: Stereopsis after congenital cataract, Invest Ophthalmol Vis Sci 34:1767–1773, 1993.
101. Gelatt KN, Myers VS, Jr, McClure JR, Jr: Aspiration of congenital and soft cataracts in foals and young horses, J Am Vet Med Assoc 165:611–616, 1974.
102. Gelatt KN, Kraft WE: A technique for aspiration of cataracts in young horses, Vet Med 64:415–421, 1969.
103. Colitz CMH, Davis JL: Ocular manifestations of systemic disease. In Gilger BC, editor: Equine ophthalmology, ed 1, St. Louis, 2005, Elsevier Saunders, pp 421–448.
104. Miller-Michau T: Equine ocular examination: basic and advanced diagnostic techniques. In Gilger BC, editor: Equine ophthalmology, ed 1, St. Louis, 2005, Elsevier Saunders, pp 1–62.
105. Nunnery C, Pickett JP, Zimmerman KL: Congenital stationary night blindness in a Thoroughbred and a Paso Fino, Vet Ophthalmol 8:415–419, 2005.
106. Sandmeyer LS, Breaux CB, Archer S, et al: Clinical and electroretinographic characteristics of congenital stationary night blindness in the Appaloosa and the association with the leopard complex, Vet Ophthalmol 10:368–375, 2007.
107. Witzel DA, Joyce JR, Smith EL: Electroretinography of congenital night blindness in an Appaloosa, J Equine Med Surg 1:226–229, 1977.
108. Witzel DA, Riis RC, Rebhun WC, et al: Night blindness in the Appaloosa: sibling occurrence, J Equine Med Surg 1:383–386, 1977.

109. Witzel DA, Smith EL, Wilson RD, et al: Congenital stationary night blindness: an animal model, Invest Ophthalmol Vis Sci 17:788–795, 1978.
110. Giuliano EA, Maggs DJ, Moore CP, et al: Inferomedial placement of a single-entry subpalpebral lavage tube for treatment of equine eye disease, Vet Ophthalmol 3:153–156, 2000.
111. Whitley RD, Lavach JD, Gelatt KN: Subpalpebral lavage system for administering frequent topical medications to the equine eye, Florida Vet J 8:10–14, 1979.
112. McMullen RJ, Jr, Gilger BC: Keratometry, biometry and prediction of intraocular lens power in the equine eye, Vet Ophthalmol 9:357–360, 2006.
113. Townsend WM, Jacobi S, Bartoe JT: Phacoemulsification and implantation of +14 diopter foldable intraocular lenses in five eyes of four adult horses (Abstract), Vet Ophthalmol 11:413–429, 2008.
114. Townsend WM, Wasserman N, Jacobi S, et al: Assessment of axial globe dimensions in juvenile horses (Abstract), Vet Ophthalmol 8:437–450, 2005.
115. van der Woerdt A, Wilkie DA, Myer CW: Ultrasonographic abnormalities in the eyes of dogs with cataracts: 147 cases (1986–1992), J Am Vet Med Assoc 203:838–841, 1993.
116. Whitley RD: Cataract removal in dogs. The presurgical considerations, Vet Med 9:848–858, 1993.
117. Williams DL: Lens morphometry determined by B-mode ultrasonography of the normal and cataractous canine lens, Vet Ophthalmol 7:91–95, 2004.
118. Brooks DE: Complications of ophthalmic surgery in the horse, Vet Clin North Am Equine Pract 24:697–734, 2009.
119. Gelatt KN: Recent advances in veterinary and comparative ophthalmology, Adv Vet Sci Comp Med 16:1–33, 1972.
120. Gilger BC: Phacoemulsification. Technology and fundamentals, Vet Clin North Am Small Anim Pract 27:1131–1141, 1997.
121. Glover TD, Constantinescu GM: Surgery for cataracts, Vet Clin North Am Equine Pract 27:1143–1173, 1997.
122. Kelman CH: Phacoemulsification in the anterior chamber, Ophthalmology 86:1980–1982, 1979.
123. Van Kruiningen HJ: Intracapsular cataract extraction in the horse, J Am Vet Med Assoc 145:773–777, 1964.
124. Wilkie DA, Colitz CM: Update on veterinary cataract surgery, Curr Opin Ophthalmol 20:61–68, 2009.
125. Coombes A, Gartry D: Incision planning and construction for phacoemulsification. In Coombes A, Gartry D, editors: Cataract surgery, ed 1, London, 2003, BMJ Books, pp 11–24.
126. Langerman DW: Architectural design of a self-sealing corneal tunnel, single-hingeincision, J Cataract Refract Surg 20:84–88, 1994.
127. Spiess BM, Bolliger J, Ruehli MB: Radiofrequency anterior capsulotomy to facilitate phacoemulsification and intraocular lens implantation, Vet Comp Ophthalmol 6:233–236, 1996.
128. Jaffe NS: Cataract surgery and its complications, ed 4, St. Louis, 1984, Mosby.
129. Wilkie DA, Willis AM: Viscoelastic materials in veterinary ophthalmology, Vet Ophthalmol 2:147–153, 1999.
130. Packard R, Buratto L: Complications. In Buratto L, Werner L, Zanini M, et al, editors: Phacoemulsification principles and techniques, ed 2, Thorofare, NJ, 2003, Slack Inc., pp 671–711.
131. Brooks DE: Complications of ophthalmic surgery in the horse, Vet Clin North Am Equine Pract 24:697–734, 2008.
132. Wilkie DA, Colitz CMH: Surgery of the canine lens. In Gelatt KN, editor: Veterinary ophthalmology, ed 4, Ames, IA, 2007, Blackwell, pp 888–931.
133. Apple DJ, Solomon K, Tetz MR, et al: Posterior capsular opacification, Surv Ophthalmol 37:73–116, 1992.
134. Bras ID, Colitz CM, Saville WJ, et al: Posterior capsular opacification in diabetic and nondiabetic canine patients following cataract surgery, Vet Ophthalmol 9:317–327, 2006.
135. Sigle KJ, Nasisse MP: Long-term complications after phacoemulsification for cataract removal in dogs: 172 cases (1995–2002), J Am Vet Med Assoc 228:74–79, 2005.
136. McMullen RJ, Jr, Clode AB, Gilger BC: Infrared digital imaging of the equine anterior segment, Vet Ophthalmol 12:125–131, 2009.
137. Obstbaum SA: Radiation cataracts: what have we learned? Arch Ophthalmol 119:119, 2001.
138. Schott HCn, Ewart SL, Walker RD, et al: An outbreak of salmonellosis among horses at a veterinary teaching hospital, J Am Vet Med Assoc 218:1152–1159, 2001.
139. Rosenberg LF, Burchfield JC, Krupin T, et al: Cat model for intraocular pressure reduction after transscleral Nd:YAG cyclophotocoagulation, Current Eye Research 14:255–261, 1995.

Chapter 8

Equine Recurrent Uveitis

Brian C. Gilger
Cornelia Deeg

Equine recurrent uveitis (ERU), also known as *moon blindness*, *iridocyclitis*, and *periodic ophthalmia*, has often been cited as the most common cause of blindness in horses.[1-6] This immune-mediated, panuveitis syndrome has a reported prevalence of 2% to 25% in horses in the United States.[2,5,6] However, field observations suggest that 1% to 2% of American horses suffer clinical disease serious enough to threaten vision.[3] Fortunately, recent advances in the treatment of horses with ERU have led to an improvement in management of this disease. This chapter discusses some important facts about ERU, its causes, and treatment options for the affected horse.

ERU is characterized by recurrent episodes of intraocular inflammation separated, in most horses, by periods of remission ("quiescence") in which there are no signs of active intraocular inflammation. These "bouts" of inflammation are separated by weeks to sometimes years. ERU generally develops after an initial bout of primary uveitis,[3,5-9] but not every case of initial equine uveitis will develop into ERU (see later in diagnosis). Cause of the primary uveitis, environmental factors, and genetic makeup of the horse all play a role in the development of ERU, and each horse that develops signs of uveitis is considered at risk for ERU until several years have passed without relapse after the primary uveitis.

ERU-like diseases have been described in horses since Vegetius wrote of recurrent eye inflammation in the 4th century AD.[1] Initially the syndrome was thought to be caused by the changes in the moon, hence the descriptive term *moon blindness*, still prevalent today. Much speculation occurred in the 18th, 19th, and early 20th centuries as to the cause(s) of ERU. Before 1940, prevailing theories included various infectious causes, hereditary predisposition, thyroid deficiency, riboflavin deficiency, climate, toxin hypersensitivity, and parasites.[1,10,11] Early reviews describing the clinical examination and pathologic findings of ERU[1,10,11] speculated further on infectious causes, and subsequent research was directed toward investigating bacterial etiologies. In 1947, Rimpau[12] presented evidence connecting some cases of the syndrome with leptospirosis, and in the following year, Heusser published data linking positive serum agglutinin titers to *L. interrogans* serogroups Grippotyphosa, Pomona, and Australis in German horses.[13] Although prevalence has varied with the geographic region, leptospirosis has been linked to initiation of spontaneous ERU around the world.[3,14-28]

Although leptospirosis has been linked to the initiation of ERU in many horses, other bacterial, viral, protozoan, and parasitic as well as noninfectious etiologies have been associ-

ated with the syndrome.[2,29-36] The pathophysiology of ERU is far more complex than a simple systemic infection or traumatic episode. Research in horses, humans, and laboratory and domestic animals has shown that recurrent intraocular inflammation is multifactorial in origin, related to the genetic makeup of the individual and strongly immune mediated. Numerous investigations have described the variety of changes that accompany the syndrome in the anterior and posterior segment at the cellular level.[7,37-45] Studies probing immune mechanisms responsible for triggering inflammatory episodes and tissue destruction, and relationships between the equine major histocompatibility complex (MHC) and ERU susceptibility are ongoing.[7,38,46] ERU is an intricate disease complex, and defining the pathogenesis and risk factors will continue to challenge scientists and clinicians as research continues for effective therapies.

CLINICAL ANATOMY AND PHYSIOLOGY

Equine recurrent uveitis is a syndrome that involves all aspects of the equine eye, so technically it would be considered a panophthalmitis, especially when most severe. However, the origin of the inflammation and the majority of the initial pathology are centered in the uveal tract, thus it is considered a panuveitis (Fig. 8-1). The uveal tract consists of the iris and ciliary body (the anterior uvea) and the choroid (posterior uvea).

ANATOMY AND PHYSIOLOGY OF THE UVEAL TRACT

The two components of the anterior uvea, the iris and the ciliary body, contain heavily pigmented connective, vascular, and muscle tissue. The iris functions as a shutter that responds to prevailing light conditions, and the ciliary body produces aqueous humor through active secretion and ultrafiltration of plasma. Both the iris and ciliary body have a large number of blood vessels within their connective tissue, and the inner aspect of both structures is lined by a double layer of epithelium, which has an important role in the pathophysiology of ERU. The layer of epithelium closest to the connective tissue is pigmented, and the boundary layer closest to the vitreous is nonpigmented. The clinical anatomy and microanatomy of the anterior portion of the uvea are described in Chapter 6, Diseases of the Uvea.

The choroid, or posterior part of the uvea, functions as the primary vascular supply of the horse retina (see Chapter 10). It lies between the sclera and the retina and contains the tapetum, the fibrous reflective layer (See Chapter 10 for a complete description of the choroid).

The uveal tract contains most of the blood supply of the eye and is in direct contact with peripheral vasculature. Therefore, diseases of the systemic circulation (e.g., septicemia, bacteremia, etc.) will also affect the uveal blood circulation. There is a barrier between this blood circulation and the internal aspects of the eye, termed the *blood-ocular barrier* (Fig. 8-2). The blood-ocular barrier consists of the blood-aqueous barrier (i.e., tight junctions between the nonpigmented epithelial cells of the ciliary body and nonfenestrated iridal blood vessels) and the blood-retinal barrier (i.e., tight junctions between the cells of the retinal pigmented epithelium and nonfenestrated retinal vessels). These semipermeable barriers normally prevent large molecules and cells from entering the eye and help the intraocular fluids remain clear. The blood-ocular barrier also limits the immune response to the internal aspects of the eye, causing the eye to be considered an immune-privileged site.[47] With trauma or inflammation, these barriers can be disrupted, allowing blood products and cells to enter the eye. Flare, cell accumulation, or haze in the aqueous or vitreous are clinically observable signs of the disruption of the blood-ocular barrier that occurs in ERU. Disruption of the barrier enables activation of various host immune responses, including antibody production to self-antigens that are not normally recognized by the horse's own immune system, as well as antibody production to foreign antigens inside the eye.

PHYSIOLOGY OF EQUINE RECURRENT UVEITIS

Because all the uveal tissues are abundantly populated with blood vessels, the physiology of early inflammation involves vascular congestion. This congestion causes dilation of the overlying episcleral blood vessels, resulting in episcleral vascular hyperemia that causes the characteristic "red eye" appearance of uveitis. Congestion and inflammation of the uveal vessels causes leakage of protein and fluid into the surrounding connective tissues as the blood-ocular barrier is disrupted. Infiltration of mononuclear cells into the uveal perivascular space is facilitated by vascular permeability, particularly in the ciliary body.

One hallmark of ERU is the accumulation of noncellular exudates adjacent to the uveal tract. Exudates contribute to uveal tissue dysfunction and hypotony of the globe as the ciliary body produces less aqueous humor. Nourishment of the photoreceptor layer of the retina with oxygen and other nutrients from the choriocapillaris is decreased. In addition, iris sphincter muscle spasm causes miosis and blocks the ability of the iris to adjust to prevailing light conditions.

The uvea and aqueous humor nourish a number of anatomically and functionally dissimilar components in the eye. Inflammation in uveitis is thus associated with inflammation and/or dysfunction in, variably, the cornea, sclera, lens, retina, and optic nerve. The physiology of inflammation in the non-uveal parts of the eye is dependent on the anatomy and physiology of each affected area (see Chapters 6, 7, and 10).

Transparency of the cornea is compromised when inflammatory mediators in the aqueous humor cause altered function of the corneal endothelium. Disruption of the endothelial sodium/potassium–adenosine triphosphatase (Na^+/K^+-ATPase) pump that normally keeps the cornea relatively dehydrated contributes to opacity changes. Resultant corneal stromal edema causes focal or diffuse opacity and general "steaminess" of the cornea. Edema can become permanent if endothelial dysfunction is severe. Corneal cellular infiltrate or extensive vascularization is not a primary feature of ERU; if present, the clinician should rule out primary corneal disease such as stromal abscessation or immune-mediated keratitis.[48,49]

Function of the lens is compromised when it becomes opacified or dislocated. Cataract occurs as the lens increases in water, electrolyte, and mineral content in response to changes in aqueous humor or adhesions of the uvea (synechia). Normal uptake of oxygen into the lens is reduced because of the abnormal aqueous humor, contributing further to loss of

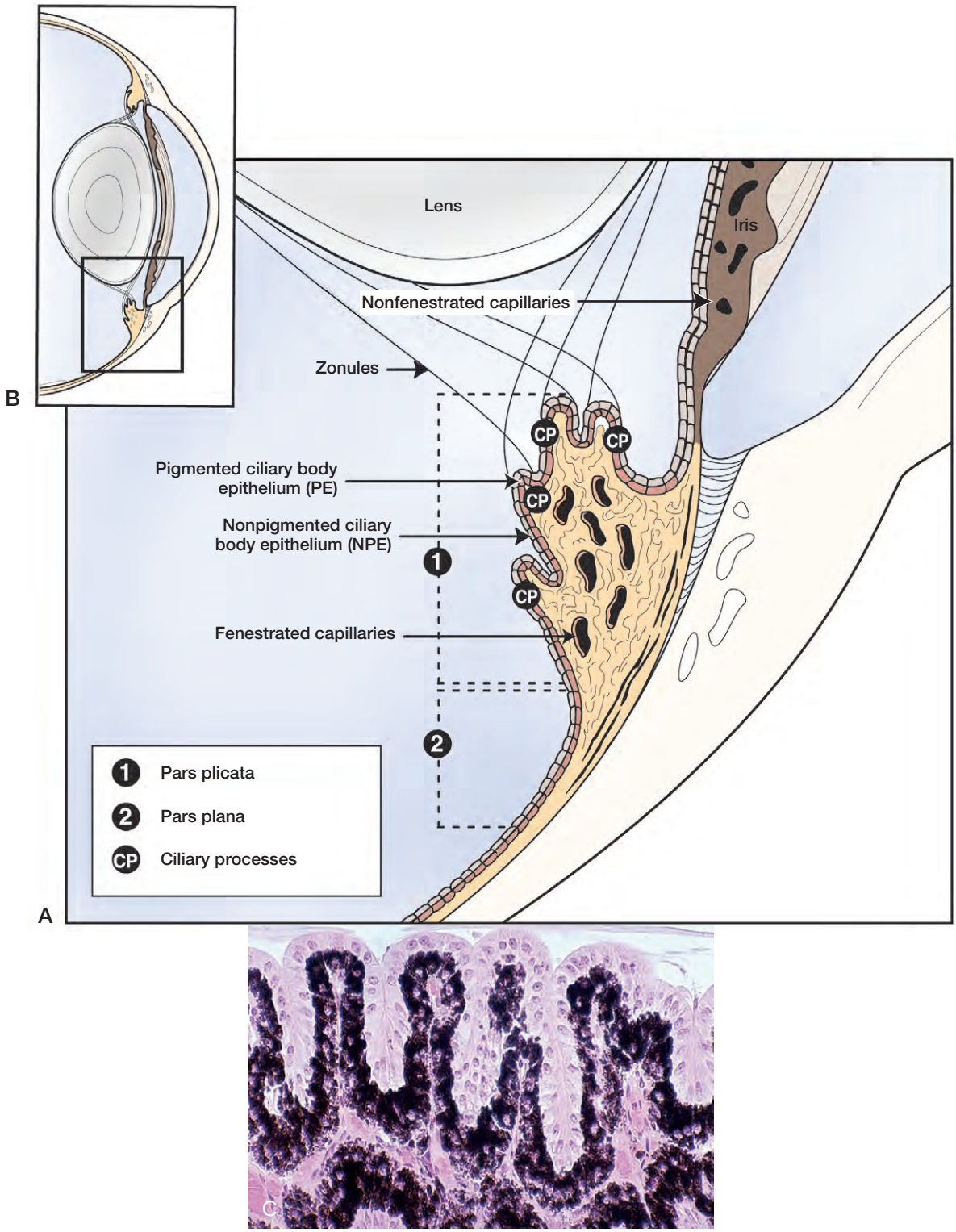


Figure 8-1. **A** and **B,** Schematic diagram of the iris and ciliary body. **C,** Normal histologic section of ciliary processes demonstrating pigmented and nonpigmented ciliary epithelium.

Continued

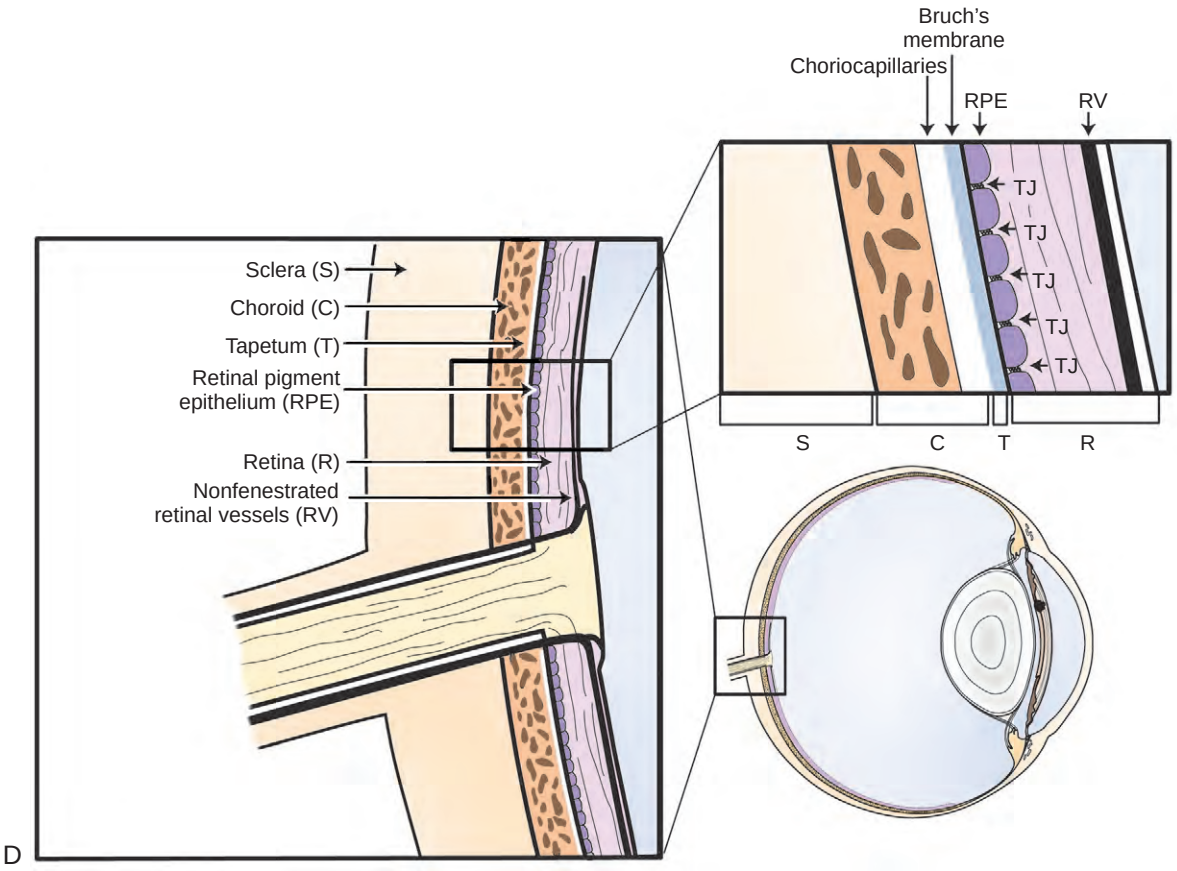


Figure 8-1, cont'd. **D,** Schematic diagram of the choroid. *TJ*, Tight junctions.

transparency. Luxation of the lens occurs when the zonular fibers, normally attached to the ciliary processes of the ciliary body, detach or degenerate because of chronic presence of inflammatory mediators.

Function of the retina is disrupted if the photoreceptors are deprived of oxygen and other nutrients normally supplied by the choriocapillaris, if inflammatory toxins from the vitreous damage cellular components, or if the retina detaches as a result of subretinal exudates and cellular infiltrate from the inner choroid. Optic nerve function is disturbed if the blood supply to the nerve is compromised due to choroidal inflammation, infarcts, or secondary glaucoma with resultant ischemia of the nerve.

The ocular media serve as collecting chambers for infiltrating cells and inflammatory byproducts. Their physiology is often altered in ERU. The anterior chamber changes transparency in instances where there is fibrin accumulation, flare, hyphema, or hypopyon. Accumulation of inflammatory cells and byproducts in the aqueous may obstruct the trabecular meshwork or uveoscleral region, resulting in secondary glaucoma. Chronically, glaucoma may occur from synechia, vascular overgrowth of the iridocorneal angle, or fibrosis of the uveal tissue.

The posterior segment of the eye may have altered clarity from leakage of blood cells, macromolecules, and plasma components from the choroid and ciliary body into the vitreous. Infiltrating mononuclear cells and inflammatory cytokines can alter waste removal and contribute to liquefaction of the normally gel-like framework of the vitreous. Loss of the viscoelastic properties, combined with traction from the collapsing collagen network of the vitreous, may exert pull on the sparsely anchored retina and contribute to detachments and vision loss.

IMPACT OF EQUINE RECURRENT UVEITIS ON THE HORSE INDUSTRY

Ocular diseases are among the most common health disorders of horses. In fact, in the 2005 U.S. Horse Council report,[50] in the study's 12 months, 6.5% of farms in the United States had at least one horse with an eye problem, and ocular disease was the fifth most common equine disorder. Of these eye diseases, inflammation of the eye, such as keratitis and ERU, are the most common causes of blindness.[50] Prevalence of infectious ocular disease and immune-mediated ocular disease in horses is higher than in any other animal other than human beings. In humans, these inflammatory ocular diseases are characterized by molecular features, and many are known to be hereditary or associated with genetic phenotypes. This is similar to horses, but much more knowledge is needed regarding genetic inheritance and ERU susceptibility. Because ERU has a high prevalence rate across horse breeds in the United States, the economic impact of this disease on the equine industry could be very high, especially when one factors in the effect of ERU on disruption of training, decreased performance, and disqualification of horses from competition (due to medication use, etc.; see more information in Chapter 2). Horses with ERU have

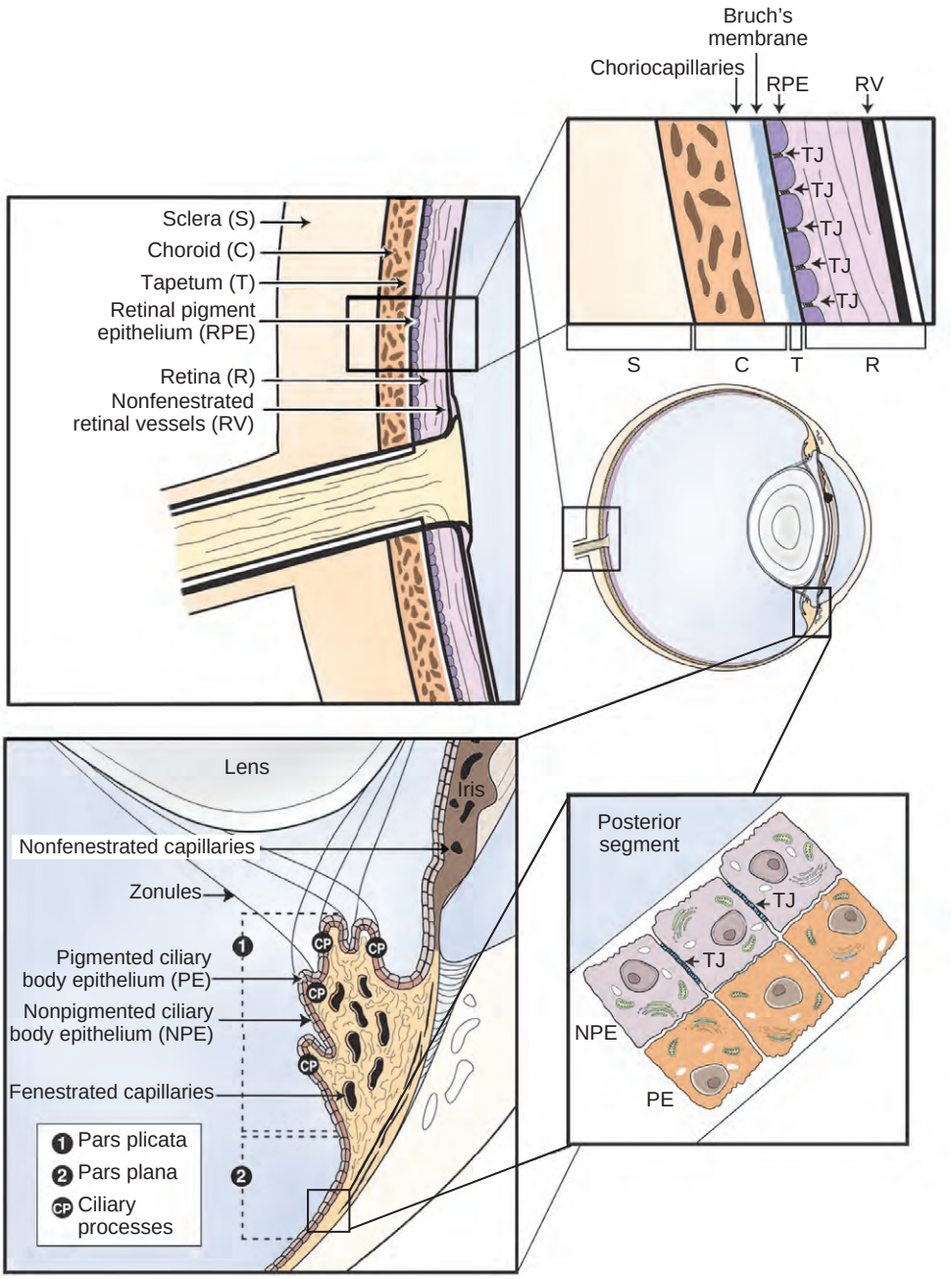


Figure 8-2. The barrier between blood circulation and internal aspects of the eye is called the *blood-ocular barrier* and consists of the blood-aqueous and blood-retinal barriers, which normally prevent large molecules and cells from entering the eye. The blood-aqueous barrier is composed of tight junctions *(TJ)* between nonpigmented ciliary epithelium and nonfenestrated iridal blood vessels. The blood retinal barrier is composed of TJ between retinal pigment epithelium *(RPE)* and nonfenestrated retinal blood vessels.

decreased value as a result of vision loss, and many horses that are blinded by ERU must be euthanized for practical and economic reasons. Treatment, veterinary care, and personnel costs add to the economic impact of the disease.

CLASSIFICATION OF EQUINE UVEITIS

The syndrome of ERU must be differentiated from primary uveitis, which is a different disease pathophysiologically. Any cause of breakdown of the blood-ocular barrier may result in problems associated with a clinical diagnosis of uveitis; however, equine recurrent uveitis is a separate disease characterized by chronic recurrent bouts of uveitis. See later discussion regarding the diagnosis of ERU and pathophysiology of the development of this syndrome. Horses experiencing an initial episode of uveitis from any cause are at risk for recurrent uveitis but are not classified as ERU cases until two or more episodes of inflammation have been observed. If several (i.e., 2 or more) years have passed without occurrence of a second episode of uveitis, the risk of development of ERU in that horse is diminished.

Equine uveitis is characterized as primary or recurrent. Recurrent uveitis is further characterized into three main clini-

Table 8-1 | **Clinical Classification of Equine Uveitis**

CLASSIFICATION		DESCRIPTION
PRIMARY UVEITIS		First or persistent bout of ocular inflammation (see Chapter 6 for causes)
SYNDROME OF EQUINE RECURRENT UVEITIS (ERU)		
Clinical classification	Classic recurrent	Active inflammatory episodes followed by periods of minimal ocular inflammation
	Insidious	Persistent low-grade intraocular inflammation without overt signs of discomfort
	Posterior	Recurrent inflammation primarily in the vitreous, retina, and choroid
Stage of chronicity	Active/acute	Actively inflamed eye with signs of intraocular inflammation
	Quiescent	No clinical evidence of active internal inflammation and a comfortable eye
	End-stage	Blind eyes with phthisis bulbi with possibly dense cataract, luxated lens, detached retina, and/or loss of normal pupillary architecture

cal syndromes in horses: classic ERU, insidious ERU, and posterior ERU (Table 8-1). Because ERU most commonly involves all areas of the uveal tract (i.e., panuveitis), the human anatomic classification of uveitis (i.e., anterior, intermediate, and posterior uveitis) is not particularly distinguishing in horses.

Classic ERU is most common and is characterized by active inflammatory episodes in the eye followed by periods of minimal observable ocular inflammation. The acute active phase of ERU predominantly involves inflammation of the iris, ciliary body, and choroid, with concurrent involvement of the cornea, anterior chamber, lens, retina, and vitreous (Fig. 8-3). After variable periods of time, the quiescent phase is generally followed by further and increasingly severe attacks of uveitis. In many horses, the repeated episodes of inflammation cause development of cataract, intraocular adhesions, phthisis bulbi, and vision loss (Fig. 8-4).[5,10,29,36,51]

Insidious ERU is characterized by a low-grade intraocular inflammation that does not manifest as outwardly painful episodes but has a gradual and cumulative destructive effect, which leads to degeneration of ocular structures and chronic clinical signs of ERU (Fig. 8-5). This type of ERU is most commonly seen in Appaloosa and Draft breed horses.

Posterior uveitis is inflammation predominantly in the vitreous, retina, and choroid (although mild anterior segment inflammation is commonly present). Clinical signs include bouts of vitreal inflammation, cloudiness, retinal detachment, and vision loss (Fig. 8-6). Chronically, these horses may develop cataracts, retinal detachments, vitreal degeneration (with or without fibrous strands), and retinal degeneration. This syndrome is most common in Warmbloods, Draft breeds, and European horses.

ERU may be further separated according to stage of chronicity, with cases labeled as "active or acute," "quiescent," or "end-stage" (see Table 8-1). Acute or active cases show active pain and observable internal inflammation manifested as blepharospasm, mild to moderate corneal edema, aqueous flare, aqueous cells, hypopyon, iris hyperemia, miosis, hypotony, vitreal cellular infiltrate, and possibly retinal inflammation and detachment (Fig. 8-7). Quiescent cases are outwardly comfortable and show little active acute internal inflammation on clinical examination. However, quiescent cases may have chronic inflammatory sequelae such as synechiae or cataracts. End-stage cases are usually eyes with chronic ERU with severe and often blinding changes such as phthisis bulbi, dense cataract, luxated lens, detached retina, and/or loss of normal pupillary architecture (Fig. 8-8).

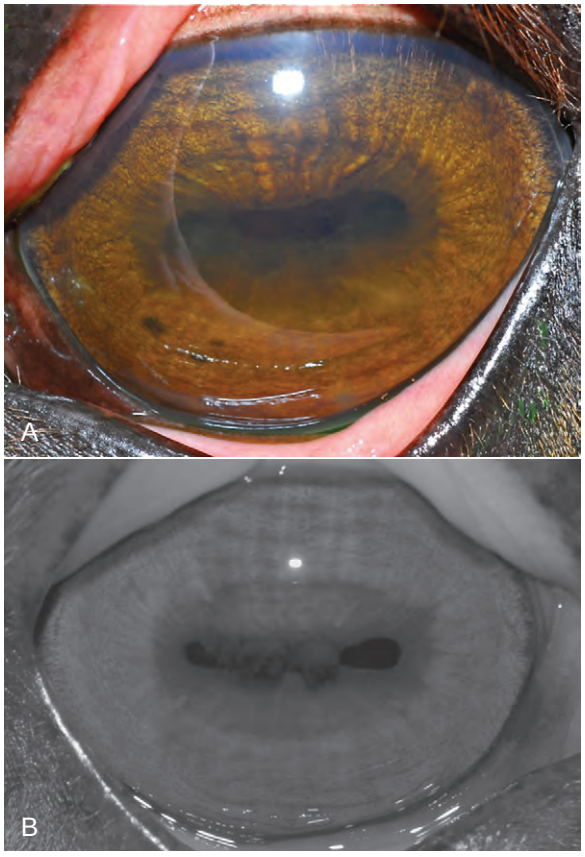


Figure 8-3. Active bout of anterior uveitis. **A,** Inflammation is observed primarily in the anterior segment, with conjunctival hyperemia, iris hyperemia/swelling, intense miosis, and fibrin in the anterior chamber. **B,** Infrared photograph of same eye as in **A,** demonstrating intense miosis and iris swelling.

CLINICAL APPEARANCE OF EQUINE RECURRENT UVEITIS

No gender predilection has been reported for ERU. Age of the initial episode is variable. One study of 160 horses with ERU found that half presented before 12 years of age, a time when horses are in their prime performance years.[3] Clinical signs are variable and depend on the stage of the episode, preexisting chronic ocular changes, the nature of the inflammation, and the anatomic location of the majority of the inflammation.

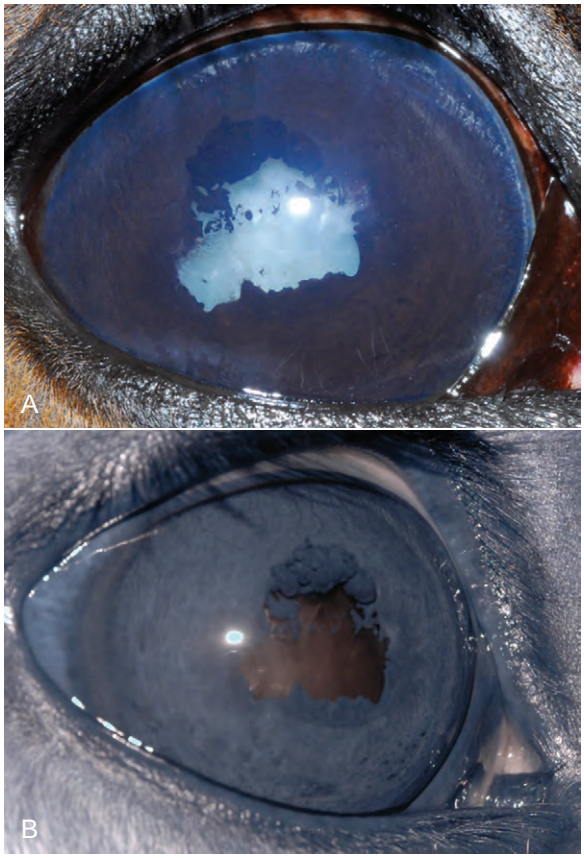


Figure 8-4. Chronic ocular changes in an eye with multiple recurrent episodes of uveitis. **A,** Mild corneal edema, multifocal posterior synechia, corpora nigra atrophy, iris hyperpigmentation, and dense cataract are visible and are all signs typical of chronic equine recurrent uveitis. **B,** Infrared photograph of same eye as in **A,** showing iris detail.

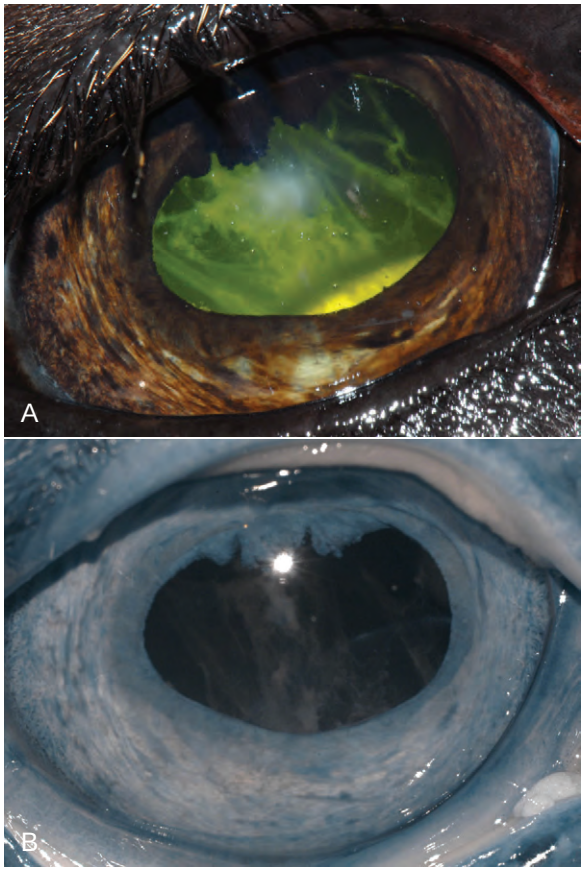


Figure 8-6. **A,** Dense vitreous opacities and yellow discoloration of the vitreous in an eye with primarily posterior uveitis. **B,** Infrared photograph of same eye as in **A,** showing iris detail.

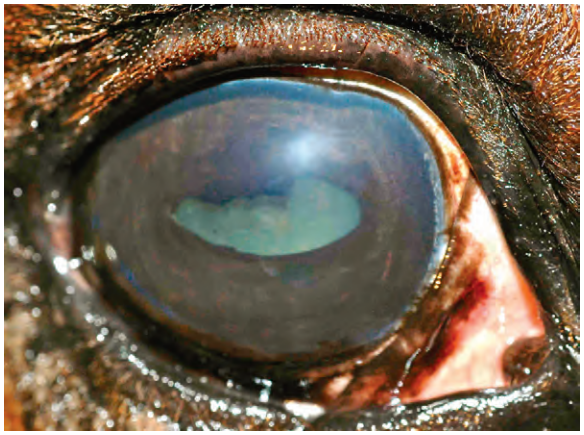


Figure 8-5. A horse with insidious uveitis. These horses do not show signs of discomfort, but ocular examination reveals chronic inflammatory changes. In this eye there is corneal edema, iris hyperpigmentation, dyscoria, corpora nigra atrophy, miosis, and cataract formation.

Figure 8-7. A horse experiencing a classic acute inflammatory episode of equine recurrent uveitis. Periocular swelling, lacrimation, corneal edema, and blepharospasm are visible.

OCULAR SIGNS: ANTERIOR SEGMENT

A horse experiencing a classic acute inflammatory episode presents with pain, lacrimation, and blepharospasm (see Fig. 8-7). The severity of the clinical signs varies from a slightly closed eye to a horse that will not tolerate any manipulation of the periocular structures without sedation. Severe blepharoedema may make ocular examination difficult. The cornea may be edematous, with the resultant opacity being most marked at the periphery. Cellular infiltrate (i.e., white or yellow corneal

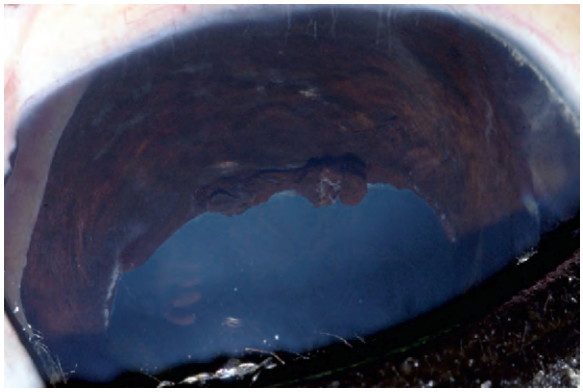


Figure 8-8. Typical clinical signs of chronic equine recurrent uveitis. Corpora nigra degeneration and/or thinning, depigmentation of the iris margin, and hyperpigmentation of the iris stoma are present.

infiltrate) or extensive corneal vascularization is not common in ERU, and their presence may suggest primary corneal disease instead of ERU. Short, deep, circumlimbal vascularization is frequent, however, and the length of the vessels are proportional to the duration of the episode. Fluorescein dye uptake will be negative, unless the horse has suffered a secondary ulcer from self-trauma. The anterior chamber may appear cloudy or hazy due to aqueous flare, and hypopyon or hyphema may be present in the ventral anterior chamber. Keratic precipitates may be visible as focal white spots on the endothelium of the cornea. A cardinal sign of active uveitis is miosis (see Fig. 8-3),[36] always present in an acute episode unless mydriatics have been administered or synechiae distort the pupil. The iris may be dull in color, show mottled pigmentation or depigmentation, or have changes in color or fibrosis (Fig. 8-9). Corpora nigra degeneration with thinning and depigmentation of the iris margin is very characteristic of ERU and may develop after several inflammatory episodes (see Figs. 8-4, 8-5, 8-8, and 8-9).

A horse with insidious ERU does not appear painful, but examination of the eyes often shows inflammatory changes suggestive of chronic inflammation. Commonly the conjunctiva and episclera are hyperemic and mild to moderate blepharitis is often observed (see Fig. 8-5). The cornea may be mildly edematous, dull, or hazy. Corneal cellular infiltrate or extensive vascularization is not a feature of insidious ERU, although focal limbal vascularization may be discernible. Fluorescein dye uptake will usually be negative. Aqueous flare (1 to 2+) is usually visible on slit-lamp biomicroscopy. The iris is discolored and hyperpigmented. Degeneration of the corpora nigrans is a hallmark clinical sign of insidious ERU and is commonly associated with iris atrophy and fibrosis (see Fig. 8-5). The pupil is usually miotic with a sluggish pupillary light reflex.

Inflammatory sequelae and scarring are often apparent in the anterior segment of both classic and insidious ERU cases. If the horse has had previous corneal disease (e.g., corneal ulcer), corneal scars may be present. Calcific band keratopathy is occasionally seen in the corneal subepithelium or outer stroma in horses with chronic ERU (Fig. 8-10). Posterior synechia, pigment on the anterior lens capsule, or pupillary occlusion are common manifestations of past damage in both classic and insidious ERU (Fig. 8-11). Focal or diffuse cataracts may be apparent (Fig. 8-12). Dense cataracts may obscure visualization

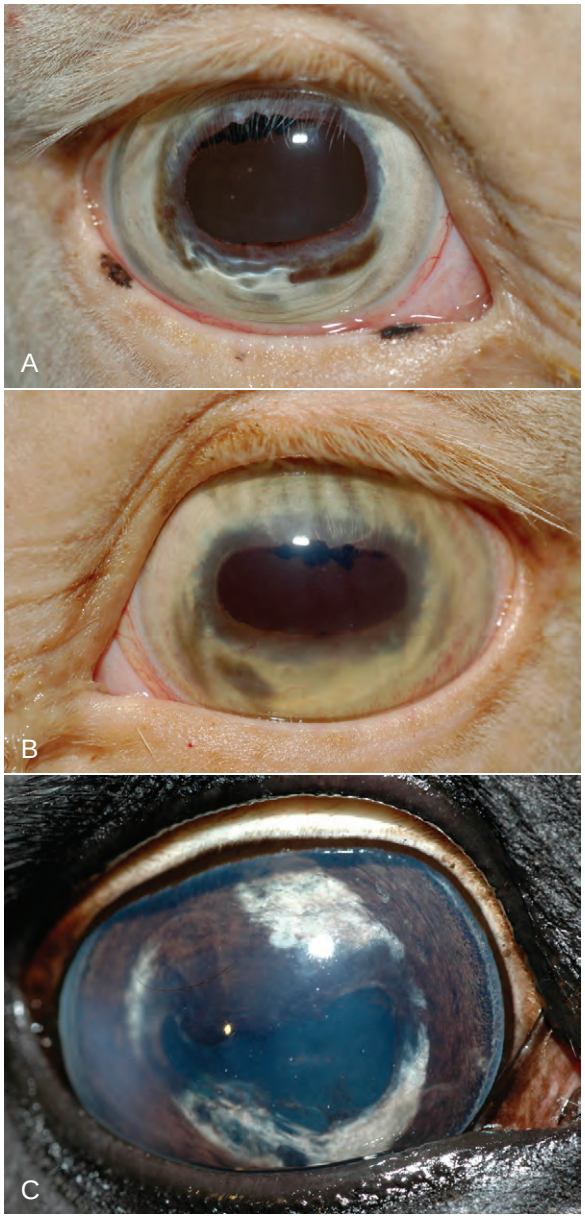


Figure 8-9. Iris color changes in equine recurrent uveitis. In acute uveitis, the iris can change to a yellow or even green color as a result of infiltration or inflammatory cells and serum. This color change is most prominent in blue or light-colored irises. **A,** Noninflamed right eye of a light-colored horse. **B,** Left eye of the same horse with a discolored iris due to active uveitis. Note peripheral corneal vascularization and miosis. **C,** Depigmentation of a dark iris also occurs but much less commonly than hyperpigmentation (see Fig. 8-8). This horse has progressive iris depigmentation associated with recurrent uveitis. Note other signs of chronic inflammation, such as corpora nigra atrophy, dyscoria, and synechia.

of the posterior segment, and lens luxation or subluxation are observed occasionally (Fig. 8-13).

Most eyes with acute uveitis are hypotensive, with intraocular pressures (IOPs) of 5 to 12 mm Hg, and commonly the anterior chamber is shallow. Glaucoma is a common sequela to all types of ERU, and this secondary glaucoma may be the most common underlying cause of glaucoma in horses (see Chapter 9). Horses that develop secondary glaucoma will have

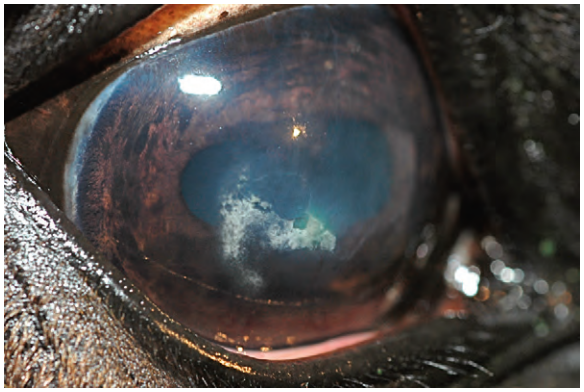


Figure 8-10. Calcific band keratopathy in a horse with chronic recurrent uveitis.

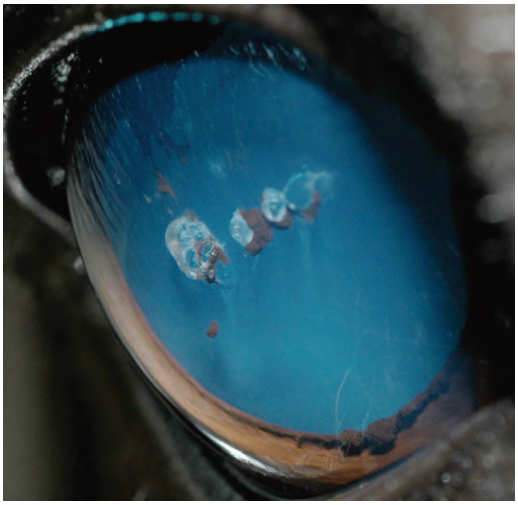


Figure 8-11. Pigment deposits ("rests") on the anterior lens capsule are common with recurrent uveitis. These are likely the results of temporary posterior synechia. Capsular and/or anterior cortical cataract and subcapsular cysts are common and are visible adjadcent to the pigment in this photograph. (Photograph courtesy Dr. Riccardo Stoppini.)

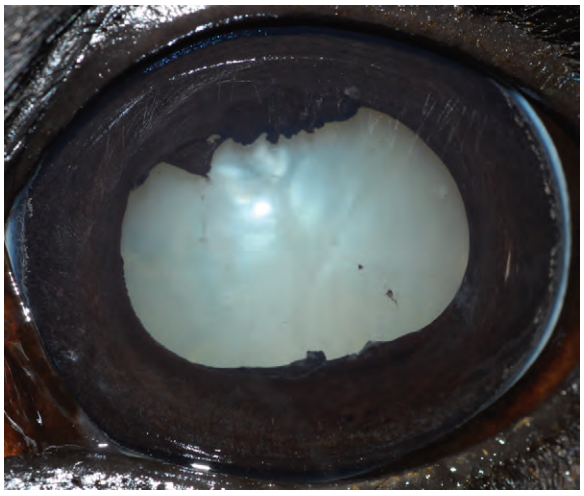


Figure 8-12. Mature, complete cataract formation in a horse with chronic recurrent uveitis. Note the iris hyperpigmentation, corpora nigra degeneration, and pigment on the anterior lens capsule—all typical signs of multiple recurrent episodes of uveitis.

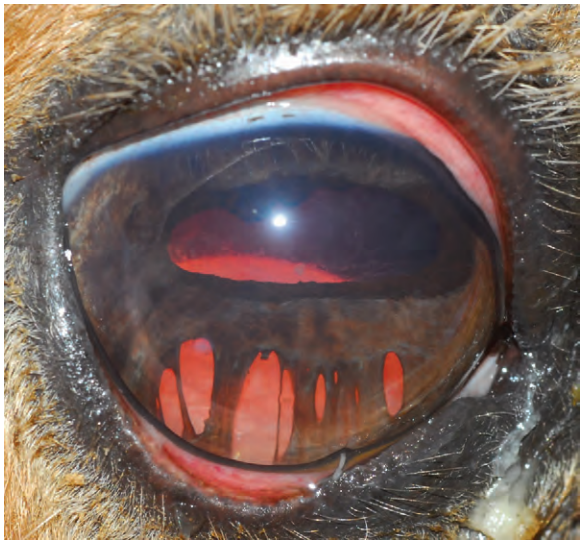


Figure 8-13. Posterior lens luxation and iris atrophy in a Miniature horse with chronic ERU. The lens has fallen posteriorly into the vitreous, and only the dorsal portion of the lens is visible in pupil.

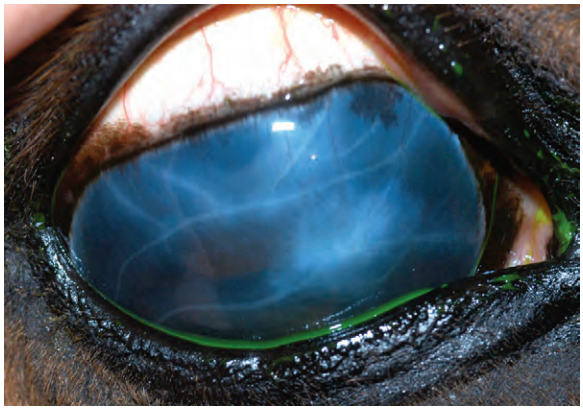


Figure 8-14. Enlarged eye secondary to glaucoma that developed as a result of chronic ERU. Note the multiple corneal striae.

diffuse corneal edema that does not respond to antiinflammatory medications, or at least does not respond as well as observed in previous bouts. IOPs typically range from 35 to 80 mm Hg in these eyes. Enlarged eyes and development of cornea striae secondary to glaucoma occur with chronic ERU (Fig. 8-14).

OCULAR SIGNS: POSTERIOR SEGMENT

In acute classic or insidious ERU, the posterior segment of the eye is usually not visible because of anterior segment cloudiness of ocular media and miosis. When these eyes are quiescent and pupils are dilated, the chronic sequelae of ERU may be observed. Posterior segment lesions are more easily observed in horses with posterior ERU because the anterior segment is relatively normal, especially early in the disease. With chronicity, however, posterior synechia, cataract, and vitreal debris will limit the view of the posterior segment even in eyes with predominantly posterior ERU.

Some horses have no observable vitritis but show chorioretinal scarring of the peripapillary region or other evidence of

retinal degeneration. The most common patterns of chorioretinal scarring are seen in the nontapetal area near the disc and present as either multiple, small, circular focal areas of depigmentation with a central area of hyperpigmentation ("bullet-hole" scarring) or wing-shaped areas of hypopigmentation nasal and temporal to the optic disc ("butterfly" lesions [Figs. 8-15 and 8-16]).

Other horses demonstrate severe vitritis where detail of the fundus is obscured and the optic disc appears orange-red owing to the vitreal inflammation and haze. Liquefaction of the vitreous is common, as are visible strands of clumped infiltrating mononuclear cells and inflammatory products (floaters [Fig. 8-17]). These opacities appear to float and move easily in the vitreous in response to eye movements. Fibrinous traction bands may be apparent as white spike-like structures that radiate from the perimeter of the optic disc (Fig. 8-18). Retinal detachments may be present and appear as a veil-like transparency that obscures fundic detail. In fact, ERU is one of the most common causes of retinal detachment in horses.[52]

CHRONIC END-STAGE EQUINE RECURRENT UVEITIS

Horses with chronic end-stage ERU show variable degrees of discomfort and inflammatory sequelae. Recurrent episodes of inflammation may subside but may be replaced by constant low-grade discomfort from blepharitis, mucopurulent lacrimation, conjunctivitis, and ocular irritation (Fig. 8-19). Some horses appear comfortable and do not have signs of recurrent episodes of inflammation. Ocular structures often become severely scarred if eyes undergo phthisis bulbi. In these eyes, corneal scarring may be dense and develop folding and anterior synechiae (Fig. 8-20). Iris architecture may be lost or indistinct. Cataracts and lens luxations are common, and the color of the

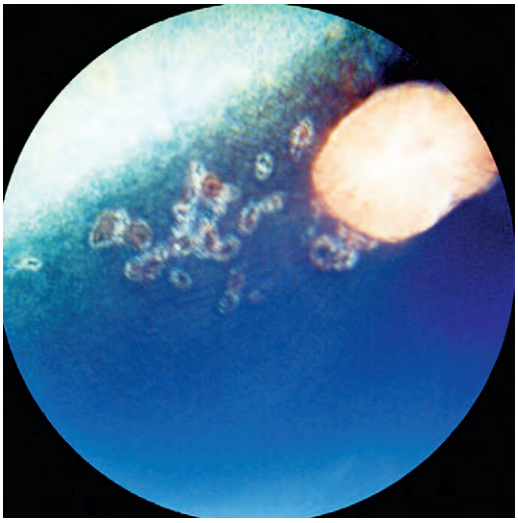


Figure 8-15. Chorioretinal scarring is in the nontapetal area near the disc and appears as multiple small, circular focal areas of depigmentation with a central area of hyperpigmentation ("bullet-hole" scarring). These lesions may be suggestive of previous uveitis.

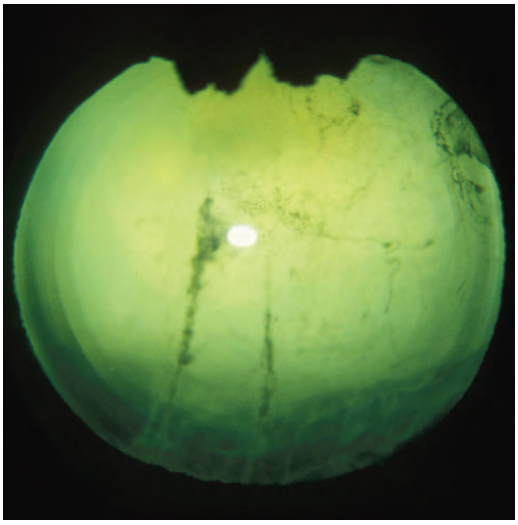


Figure 8-17. Vitreal degeneration and cellular infiltrate in vitreous. Liquefaction of the vitreous is common in ERU, as are visible strands of clumped, infiltrating mononuclear cells and inflammatory products.

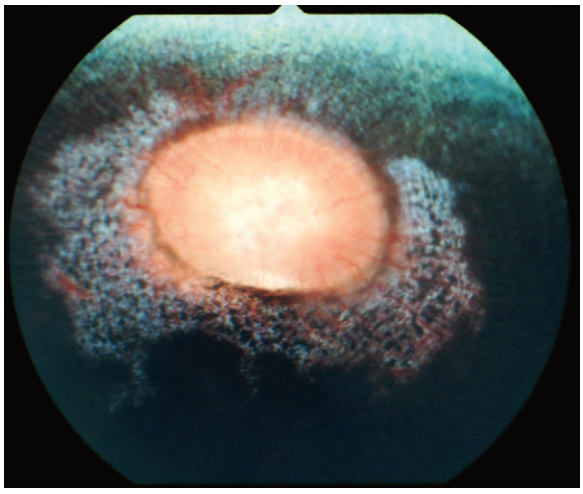


Figure 8-16. Wing-shaped areas of hypopigmentation nasal and temporal to the optic disc ("butterfly" lesions) suggestive of previous uveitis.

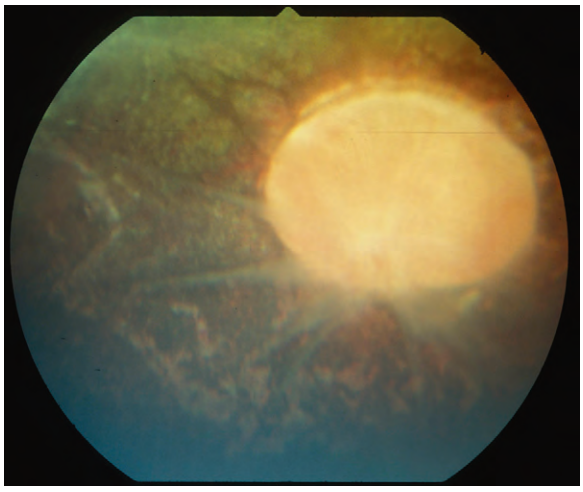


Figure 8-18. Fibrinous traction bands that radiate from the perimeter of the optic disc.

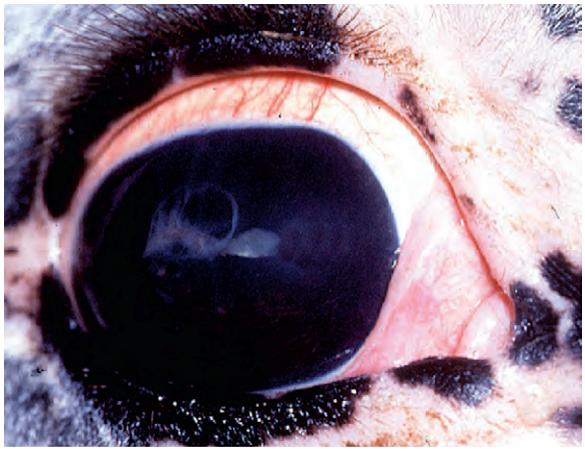


Figure 8-19. Chronic end-stage recurrent uveitis in an Appaloosa. This horse had the insidious form of recurrent uveitis and did not demonstrate discomfort. There is phthisis bulbi, miosis, corpora nigra atrophy, synechia, and cataract formation.

Figure 8-20. Chronic end-stage recurrent uveitis in an eye with phthisis bulbi, dense corneal scarring and wrinkling, and extensive anterior synechiae.

lens may become yellow. Complete retinal detachment is also common. The nictitans may become elevated or prolapse as the globe becomes phthisical, and the mucosa may show chronic inflammation. A head tilt or "star-gazing" head posture is sometimes observed in blind horses with end-stage ERU (Fig. 8-21).

BILATERAL VERSUS UNILATERAL OCULAR INVOLVEMENT

The initial episode of uveitis may be bilateral or unilateral. Recurrences may occur in one or both eyes. Sometimes one eye suffers initial inflammation, and then the other eye becomes inflamed at a later interval. In other instances, inflammation remains in just one eye. A horse that has had unilateral ERU for 2 or more years but no inflammation in the fellow eye during that time has a greatly reduced chance of the second eye developing ERU. The majority of cases of insidious ERU are bilateral, but one eye may be more severely affected than the other.

One study found that approximately 50% of eyes with leptospiral-induced ERU were bilateral.[53] In this same study, 81% of Appaloosa horses with ERU had bilateral involvement.[53] Of a small series of 32 horses that were seronegative to *L. interrogans* serogroup Pomona and were of non-Appaloosa breeding, 38% had bilateral involvement (Table 8-2).[53] In a recent study reviewing 186 cases of ERU that received a cyclosporine implant, only 16% had bilateral disease.[54]

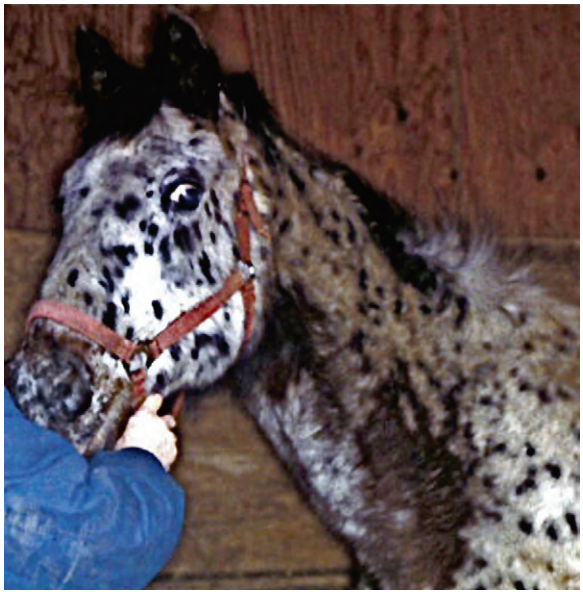


Figure 8-21. A head tilt or "star-gazing" head posture is sometimes observed in blind horses with end-stage equine recurrent uveitis. (Photograph courtesy Dr. Ann Dwyer.)

IMMUNOLOGIC ASPECTS OF EQUINE RECURRENT UVEITIS

Pathogenesis of ERU is immune mediated. Although the etiology of ERU is still under discussion, there is agreement that a dysregulated immune response causes the disease.[7] It explains the recurrences of inflammation, the positive effect of corticosteroids (or other more selective immunosuppressive agents), and the insufficient therapeutic success of antibiotics. The relevance of the inflammatory reaction is underscored by the successful therapeutic strategy of immunosuppression, the gold standard therapy to control ERU for decades.[55] Use of corticosteroids is the therapy of choice, but a more precise local targeting of T cells only has been shown to be effective in controlling recurrent disease by using an intraocular cyclosporine device.[54-58]

GENERAL FEATURES OF OCULAR IMMUNOLOGY AND EQUINE RECURRENT UVEITIS

Physiologically, the inner eye is devoid of immune cells, and the eye maintains an immunosuppressive environment through, for example, factors expressed in the vitreous such as transforming growth factor β (TGF-β). The eye has long been recognized as an immune-privileged organ. Immune privilege in the eye was originally ascribed to its separation from the systemic immune system by the blood-ocular barrier, lack of lymphatics, and the presence of limited numbers of resident leukocytes. But extensive detailed work has demonstrated that

Table 8-2 | **Outcome, Chronic Ocular Changes, and Concurrent Ocular Problems in Appaloosa and Non-Appaloosa Horses That Are Seropositive or Seronegative for *Leptospira* Pomona***

	APPALOOSA HORSES				NON-APPALOOSA HORSES				TOTAL	
SEROLOGY TO *LEPTOSPIRA* POMONA	POSITIVE		NEGATIVE		POSITIVE		NEGATIVE		TOTAL	%
Total # with uveitis	14		28		86		32		160	100%
Unilateral equine recurrent uveitis (ERU)	5	36%	3	11%	48	56%	20	62%	76	48%
Bilateral ERU	9	64%	25	89%	38	44%	12	38%	84	52%
Vision loss (1 or 2 eyes)	14	100%	20	72%	44	51%	11	34%	89	56%
Bilateral vision loss	7	50%	8	29%	15	17%	2	6%	32	20%
CHRONIC OCULAR CHANGES										
Corneal striae	2	14%	5	18%	4	5%	2	6%	13	8%
Corneal scars	4	29%	10	36%	22	26%	6	7%	42	26%
Corneal calcium deposits	1	7%	1	4%	8	9%	0		10	6%
Corneal streaks	6	43%	4	14%	5	19%	0		15	9%
Corneal opacity, other	0		0		3		0		3	8%
Corpora nigrans excess	0		4	14%	5	19%	3	9%	12	2%
Iris atrophy	7	50%	16	67%	16	19%	2	6%	41	26%
Iris color change	5	36%	12	43%	13	22%	3	9%	33	21%
Anterior synechiae	1	7%	0		3	3%	0		4	3%
Posterior synechiae	6	43%	11	39%	23	27%	5	16%	45	28%
Lens luxation	4	29%	8	29%	6	7%	4	13%	22	14%
Diffuse cataract	10	71%	21	75%	26	30%	9	28%	66	41%
Focal cataract	5	36%	4	14%	16	19%	3	9%	23	14%
Vitritis	0		6	21%	23	27%	7	22%	41	26%
Vitreal traction bands	0		2	7%	7	8%	2	6%	11	7%
Detached retina	0		2	7%	9	10%	0		11	7%
Peripap alar depigment	1	7%	5	18%	5	19%	8	25%	19	12%
Peripap focal depigment	3	21%	1	4%	11	13%	9	28%	24	15%
Glaucoma	1	7%	8	29%	6	7%	3	9%	18	11%
Phthisis bulbi	7	7%	3	11%	13	15%	1	3%	24	15%
CONCURRENT PROBLEMS										
Corneal ulcers	4	29%	12	42%	19	22%	8	25%	43	27%
COPD (heaves)	1	7%	6	21%	0		1	3%	8	5%
Laminitis	2	14%	3	11%	2	2%	0		7	4%
Abortion	0		0		2	2%	0		2	1%
Fever in past	0		0		7	8%	0		7	4%
Night blindness	0		3	11%	0		0		3	2%
Neoplasia	1	7%	1	4%	2	2%	3	9%	7	4%
Cushing's	0		1	4%	0		0		1	0%
Enucleations	0		3	11%	2	2%	1	3%	6	4%
Injuries secondary to blindness	1	7%	3	11%	6	7%	4	13%	14	9%
Died or euthanized due to blindness	2	14%	6	22%	7	8%	0		15	9%

*Data collected by Dr. Ann Dwyer, Scottsville, NY.

privilege is in fact a far more active process than this. The blood-ocular barrier is a specialized endothelium with tight junctions that control cell traffic in a highly regulated fashion. Naïve T cells cannot cross the normal blood-retinal barrier because of the high shear stress in the retinal vessels and the lack of appropriate adhesion molecules. Expression of chemokines such as RANTES in the ciliary epithelium may play a role in recruitment and activation of leukocytes in diseased eyes.[41] Furthermore, inner and outer blood-retinal barriers keep cells from the healthy inner eye.[59] Retinal blood vessels that are similar to cerebral blood vessels maintain the inner blood-ocular barrier. This physiologic barrier comprises a single layer of nonfenestrated endothelial cells which have tight junctions. The retinal pigment epithelium maintains the outer blood-retinal barrier.[59] Since the horse retina is mainly avascular, the outer blood-retinal barrier (retinal pigment epithelium) mainly keeps the immune effector cell-free environment in equine eyes.[60]

In ERU, considerable amounts of leukocytes are able to enter the inner eye and cause damage to the inner ocular tissues.[38] Analysis of the infiltrating cells revealed that the majority of cells are lymphocytes in most ERU cases.[38] These cells are predominantly CD4-positive T cells that secrete pro-inflammatory cytokines such as interleukin 2 (IL-2) and interferon γ (IFN-γ).[40] The IFN-γ-producing phenotype is named *T_H1 helper cell*. T_H cells are involved in activating and directing other immune cells and are particularly important in the immune system. They are essential in determining B-cell antibody class switching, in the activation and growth of cytotoxic T cells, and in maximizing activity of macrophages.[61] It is this diversity in function and their role in influencing other cells that gives helper T cells their name. Until recently, this cell type of IFN-γ-producing T_H1 effector cells was considered the main pathogenic pathway in autoimmune diseases. T_H17 cells are a newly identified subset of $CD4^+$ T-helper cells producing IL-17.[62] They are found at interfaces between the external environment and the internal environment, such as the skin and lining of the GI tract. Numerous immune regulatory functions have been reported for the IL-17 family of cytokines, presumably due to their induction of many immune signaling molecules. Most notably, IL-17 is involved in inducing and mediating

proinflammatory responses.[62] IL-17 induces the production of many other cytokines, chemokines, and prostaglandins from many cell types. The increased expression of chemokines attracts other cells, including neutrophils but not eosinophils. T_H17 lymphocytes are implicated in a variety of immune-related diseases, including rheumatoid arthritis.[63] Recently, T_H17 and IL-17 have been found to increase in patients with juvenile idiopathic arthritis (JIA) and Behcet's disease, each of which may be associated with uveitis.[64] Novel data from experimental uveitis models in rodents also point to a significant role of IL-17 in uveitis.[65,66] It is interesting to note that whereas the T_H17 line typically recruited a mostly granulocytic inflammatory infiltrate into the eye, the T_H1 line recruited a predominantly mononuclear infiltrate. Notably, the severity of tissue pathology induced by T_H1 cells was no less than that induced by T_H17 cells.[67] To date, it is not known if a certain percentage of ERU cases are caused through T_H17 cells, because adequate tools to address this question are lacking at the moment. Interestingly, a few ERU cases had a pure granulocytic infiltrate in the inner eye.[39] This was also seen in an experimental model of induced uveitis in horses using interphotoreceptor retinoid-binding protein (IRBP) as an autoantigen. Inflammatory cells differed between experimental horses.[68] Differences in the immunologic response profile could account for pathologic and clinical disease manifestation differences, but this is speculative to date.

AUTOANTIGENS AND EQUINE RECURRENT UVEITIS

Uveitis is a clinically heterogeneous disease. Although the antigenic triggers of autoimmune uveitis are still under discussion, there is a large body of evidence implicating responses to retinal antigens in the etiology and/or progression of the disease. One of the explanations that has been offered for the clinical heterogeneity of uveitis cases is a difference in the antigens being recognized. Many, though certainly not all, ERU cases have detectable immunologic responses to retinal antigens, most often to IRBP.[39] IRBP is a large glycoprotein (140 kD) known to bind retinoids and found primarily in the interphotoreceptor matrix of the retina between the retinal pigment epithelium and the photoreceptor cells. It is thought to transport retinoids between the retinal pigment epithelium and the photoreceptors, a critical role in the visual process. Further, immune reactions of diseased horses are additionally directed against S-antigen (S-Ag),[69,70] a photoreceptor protein found in rods and in the pineal gland, exerting an inhibitory function in the light transduction cascade. In almost all ERU cases, serum and vitreal autoantibodies against both autoantigens are detectable. Since antiretinal antibodies do not seem to be essential for the induction of uveitis, as shown in several EAU models,[71] and the predominating infiltrates in eyes of ERU horses are T-helper cells, the T cell specificity is even more interesting. Vitrectomy, as a therapeutic procedure, allows one to obtain sufficient numbers of vitreous infiltrating cells from diseased horses for immunologic studies and compare the reactions of peripheral and intraocular lymphocytes.

Whereas peripheral blood-derived lymphocytes (PBL) do not proliferate after in vitro stimulation with retinal antigens,[39,72] cells from the eye strongly responded.[39,72] In most cases, a clear response to one or several IRBP-derived peptides was observed. This is in accordance with other autoimmune diseases, where responses to autoantigens are also rarely seen with peripheral lymphocytes. Only in some patients or at certain time points will PBL respond to autoantigens.[73] The low frequency of antigen-specific peripheral blood lymphocytes, even in advanced cases of uveitis, has been discussed as one reason for poor results in proliferation assays.

Further analysis of the immune response pattern of ERU cases revealed a novel yet unknown protein as a uveitis autoantigen. An immune response to cellular retinaldehyde-binding protein (CRALBP)[74] was detectable in a large percentage of ERU cases. CRALBP was detected as a novel uveitis autoantigen. Screening the immune response of ERU cases to a map of retinal proteins, CRALBP could be verified as a novel ERU autoantigen[74] and was subsequently tested with samples of human autoimmune uveitis patients.[75] Fifty-four percent of tested patients were CRALBP autoantibody positive, thereby underscoring the relevance of ERU as a model for human autoimmune uveitis. Considerable evidence indicates that CRALBP is a component of the rod and cone visual cycles, the sequences of reactions responsible for the regeneration of 11-*cis*-retinal after photoisomerization. The protein is abundant in RPE cells, where many of the reactions of the rod visual cycle take place, and in Mueller cells, which have been implicated in cone visual pigment regeneration.

Earlier studies had shown that experimental uveitis induced in guinea pigs with soluble retinal proteins also led to involvement of the pineal gland in the inflammatory process.[76] Pineal glands were infiltrated by lymphocytes and observable before retinal involvement.[76] Interestingly, the same group later also demonstrated pinealitis in ERU cases.[43,77,78] Septal areas of pineal glands from horses with uveitis had clusters of MHC class II antigen-expressing cells and T lymphocytes.[77]

PATHOGENESIS OF RECURRENT DISEASE

Current concepts to explain the origin and perpetuation of autoimmune diseases include molecular mimicry,[79] bystander activation,[80] and epitope spreading.[81,82] These mechanisms do not exclude each other but could appear together and even interact. *Epitope spreading* is defined as the diversification of epitope specificity from the initial focused, dominant, epitope-specific immune response, directed against a self or foreign protein to cryptic epitopes on that protein (intramolecular spreading) or other proteins (intermolecular spreading).

The immune response consists of an initial magnification phase and a later downregulatory phase to return the immune system to homeostasis. In most autoimmune diseases, several autoantigens participate in the pathogenesis,[83] and epitope spreading is accountable for disease induction, progression, and inflammatory relapses.[84-88] The shifts in immunoreactivity could account for the remitting/relapsing character of ERU. Different target antigens may be important for a given individual, depending on the MHC background. Genetic background and antigens encountered influence the direction and extent of epitope reactivity and probably play an important role in the heterogeneous clinical manifestations of disease.[89] In many autoimmune diseases, epitope spreading is suspected to occur as a result of an immune response against endogenous

target antigens first and secondary to the release of self-antigen during the chronic autoimmune response.[89] The formation of new antibodies may determine a different clinical picture. For example, the transformation of anterior uveitis to posterior uveitis may be an excellent example of the effects of epitope spreading. Through tissue damage, cryptic or hidden epitopes on the same molecule will be suddenly presented to the immune system. The end result is that every target antigen generally contains several epitopes, each of which reacts with a T cell or antibody response of different specificity and affinity. Thus, epitope spreading in autoimmune diseases results in the detection of an increasing array of autoantibodies against various target antigens. Studies characterizing the shifting immune response of ERU-diseased horses are currently underway, but initial studies have confirmed epitope spreading in a high percentage of cases.[37]

Analyses of autoantigen and epitope specificity of autoaggressive T cells from ERU cases already revealed evidence for inter- and intramolecular epitope spreading.[37] Epitope spreading is only pathogenesis associated if the targeted epitope has pathogenic potential. Therefore, it was essential to evaluate the uveitogenic potential of all involved autoantigens directly in the horse. Surprisingly, S-antigen, which is seen as the major uveitis autoantigen in human autoimmune uveitis and is used by many researchers as autoantigen to experimentally induce uveitis in Lewis rats for uveitis research, widely failed to induce uveitis in horses.[90] S-Ag-induced uveitis is monophasic in rats[69] and was also monophasic in one horse that developed uveitis after S-Ag injection.[90] In contrast, CRALBP and IRBP proved their uveitogenicity in the horse with an incidence of 100%.[74] Further, both autoantigens were capable of reinducing uveitis in the horse,[74] closely resembling the clinical course of spontaneous ERU. Equine experimental uveitis induced with CRALBP or IRBP is to our knowledge the only animal model where relapses of an autoimmune disease can be reinduced in a well-defined and predictable manner.

Uveitic relapses are notable even in phthisical and blind eyes.[91] Histopathologic examination of ERU eyes and eyes from experimentally induced uveitides revealed an almost complete loss of the photoreceptor outer segments in advanced stages of disease.[38,69] Since the photoreceptor outer segments host two major autoantigens, retinal S-Ag (arrestin) and IRBP,[92] the ongoing immune pathology after destruction of the physiologic expression sites of these proteins was difficult to explain. In other autoimmune diseases, such as Hashimoto's thyroiditis, a termination of autoimmune attacks is notable after depletion of autoantigens.[93,94] We therefore examined autoantigen expression levels of IRBP, S-Ag, and CRALBP in uveitic retinas of several clinical stages in comparison to healthy control retinas. IRBP, S-Ag, and CRALBP were clearly detectable in proteomes of normal equine retina and in retinas with different stages of uveitis. Although the composition of retinal proteomes differed considerably between healthy and diseased state,[95] IRBP, S-Ag, and CRALBP amounts remained unchanged.[96] Substantial photoreceptor damage in uveitic retinas tested in this study was evident by measuring rhodopsin expression levels that were reduced to 27% of original expression. The unchanged total amount of three major retinal autoantigens indicates that the autoantigenic target protein is present despite considerable destruction of its hosting structures and can thus trigger unabated relapses in patients with blind eyes.

DIFFERENTIALLY REGULATED PROTEINS IN EQUINE RECURRENT UVEITIS

Although retinal autoantigen–specific T_H1 cells have been demonstrated to trigger disease progression and relapses, the molecular processes leading to retinal degeneration and consequently blindness remain as yet unknown. Systematic exploration of the intraocular proteomes of spontaneous uveitis and healthy controls has made it possible to identify several differentially regulated proteins that belong to pathways involved in immune response and the maintenance of the blood-retinal barrier.[95,96]

One upregulated candidate in the retina in ERU is, amongst others, complement component C3.[97] Novel data indicate an activated complement system also in sera of ERU cases.[97] This is interesting, because intraocular complement activation, specifically engagement of complement receptor 3, had a significant impact on disease activity in experimental autoimmune uveitis in rats.[98,99] The role of complement system activation in ERU merits further exploration in the pathogenesis of ERU. Another candidate is pigment epithelium-derived factor (PEDF), a neurotrophic factor and a potent inhibitor of angiogenesis.[100] PEDF is produced by the RPE cells and retinal Mueller glial cells and is significantly downregulated intraocularly in uveitis to around 20% of the normal expression level.[101] PEDF operates as a regulator of inflammatory factors and suppresses endothelial permeability by protecting tight junction proteins.[102] In ERU, a direct link between downregulation of PEDF and concomitant appearance of vascular endothelial growth factor (VEGF) and IFN-γ in the retina has been demonstrated.[95] Additionally, uveitic changes in the retina were accompanied by upregulation of glial fibrillary acidic protein (GFAP) and vimentin as well as downregulation of glutamine synthetase.[95,101] These expression patterns point to an activated state of retinal Mueller glial cells (RMG) in the disease process.[103] The activated RMG downregulate the expression of PEDF and begin expressing IFN-γ, a proinflammatory cytokine typical for T_H1 cells.[95] Therefore, RMG may play a fatal role in uveitic disease progression by directly triggering inflammation processes through the expression and secretion of IFN-γ. Most interesting, a significant downregulation of PEDF could also be demonstrated in sera of ERU cases, consistent with earlier observations in ERU vitreous[101] and retina.[95] This suggests that the down-regulation of PEDF under inflammatory conditions is not only limited to the eye. It was shown that PEDF concentration in blood is sufficient to have functional significance.[104] In rats with endotoxin-induced uveitis, drastically decreased PEDF levels are detectable in retina and plasma, which suggests that PEDF is a negative acute-phase protein.[102] The findings of a significantly lower PEDF expression in ERU cases, in not only the target organ but also the serum, proves PEDF as a promising uveitis biomarker. The possible predictive value in clinical patients of PEDF downregulation for ERU now merits closer examination.

Initiating events of the immunopathology in ERU remain obscure. In many autoimmune disorders, infections have been discussed as triggering events, either by antigenic mimicry with a pathogen's antigen or as a bystander effect due to the general systemic or local immune stimulation by the pathogen. The historical association between leptospiral infection and development of ERU suggests this pathogen is a potent activator of

the immunopathology in ERU (see section later in this chapter on leptospirosis).

PATHOLOGY OF EQUINE RECURRENT UVEITIS

ANTERIOR UVEA

The pathology of early ERU involves congestion of the vessels of the anterior uvea and infiltration of the uveal tract with inflammatory cells. The iris and ciliary body are infiltrated first by neutrophils. The neutrophils, which may escape into the anterior chamber to cause visible hypopyon, are soon replaced by large numbers of lymphocytes as well as some plasma cells and macrophages. Exudates of fibrin, serum proteins, and other substances are a predominant feature. Gross or histopathologic examination of eyes acutely affected with ERU show notable exudates on the surface of the iris, ciliary body, and ciliary processes and over the lenticular capsule. Serous and cellular exudates are also noted in the iridic stroma, in trabecular meshwork, and in the aqueous and vitreous humors. Simultaneous congestion and infiltration occurs in the conjunctiva. The retina is relatively unaffected in the first few attacks of inflammation.

With chronicity and further recurrences, organization of the lymphocyte infiltrate is evident. The ciliary body and base of the iris regularly demonstrate prominent lymphocytic nodules (Fig. 8-22). The lymphocytes in the center of the nodules are B lymphocytes, whereas those on the periphery of the nodules, and most of the diffuse infiltrating population, are T lymphocytes.[42,44] Lymphocyte follicles may also be seen in the conjunctiva adjacent to the limbus. The function of these lymphoid follicles is very interesting and could account for the relapses, since immunologically primed cells remain directly in the eye after the uveitic attack. Although T cells dominate the inflammation in ERU, autoantibodies are also detectable in sera and ocular tissues and can be used to detect autoantigen specificity.

As pathologic damage continues, the epithelium of the ciliary processes and uveal blood vessel walls thickens. Exudates occur in the uvea and are easily seen occupying space over the ciliary processes and on the posterior epithelium of the iris. Histopathology of the ciliary body[105,106] of spontaneous ERU have demonstrated three characteristic features: (1) presence of a thick, noncellular hyaline membrane tightly adherent to the inner aspect of the nonpigmented ciliary epithelial cells (NPE), (2) eosinophilic linear inclusions in the cytoplasm of the NPE, and (3) accumulation of clusters of lymphocytes and plasma cells directly within the NPE layer of the posterior iris and ciliary body.

The finding of the hyaline membrane adjacent to the posterior aspect of the iris (Fig. 8-23) (characteristically staining orange-red with Congo red stain), coupled with the presence of the linear cytoplasmic inclusion bodies in the adjacent NPE (Fig. 8-24) is highly suggestive of the presence of ERU.[105,106]

POSTERIOR SEGMENT

Although acute cases of ERU show pathology that is most distinct in the anterior uvea, recurrence and chronicity of inflammation bring many changes to the retina and adjacent choroid. Scattered foci of T-lymphocytic infiltration are seen,

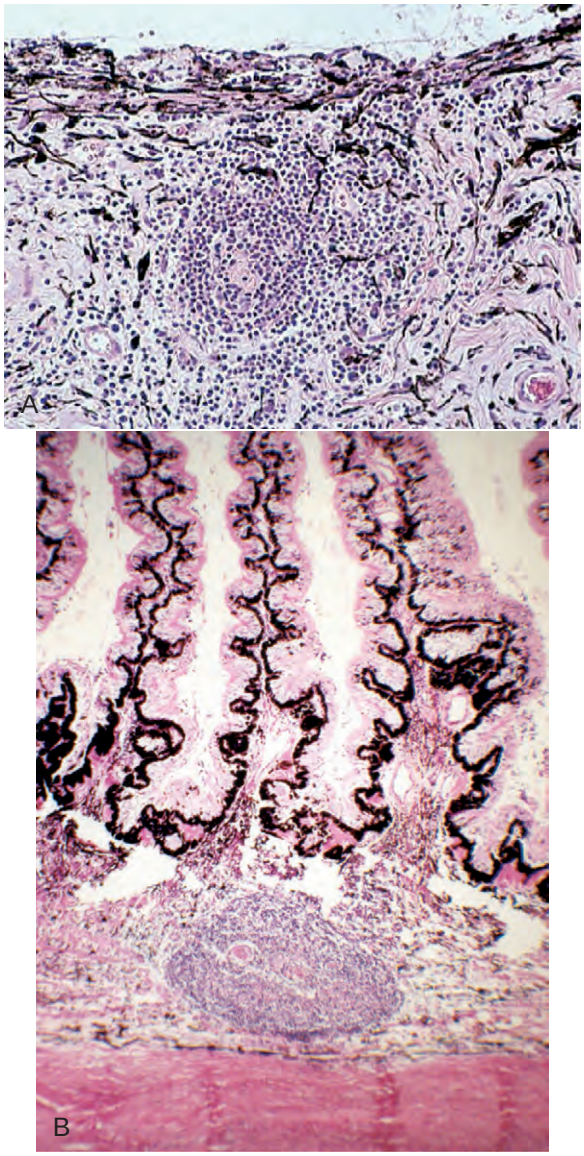


Figure 8-22. **A,** Lymphocytic follicle or nodule formation at the base of the iris, a common feature in eyes with recurrent uveitis (H&E ×400). **B,** Lymphocytic follicle or nodule formation at the base of the ciliary body, a common feature in eyes with recurrent uveitis (H&E ×400).

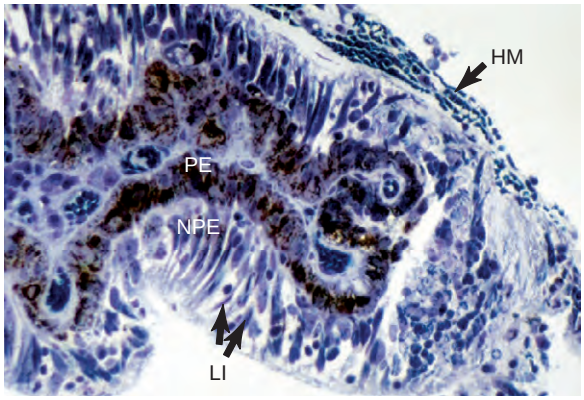


Figure 8-23. Ciliary process from an eye with chronic equine recurrent uveitis. *HM*, Hyaline membrane; *LI*, linear cytoplasmic inclusions in the NPE; *NPE*, nonpigmented epithelium; *PE*, pigmented epithelium (H&E ×400). (Photograph courtesy Dr. Penny Coolie.)

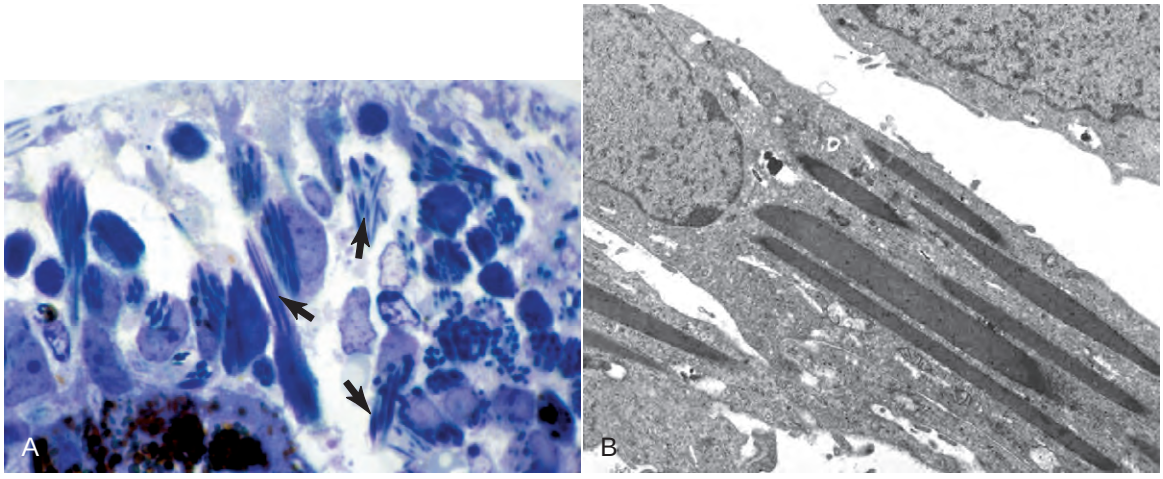


Figure 8-24. A, Linear cytoplasmic inclusions *(arrows)* in the nonpigmented epithelium from an eye with chronic recurrent uveitis (H&E ×1000). **B,** Transmission electron microscope image of the nonpigmented epithelium linear cytoplasmic inclusions (×5000). (Photographs courtesy Dr. Penny Coolie.)

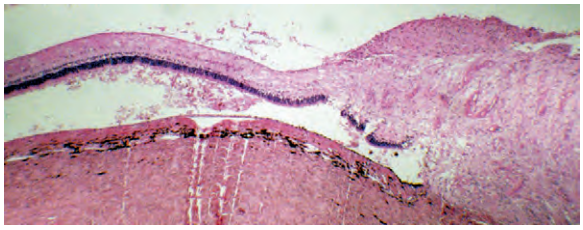


Figure 8-25. Serofibrinous exudate is commonly seen between the retinal pigmented epithelium and the photoreceptors in horses with ERU. This photograph shows optic nerve involvement and retinal detachment with exudates (H&E ×31.25). (Photograph courtesy Dr. Carolyn Kalsow.)

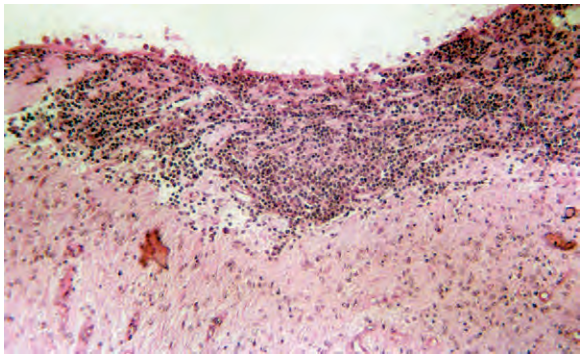


Figure 8-26. Pathologic changes observed around the optic nerve head in horses with ERU include surface infiltrate, occasional lymphocyte nodule formation, and retinal traction folds around the margin of the nerve. This photograph shows optic nerve infiltrate. This is the same horse as shown in Fig. 7-20 (H&E ×31.25). (Photograph courtesy Dr. Carolyn Kalsow.)

particularly near the ora ciliaris retinae and optic nerve head. The retinal pigmented epithelium (RPE) may undergo focal hypertrophy or degeneration. Serofibrinous exudate is commonly seen between the RPE and the photoreceptors and can be so extensive that it replaces the vitreous in a portion of the posterior chamber (Fig. 8-25). Loss of rods and cones secondary to macrophage activity, destruction of the inner nuclear layer,[38] and detachment of the retina may follow, with the RPE remaining attached to Bruch's membrane of the choroid, and the rest of the retina collapsing into the posterior chamber.

Pathologic changes observed around the optic nerve head of horses with ERU include surface infiltrate (Fig. 8-26), occasional lymphocyte nodule formation, and retinal traction folds around the margin of the nerve. Infiltrating cells in the perivascular and parenchymal space of the nerve are immunoreactive. The optic nerve itself can show swelling or may be cupped or atrophied if secondary glaucoma is present.[42]

ACCESSORY STRUCTURES

The lens often shows thick exudates adherent to the capsule, particularly on the posterior aspect, in early ERU. The lens capsule proliferates, and over time cataracts develop. Luxation of the lens is common as deterioration of the zonules occurs. Wrinkling of the lens capsule (secondary to a hypermature, resorbing cataract) or osseous metaplasia occasionally occur.

Many cases of ERU will develop perilimbal vascularization of the cornea, although superficial and extensive vascularization is not characteristic of ERU. Histology of these cases shows that the new vessels start out as tiny capillary offshoots from the scleral vessels that grow into the lamina propria of the cornea below the epithelium. They may only be present on the inferior limbus, or they may extend all around the periphery in a radial pattern. Cellular infiltrate is rarely present in the stroma of the cornea in horses with ERU. If the cellular infiltrate is prominent, then the uveitis may be caused by primary corneal disease, such as stromal abscessation or immune-mediated keratitis (Fig. 8-27).

Several studies have shown that ERU is accompanied by inflammation in the pineal gland of the brain. The inflammation is variable and may be transient. It involves immunoreactive cells and is similar to inflammation seen in experimental induction of recurrent uveitis in laboratory animals.[43,76-78]

Acute classic ERU episodes are followed by periods of quiescence when the eye is outwardly comfortable, and gross

Figure 8-27. Corneal edema, vascularization, and cellular infiltrate of the cornea with a corneal stromal abscess. ERU, which rarely has extensive corneal vascularization, must be differentiated from primary corneal disease, such as this abscess.

disease evidence is restricted to observable sequelae (synechiae, cataract, peripapillary scarring) from previous episodes and occasionally subtle aqueous flare. Histopathology and immunohistopathology of quiescent eyes reveal that inflammation does persist in these eyes microscopically. Lymphocyte nodules are frequently present in the ciliary body, and infiltrating lymphocytes are identifiable in the uveal stroma and in many accessory eye structures. Immunoreactivity is demonstrable during periods of quiescence as well.

Many chronic ERU eyes develop phthisis bulbi (see Fig. 8-20). Others maintain normal globe size but show extensive posterior synechiae, loss of normal iris shape and motility, and dense cataract. Histologic examination of end-stage ERU with blinding consequences shows a shrunken globe with thickened sclera, cataracts with posterior and anterior synechiae, and a torn distorted iris. The lens may be luxated and may be surrounded by thick exudates. Iris vessels are thick walled, and the ciliary body is filled with organized exudates. The retina is detached, and exudates may fill the posterior chamber. Some others retain a functional ocular structure with less inflammatory sequelae.

DIFFERENTIAL CONSIDERATIONS AND DIAGNOSTIC METHODS

The clinical diagnosis of ERU is based on the presence of characteristic clinical signs and history of documented recurrent, or in the case of insidious ERU, persistent episodes of uveitis. Both features are required to make this clinical diagnosis, especially to differentiate ERU from non-ERU uveitis (i.e., primary uveitis) and other causes of recurrent or persistent ocular cloudiness and/or inflammation, such as herpesvirus keratitis, immune-mediated keratitis, glaucoma, and stromal abscessation (Box 8-1 and Table 8-3). These and many other primary conditions of the eye result in ocular clinical signs typical of ERU, particularly pain, blepharospasm, photophobia, miosis, and altered corneal transparency. If the eye has clinical signs consistent with uveitis, it is critical that the clinician differentiate between primary uveitis and recurrent uveitis. These are two separate diseases.

Box 8-1 | **Causes of Uveitis in Horses**

Any injury to a horse's eye may result in uveitis and possible development of the syndrome of equine recurrent uveitis (ERU). Some examples include:

Trauma

Blunt or penetrating injury

Bacterial Organisms

Leptospira
Brucella
Streptococcus
Rhodococcus equi
Borrelia burgdorferi (Lyme disease)

Viral Organisms

Equine influenza
Equine viral arteritis
Parainfluenza type 3
Equine herpesvirus types 1 and 2

Parasites

Onchocerca
Strongylus
Toxoplasma

Miscellaneous

Endotoxemia
Septicemia
Tooth root abscesses
Neoplasia

It is also particularly important to differentiate primary corneal disease from ERU. Deep nonulcerative infectious keratitis (i.e., stromal abscesses), such as that associated with fungal infections,[49] is commonly misdiagnosed as ERU. Deep stromal abscesses wax and wane in severity (although they are generally progressive) and are associated with severe pain, aqueous flare, miosis, corneal edema, and hypopyon. Treatment of infectious keratitis with topical corticosteroids, a common treatment of ERU, can result in substantial worsening of the stromal abscess. Use of topical corticosteroids is contraindicated for most primary corneal problems, and failure to properly treat ulcers or other problems (e.g., corneal ulcer or foreign body, stromal abscess, unusual keratitis, glaucoma, corneal or intraocular neoplasia) may have disastrous consequences. These diseases are referred to as "masquerading syndromes" of ERU (see Table 8-3).

A thorough ocular examination is needed, with careful inspection of the eyelids and cornea to rule out primary corneal disease. If palpebral and conjunctival swelling obstructs a portion of the cornea, a repeat examination may be needed after nonsteroidal antiinflammatory drug (NSAID) therapy has reduced pain and swelling. Scrutiny for other differentials requires a careful inspection of all accessory anatomic structures of the eye, looking for masses, pigment changes, scars, opacities, accumulation of fluid in the ocular media, and

Table 8-3 | **Differentiating Equine Recurrent Uveitis from Other Causes of Ocular Inflammation***

SYNDROME	COMMENT	DIAGNOSTIC AID
Non-ERU uveitis	Anterior or posterior uveitis	History of no recurrence of uveitis
Corneal ulcer	Self-trauma, corticosteroids contraindicated	Fluorescein dye positive, focal opacity or defect
Stromal abscess	Past trauma, corticosteroids contraindicated	Fluorescein dye negative, focal yellow-white opacity
Immune-mediated keratitis	Appearance may change often, severity varies, recurrent inflammation possible	Fluorescein dye negative, multiple opacities, variable pattern
Herpes keratitis	Variable pain, may retain rose bengal	Fluorescein dye variable, multiple punctate or linear opacities
Corneal foreign body	May be vascularized focally, may be visible	Fluorescein dye variable
Corneal neoplasia	Squamous cell carcinoma, melanoma	Mass or cellular infiltrate visible on corneal surface or through epithelium
Intraocular neoplasia	Melanoma, medulloepithelioma, anterior or posterior segments	Ocular ultrasonography, or may visualize in anterior chamber
Glaucoma	Often secondary to ERU, persistent corneal edema	Tonometry

ERU, Equine recurrent uveitis.
*"Masquerading syndromes" of ERU.

changes of the fundus, particularly the peripapillary region. The clinician should perform a complete ophthalmic examination in both eyes of the animal, even if only one eye has active inflammation. Tonometry is recommended in all cases to rule out glaucoma or document hypotony that often accompanies ERU. A complete ophthalmic examination is also important in quiet, comfortable (i.e., quiescent) eyes to document clinical signs consistent with past uveitis (synechiae, pigment on the anterior lens capsule, diffuse cataract, peripapillary scarring, etc.).

A careful history of previous episodes of inflammation should be taken, including a description of the signs observed by the owner. If the owner reports that the horse has had brief or protracted episodes of ocular pain or swelling in the past, the scenario is strongly suggestive of ERU. However, if owners report that the horse has had no observable eye inflammation or do not know the history of the animal, these horses may have the insidious form of ERU (especially if the horse is an Appaloosa or draft breed), or horses may have classic ERU but have not had an episode that has been witnessed by the owner. In cases where the history is unknown but recurrent uveitis is suspected, at least three signs of disease (corpora nigra atrophy, pigment on anterior lens capsule, synechiae, iris fibrosis or color change, cataract, lens luxation or subluxation, vitreal opacities, retinal detachment or traction bands, peripapillary scarring in a focal or alar pattern) AND a history of recurrent ocular disease is needed before making a presumptive diagnosis of previous ERU.[5]

Other tests that may be used in assessing the horse that presents with acute primary uveitis or signs compatible with previous disease include complete blood count and blood chemistry. Leptospiral serology is useful for testing previous exposure to this well-known risk factor but may not be particularly helpful in determining treatment. Aqueous humor and serum leptospiral serology (microagglutination titers [MAT]) may be more helpful, because a positive C value (i.e., aqueous humor MAT value/serum MAT value) suggests intraocular production of antibodies against the organism.[107] In this case, definitive treatment for *Leptospira* may be helpful (see later). Equine leukocyte antigen (ELA) typing may also help determine if the animal is genetically susceptible to ERU.[46] In addition to leptospiral MAT serology, blood may be submitted to test for exposure to Lyme disease (serum titer and Western blot analysis) and/or equine viral arteritis. Fecal parasite analysis is indicated, as well as a full physical examination of other body systems to check for concurrent problems (see Box 8-1 and Table 8-3). Please see Chapter 6, Diseases of the Uvea, for more information on the diagnosis and workup for primary uveitis in the horse.

Owner education and counseling is indicated whenever signs of ERU are detected during a routine ophthalmic exam. The owner should be educated about the disease syndrome, and a frank discussion of visual prognosis should occur. It is best to stress the possible scenarios early and prepare owners for the expense, treatment effort, and progression associated with overt future attacks. Frequent veterinary follow-up exams should be recommended. In cases where the veterinarian suspects either insidious or classic ERU that has been unobserved by the current owner, biannual examination coupled with immediate evaluation if the horse suffers pain in one or both eyes should help sort out the diagnosis. Referral to a board-certified veterinary ophthalmologist may be helpful in providing a complete examination of cases of uncertain etiology.

EQUINE RECURRENT UVEITIS AND LEPTOSPIROSIS

Although many different endogenous and exogenous inciting factors have been associated with ERU, leptospiral infection has been linked to the development of spontaneous cases of ERU around the world and has been studied extensively.

FEATURES OF LEPTOSPIROSIS

Leptospirosis is a bacterial disease affecting domestic animals, wildlife, and humans. Leptospirae are the smallest spirochete bacteria, measuring less than 0.3 microns in width and 6 to 30 microns in length. They have a tightly wound spiral shape with a distinctive hook on one or both ends. Other genera of related pathogenic spirochetes include *Treponema* (agents of syphilis and swine dysentery) and *Borrelia* (agents of relapsing fever and Lyme disease). The organism is motile and able to enter hosts by penetrating mucous membranes or abraded skin. It does not stain with conventional pathology stains, requiring special silver impregnation stains for identification. Clinical tests available to diagnose leptospiral infections include direct culture of infected organs or body fluids, microscopic aggluti-

nation testing of sera or ocular fluids, PCR analysis of ocular fluids, and fluorescent antibody testing of urine samples.

Leptospirae are aquatic unicellular organisms found in river and lake waters and in sewage. *L. interrogans* is host adapted, and infective strains are maintained in a variety of mammalian species. The principle reservoirs for the serogroups associated with ERU are deer, cattle, swine, and rats. The organisms multiply in the kidneys of adapted hosts and are shed in the urine. Pathogenic leptospires can only survive for short periods in soil outside a host but are able to live for up to 6 weeks in ground water if environmental conditions include slightly alkaline conditions (pH 6.2 to 8), low salinity, and moderate temperatures above 22°C.

LEPTOSPIROSIS IN HORSES

Exposure to the organism occurs when horses drink contaminated ground water that contains urine shed from a host-adapted species. Horses pastured next to unvaccinated cattle or pigs, and horses that live on farms frequented by deer or infested with rats are at increased risk for exposure. Ponds on the property, the use of pond water as drinking water, and close proximity to a river are other frequently observed risk factors (Fig. 8-28).[3] Clinical infections are thought to be most prevalent during rainy periods in the spring and fall. The inciting organisms enter the body through mechanical penetration of mucous membranes or abraded skin and rapidly gain access to the vascular space. Bacteremia persists about 8 days. Invasion of many internal organs occurs, and infection induces a strong host antibody response that is first detectable in the serum 4 to 8 days post exposure.[108] Organisms are eliminated rapidly from the blood and most organs by host mechanisms. However, localization of organisms in the genital tract and renal tubules[109,110] may occur, and the infected horse may shed pathogenic leptospires in the urine for up to 3 months.[108]

Acute signs of leptospirosis in the horse include transient depression, fever, icterus, anemia, and anorexia. Sporadic reports of severe disease in neonates or adult horses exist,[111,112] and the disease has been associated with many equine abortions in Kentucky,[113,114] but most infections are outwardly self-limiting. Clinical diagnostics that would confirm acute infection in the horse are rarely performed, because observable initial illness is generally mild and brief. Serologic surveys in horses have shown that exposure to leptospires is common but

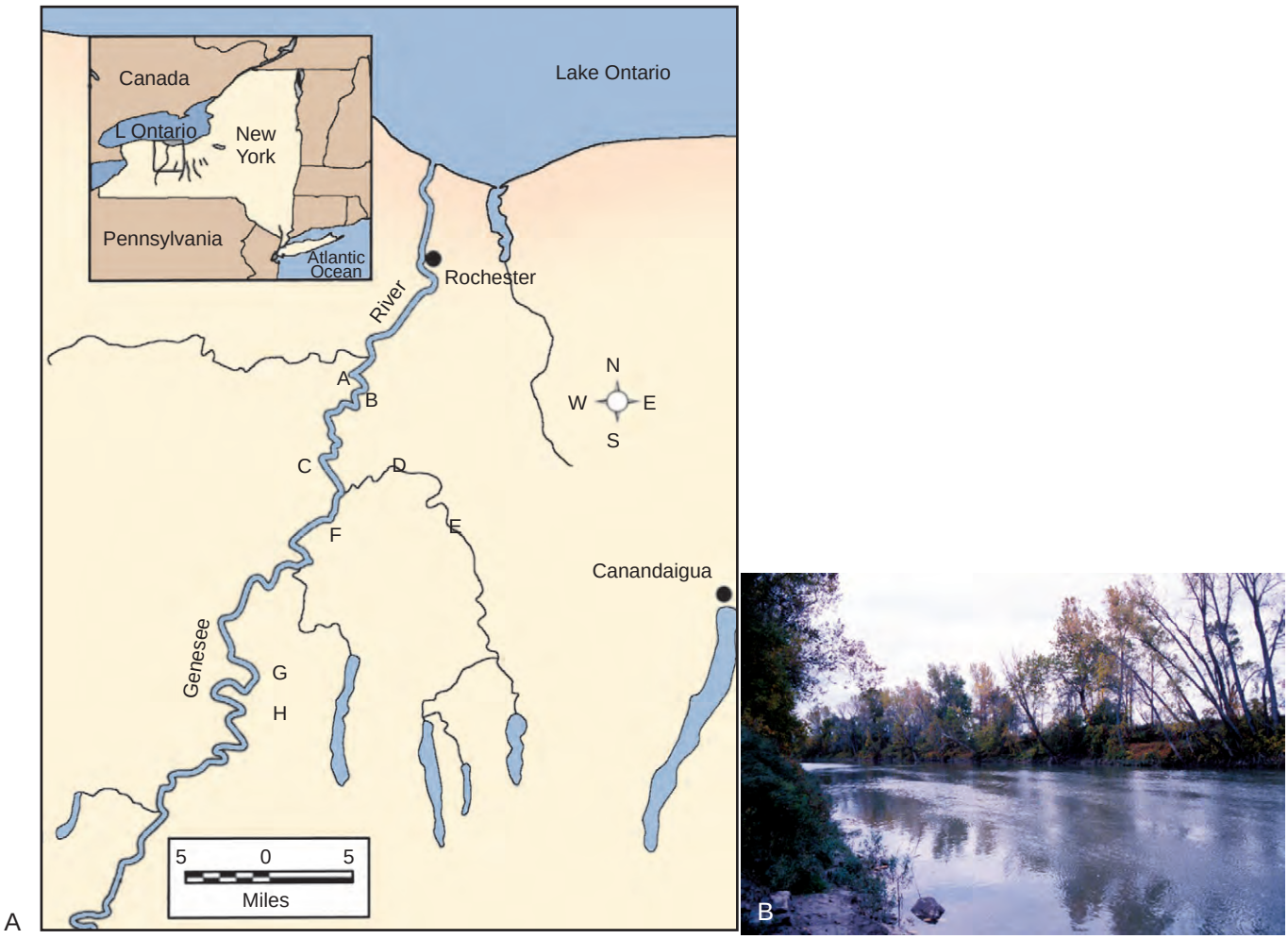


Figure 8-28. A, Map of farms that have multiple cases of *Leptospira* Pomona–associated equine recurrent uveitis, showing proximity to the Genesee River of New York State. **B,** Genesee River.

variable according to geographic region and climate. Seropositivity rates tend to be highest in tropical climates[109] and in river valleys in temperate climates, especially in the Ohio, Delaware,[115,116] Genesee,[3] and Mississippi[24] River valleys in North America. These regions also have high rates of ERU in resident horse populations.[3,24]

CLASSIFICATION AND CLINICAL TESTING FOR LEPTOSPIROSIS

Biologically, leptospirae are classed into two large species: *L. biflexa*, the nonpathogenic, free-living and saprophytic complex and *L. interrogans*, the parasitic species complex that causes disease. *L. interrogans* is further classified into over 20 serogroups. Diagnostic laboratories distinguish exposure to these serogroups by performing serial microagglutination titers (MAT) on equine sera or ocular fluids, looking for antibodies to leptospiral surface antigens. The *L. interrogans* serogroups most often incriminated in equine disease are Pomona and Grippotyphosa.* In some studies, the serogroup most often associated with ERU in North and South America was Pomona,[3,18,24,117] while in other studies, the serogroup Grippotyphosa predominated.[16,26,107,110] Sporadic reports have also associated serogroups Autumnalis,[5] Icterohemmorrhagiae,[24,107] Australis, Sejroe, and Javanica[20] with ERU.

Most public diagnostic laboratories perform MAT for five to seven serogroups (Pomona, Icterohaemorrhagiae, Grippotyphosa, Canicola, Hardjo, and sometimes Bratislava and Autumnalis). Interpreting serology for leptospiral reactivity can be confusing. A large number of horses that live in temperate or tropical climates demonstrate low titers to one or more serogroups, and exposure analysis is often not performed until years after episodes of ERU have begun, when titer levels in these animals are usually low.

Acute infections are characterized by high titer seroreactivity to at least one serogroup by the eighth day.[108] Cross-reactivity to one or more other serogroups is common due to surface antigen overlap and is usually detectable at the same time but at reduced titer levels. Over time, the titer to the predominant serogroup falls to lower dilution levels, but positive seroreactivity to the original panel of serogroups persists for many years and probably for life. Usually the predominant serogroup titer will be elevated above the cross-reacting serogroups for the first several years after infection. Reactivity to serogroup Pomona is often associated with seroreactivity to serogroup Icterohemmorrhagiae.[3,24,118] The horse has been shown to be an adapted host that can maintain the Bratislava serogroup,[110] but to date, this serogroup has not been associated with ERU.

One study has shown that 56% of horses with ERU from an upstate New York river valley were seropositive for *Leptospira* Pomona while only 9% of normal horses were seropositive.[3] Other studies have demonstrated leptospiral seroreactivity[13,24] or evidence of *Leptospira* in ocular media[13,16,18,24,26] in a majority of their affected study populations. These data imply that any positive Pomona titer in a horse (i.e., ≥1:400) should be considered a risk factor for ERU. In some studies, analysis of the ocular fluids or tissues of affected horses has shown that leptospiral organisms or leptospiral DNA can be isolated from ERU horses that are seronegative for leptospiral reactivity,[18,26] but in other studies no evidence of *Leptospira* could be found.[107,119] This means that although positive seroreactivity to pathogenic groups of leptospires, particularly Pomona and Grippotyphosa, is often linked to ERU etiology, positive or negative seroreactivity does not rule in or out leptospirosis as a contributing factor to the disease.

*References 3, 13, 16, 18, 23-26, 112-114, and 117.

THE ROLE OF LEPTOSPIROSIS IN EQUINE RECURRENT UVEITIS

The initial association of leptospirosis with ERU reported in Germany in the 1940s by Rimpau[12] and Heusser[13] was followed by case reports of an outbreak of acute leptospirosis on two horse farms in Ithaca, New York.[9,23,117,120,121] Analysis of events on one of the Ithaca farms showed that in the spring of 1952, 6/15 resident horses developed acute systemic disease confirmed as infection with *L. interrogans* serogroup Pomona.[120] All horses recovered, but one of the six developed intraocular inflammation during acute disease that later become recurrent.[23] The majority of the remaining horses developed ERU 18 to 24 months after the initial infection. This pattern is typical of leptospiral-associated ERU—ocular signs at the time of acute infection are generally absent or mild, but overt ocular inflammation develops months to years later. Recurrence of uveitis is typical, with subsequent episodes of inflammation often increasing in severity and threatening vision.

Experimental work to try to reproduce this unusual pattern ensued in the 1960s at Purdue University. Morter[108] succeeded in inducing leptospiral-associated uveitis by subcutaneously injecting guinea pig blood containing live *L. interrogans* serogroup Pomona organisms into a group of ponies. All the ponies developed systemic leptospiral infections that resolved but were followed by the development of ocular inflammation in the ensuing 15 months post exposure.[108,122,123] The ponies had recurrent uveitis that varied in intensity but resulted in blinding sequelae in many cases. Subsequent analysis of the ocular tissues of this same set of ponies in recent studies has shown that the pathology and immunohistopathology of the experimental disease was quite similar to that of spontaneous cases of leptospiral-induced ERU.[42,106]

PATHOGENESIS OF LEPTOSPIRAL-INDUCED EQUINE RECURRENT UVEITIS

A large body of research has been stimulated by the early reports of clinical and experimental leptospiral-related ERU, but the precise pathogenesis of induction of uveitis and the role of the organism in recurrent disease is poorly understood, although much progress has been made recently. In 1985, clinicians at the University of Florida used enzyme-linked immunosorbent assay (ELISA) to detect antibodies specific to *L. interrogans* serogroup Pomona in the sera, aqueous, and vitreous humor of horses with ERU. Their data suggested that antibodies in the ocular media may be synthesized in the eye rather than just leaking across the blood-ocular barrier.[19,124] Analysis of aqueous and vitreous humor samples from horses support the concept that some horses with ERU have intraocular antibody synthesis to *Leptospira*.[16,17,39,107,125]

In 1985, Argentinean researchers demonstrated an antigenic relationship between *Leptospira* and the equine cornea, sug-

gesting that molecular mimicry occurs between the bacteria and host tissues.[126] Subsequent work has demonstrated that tears and aqueous humor from horses inoculated with *Leptospira* contain antibodies that bind to the cornea[127] and that the antigenic relationship between the bacteria and ocular tissues includes the lens as well and involves a peptide fragment.[128] A leptospiral DNA fragment was found to encode cross-reacting epitopes toward equine cornea. This fragment was found in several pathogenic *L. interrogans* subgroups but not in the nonpathogenic *L. biflexa*.[21] Furthermore, in aqueous and vitreous humor from equine eyes with uveitis, immunoglobulin (Ig) A and IgG to *L. interrogans* lipoproteins LruA and LruB were significantly higher than in companion sera, indicating intraocular antibody production.[45] Also, LruA- and LruB-specific antisera cross-reacted to normal equine lens, ciliary body, and retina, suggesting an immunopathogenic role in leptospiral-induced ERU.[45] In humans with both leptospiral-associated and known autoimmune uveitis (i.e., Fuchs uveitis or Behcet's syndrome), serum antibodies cross-reacted with LruA and LruB lipoproteins, suggesting similarities in the disease pathogenesis.[129] This strongly suggests that leptospiral infections are potent initiators of autoimmune disease in the eye through a "molecular mimicry" pathogenesis.

Isolation of *L. interrogans* serogroup Pomona from the aqueous humor of horses affected with ERU was reported in 1977.[130] Leptospiral organisms have been cultured from equine eyes with uveitis in California[18] and Germany,[26] and in these studies there were some instances where leptospiral DNA was detected in samples that were culture negative.[16,18] A clear differentiation between primary equine uveitis and ERU was not carefully done in all these studies, but they do suggest that leptospiral organisms may persist in the eyes of ERU horses. The precise role the organisms play in mediating recurrences remains to be clarified; however, the presence of leptospiral organisms, organism fragments, or DNA would likely heighten the chance of development of autoimmune disease.

The exact interaction that occurs between bacterial infection and the host immune system in ERU is a subject of debate. Strong evidence of antibodies against *Leptospira* in the eye, coupled with demonstration of molecular mimicry between leptospiral DNA fragments and equine cornea and lens, supports an autoimmune component, as does the existence of antiretinal seroreactivity in leptospiral-related ERU horses. The presence of MHC class II expression and Ig deposition on resident and infiltrating cells in the eyes and pineal glands of these horses suggests that leptospiral infection may modulate the immune response of the eye. Because the disease has an immune pathogenesis, it is likely the genetic makeup of the individual, specifically the MHC, also plays a role in determining both susceptibility to leptospirosis as an inciting trigger and severity of subsequent inflammatory episodes.

A likely scenario regarding the pathogenesis of the immune-mediated leptospiral-associated ERU is as follows. When the inflammatory and uveitis process has been initiated, possibly by leptospiral infection (or other ocular disease), there is a general loss of ocular immune tolerance. In this environment, activated antigen-presenting cells in the uveal tract will effectively present autoantigens to the adaptive immune system, and cross-reaction between infectious agents and self-antigens can occur. *Leptospira* organisms (lipoprotein fragments and DNA) have been demonstrated to be particularly cross-reactive with equine ocular tissues.* When cross-reactivity occurs and self-antigens are recognized and processed, the specific subcellular site, or epitope, is processed within cytoplasmic endosomes to ultimately present to T cells. Autoantigen cleavage in these endosomes can create neoepitopes, either from novel conformations or realignment of protein sequences.[37] This process can lead to intramolecular epitope spreading, which is the development of autoantibodies against additional components of the autoantigen.[37] Similarly, autoantibodies specific for one antigen may bind to apoptotic bodies or other similar autoantigens produced or recognized during inflammatory processes, leading to activated antigen-presenting cell uptake of this material and reamplification of inflammatory response (i.e., intermolecular epitope spreading).[37] This reamplification of the inflammatory response to these neoepitopes likely explains the recurring nature of inflammation characteristic of ERU.[37]

EQUINE RECURRENT UVEITIS IN APPALOOSA HORSES

Early ERU literature claimed that there was no breed predilection. However, in 1988, clinicians at Cornell analyzed admission records of 16,242 cases and found that the Appaloosa breed had a significantly higher risk of developing uveitis relative to Thoroughbreds, and that Standardbreds had a reduced risk for the syndrome.[131] This study supported the observations of many equine practitioners who had diagnosed insidious uveitis in a large number of their Appaloosa patients, many of whom developed blindness or other secondary complications. A field study of a large number of cases in New York confirmed the breed predilection and reported the odds of finding uveitis were 8.3 times greater in Appaloosas than in all other breeds combined.[3]

Uveitis in the Appaloosa breed is often clinically distinct from classic ERU reported in other breeds. Many affected horses show an insidious course of disease without overt recurrent episodes of pain, so lumping these cases with horses that exhibit classic recurrences may be misleading. In fact, uveitis in the Appaloosa horse may have a different disease cause and pathogenesis than classic ERU, and further study is needed. Age of onset is variable and often difficult to determine, because the owner of an affected horse may be unaware of a problem until a veterinary examination is done or the horse shows overt vision loss.

Secondary complications and severe degeneration of ocular tissues are common sequelae of uveitis in Appaloosas. Analysis of records of 160 cases of horses with uveitis in New York showed that 25%, or 42, of these cases occurred in Appaloosas, and that this subset of 42 horses had many characteristic chronic ocular changes and concurrent medical problems (see Table 8-2).[53] Over 80% of cases were bilateral. During an 11-year period of observation, 38% of the afflicted horses were treated for acute corneal ulcers, and corneal scars indicating previous ulcers were apparent in a third of the cases. Glaucoma signs were present in 21%. Over half of the Appaloosas followed showed iris atrophy, and slightly less than half had developed or presented with posterior synechiae. Diffuse cataract devel-

*References 16, 18, 45, 126, 127, and 129.

oped in nearly three-quarters of the group, and a third of them experienced lens luxation or subluxation. Posterior changes like vitritis, chorioretinitis, or detached retina were common but hard to quantify because many of the horses developed cataracts that obscured visualization of these structures. Nearly a quarter of the cases went on to develop phthisis bulbi in one or both eyes (see Table 8-2).[53]

Coat color pattern of affected horses trended towards horses with overall light base coats and focal darker spots ("Foundation-type" or "leopard" appaloosas). Appaloosas that had dark basic coat patterns with a light "blanket" over the rump were less likely to develop ERU. Affected horses often showed annual coat color changes, with their base coat becoming lighter as they aged (Fig. 8-29). Night blindness was only rarely associated with uveitis, being confirmed in just 3 of 42 cases, which is much less frequent than recently reported.[132] Interestingly, 17% of affected Appaloosas showed signs of recurrent obstructive airway disease (heaves), often severe in nature.[53]

Appaloosas that live in river valleys or other temperate areas may become infected with leptospirosis because of environmental risks. One study showed that Appaloosa horses seropositive to *L. interrogans* serogroup Pomona have a particularly severe clinical course and a nearly 100% incidence of blindness in one or both eyes.[3] These cases often showed clinical disease that was a hybrid between classic and insidious forms of uveitis—the horses would experience recurrent episodes of fulminant ocular inflammation and severe pain and also show signs of progressive deterioration in the interludes between episodes.

Any disease that has a breed proclivity likely has a genetic basis. In Appaloosas, it is suspected that the equine MHC may play a role in susceptibility.[133] ERU is strongly associated with the MHC class I haplotype ELA-A9 in a population of German Warmblood horses.[46]

Figure 8-29. A, Example of an Appaloosa horse with an annual coat color that changes with its base coat and becomes lighter as the horse ages. This type of Appaloosa horse may be more likely to have equine recurrent uveitis. **B,** Example of an Appaloosa horse with a dark basic coat pattern with a light "blanket" over the rump. This type of Appaloosa horse is less likely to have recurrent uveitis.

PROGNOSIS OF HORSES WITH EQUINE RECURRENT UVEITIS

INFLAMMATORY SEQUELAE IN EQUINE RECURRENT UVEITIS

Data on the long-term outcome and ocular sequelae of horses with ERU are scarce. The visual prognosis of 112 cases of ERU that were followed for a 7-year period in the Genesee River Valley were reviewed,[3] and the visual outcome, chronic ocular changes, and concurrent medical problems in a group of 160 cases (including the original 112) were followed over 11 years.[53] The horses were segregated by breed and seroreactivity to *L. interrogans* serogroup Pomona. Of the total group of 160 horses, 20% (32) had no known risk factor for ERU—that is, they were seronegative and non-Appaloosas. Of the remaining 128 horses, 86 were leptospiral seropositive non-Appaloosa horses, 28 were Appaloosa horses with insidious uveitis, and 14 were horses that were both Appaloosas and seropositive to *L.* Pomona. Table 8-2 summarizes the chronic ocular changes observed in these four groups, concurrent medical problems observed, and the eventual visual outcome. Common ocular sequelae seen in these ERU horses included corneal focal scars, calcium deposits, and other corneal opacities. Leptospiral-seropositive horses experienced a high rate of calcific band keratopathy. Striae and dense corneal streaks were common in Appaloosas, and their presence was associated with blindness. Iris atrophy and color change were common, especially in Appaloosas and seropositive horses. Anterior synechia were rare unless phthisis bulbi was present, but posterior synechia occurred in nearly a third of all cases and 40% of Appaloosas. Diffuse cataract(s) developed in 41% of all cases, and nearly three-fourths of the Appaloosas. These were a common cause of blindness. Lens luxation was common in Appaloosas (29%). Severe vitreal opacity (vitritis) was observed in nearly a third of the cases. Peripapillary scarring (focal or alar) was also present in about a third of the horses. Cataracts and synechiae often obstructed posterior segment evaluation, so inflammatory changes were probably underreported. Appaloosas had the highest rate of glaucoma (21%). Phthisical eyes developed most often in Appaloosas and leptospiral-seropositive horses.

Owners are often concerned that horses with ERU will have to be enucleated. In the described series, only 4% (6/160) were enucleated for complications from corneal infection or glaucoma. Of more concern is the fact that 43 of the 160 horses (27%) were treated for corneal ulcers over the observation period. Risk of corneal ulcers in ERU horses should be stressed, as owners often choose to medicate horses with painful eyes themselves, and they may potentiate serious infections by

applying corticosteroids and delaying proper diagnosis. Additionally, in this study, 10 horses suffered from calcific band keratopathy.

VISUAL PROGNOSIS OF EQUINE RECURRENT UVEITIS

The presenting signs, response to treatment, and recurrence rate of ERU are highly variable and likely related to a variety of environmental, genetic, and immune factors as well as inciting triggers that produce disease.

The overall prognosis for sight in horses with uveitis has been described as poor.[10] Limited data have been published regarding actual rates of vision loss in horses with ERU. In the New York study, complete blindness was noted in 20% (32/160) of all the horses followed long term. Unilateral blindness occurred in 36% (57/160). Overall, 56% of all horses experienced blindness in one or both eyes.[53]

Appaloosas and seropositive horses were at increased risk for blindness. Seropositive Appaloosas had the worst visual prognosis: all lost vision in at least one eye, and 50% became completely blind. Appaloosas that had never been exposed to *L.* Pomona and who suffered insidious disease fared a little better. The rate of vision loss in one or both eyes was 72%, with 29% experiencing total blindness. Horses that had been exposed to *L.* Pomona but were not Appaloosas lost vision in one or both eyes 49% of the time and had a total blindness rate of 17%. Horses that were seronegative to *L.* Pomona and were not Appaloosas had the best visual prognosis; 34% became blind in one or both eyes, and total blindness occurred in only 6%.[53]

MANAGEMENT OF EQUINE RECURRENT UVEITIS

The main goals of therapy for ERU are to preserve vision, reduce and control ocular inflammation in an attempt to limit permanent damage to the eye, control pain, and prevent recurrence. In horses where a definite inciting cause has been identified, treatment is directed at eliminating the primary problem, and initial tests to isolate an inciting agent are performed (see section on diagnosis earlier in this chapter). Usually, however, due to the immune-mediated pathogenesis of ERU, a particular cause cannot be isolated. In these instances, therapy is directed at treatment of symptoms and reducing ocular inflammation.

PRACTICAL AND STABLE-MANAGEMENT PRACTICES TO DECREASE EQUINE RECURRENT UVEITIS

Practices that decrease ocular injury or minimize the inflammatory stimuli may decrease or eliminate the development of recurrent episodes of uveitis in ERU (Box 8-2). It may be possible to eliminate environmental triggers (e.g., allergens, antigens, etc.) of the recurrent episodes of uveitis by changing the horse's pasture, pasture mates, or stable, increasing insect and rodent control, decreasing sun exposure, or changing bedding type. Trauma to the eye(s) can also be decreased by eliminating sharp edges, nails, and hooks in the stable, taping up exposed handles on feed and water buckets, removing low tree branches in the pasture, reducing the training and show schedule, minimizing trailering, and implementing the constant use of a quality fly mask. Ensuring that the horse has proper hoof care, an optimal anthelmintic schedule, and proper diet may also reduce uveitis episodes by minimizing infectious disease occurrence and optimizing systemic health.

Box 8-2 | **Practical and Stable-Management Practices to Decrease ERU**

Environmental

- Change pasture/stable/pasture mates
- Increase insect and rodent control
- Decrease dust
- Decrease sun exposure
- Change bedding type

Health Maintenance

- Proper hoof and dental care
- Optimal anthelmintic and vaccination schedule
- Avoid large multivalent vaccines; split up immunizations
- Proper diet; minimize weeds in pasture

Decrease Ocular Trauma

- "Soften" stable (eliminate sharp objects), tape up bucket handle hooks
- Eliminate low tree branches and burdock plants in pasture
- Decrease training and show schedule
- Minimize trailering
- Do not feed from hay nets
- Use quality fly mask

Anecdotal reports have suggested that vaccination with multivalent vaccines or administration of a number of different individual vaccines on the same day is sometimes associated with a relapse of signs of ocular inflammation. For this reason, it is recommended that horses with ERU be given their annual vaccinations in at least two sessions spaced a week or more apart, rather than all at once. Also, pretreating with a systemic NSAID 24 hours prior to vaccination and repeating the NSAID at the time of vaccination may prevent a flare-up. The attending veterinarian should determine the appropriate immunizations and the route and frequency of administration of the products.

VACCINATION OF HORSES AGAINST LEPTOSPIROSIS

Vaccination of horses with a leptospiral bacterin has been proposed as a preventive measure for leptospiral-associated ERU.[117] Several bovine vaccines that contain bacterins of pathogenic leptospiral serogroups are available commercially, but there is no approved equine vaccine, and all are labeled solely for use in the bovine or porcine species. Insofar as ERU has been shown to have a strong immune-mediated component, and research has demonstrated molecular homology between equine ocular tissues and leptospiral proteins, it is not known if vaccination carries any risk of exacerbating the immune response or precipitating inflammation.

Anecdotal reports suggest that selective use of a bacterin on farms with demonstrated risk of exposure to *Leptospira* has reduced incidence of eye disease.[117] However, acute uveitis signs have also been observed shortly after vaccine administration in a few horses who had unknown past exposure to the bacteria. A study of the effect of an inactivated bovine vaccine against six serovars of *L. interrogans* in small number of ERU horses demonstrated no significant increase or decrease in recurrent episodes of inflammation after vaccination compared to control groups receiving adjuvant only.[134]

Vaccination may be considered on farms in the known geographic risk zones that have had multiple cases of ERU in the past, assuming the clinician and horse owner have discussed the risks versus benefit of the vaccination, and signed owner consent is obtained. Before any decision is made to immunize, all horses on those farms should have leptospiral serology performed. Vaccine administration should be limited to horses that are seronegative to *L. interrogans* and have normal eyes. This conservative approach seems to have reduced the incidence of new cases of ERU on the at-risk farms and to date has not resulted in any ocular inflammation that has been associated with this vaccine administration protocol.[135]

MEDICAL THERAPY FOR EQUINE RECURRENT UVEITIS

Because vision loss is a common long-term manifestation of ERU, initial therapy must be aggressive (Table 8-4). The two main goals of therapy are to reduce discomfort, which is achieved through mydriatic-cycloplegics (e.g., topical atropine), and to reduce inflammation with systemic medications (e.g., corticosteroids and NSAIDs). Topical atropine 1% is generally given to effect and then continued as required to maintain pupil dilation, usually once a day. If the pupil does not dilate after topical atropine use, addition of 10% phenylephrine HCl topically (every 6 hours) for 24 to 48 hours may help achieve mydriasis. Phenylephrine is an alpha agonist but has poor mydriatic and cycloplegic effect in horses.[136] When used in combination with topical atropine, there may be a slightly improved mydriatic effect than that observed with atropine alone. Poor response to mydriatics in general suggests that severe intraocular inflammation is present, therefore control of the inflammation is required to allow the mydriatics to function. Increasing frequency of topical atropine (e.g., greater than every 6 hours) or increased concentrations of atropine (e.g., 2% to 4%) is rarely indicated and could predispose the horse to colic.[137]

Topical corticosteroids are most commonly used to decrease inflammation. Prednisolone acetate 1% and dexamethasone HCl 0.1% are the most commonly used topical corticosteroids. Both medications have excellent ocular penetration. Frequency of therapy varies according to the severity of the disease and ranges from hourly topical application to once-daily application. Dexamethasone is used most often in clinical situations because it is available in an ointment form and inexpensive. Topical corticosteroids have side effects, including the ability to potentiate infections and collagenase enzymes (melting of the cornea), delaying epithelialization of corneal ulcers and possibly the potentiation of calcific band keratopathy.

Table 8-4 | **Medical Therapy for Equine Recurrent Uveitis**

MEDICATIONS	DOSE	INDICATION	CAUTION
TOPICAL MEDICATIONS			
Prednisone acetate 1%	q1-6h	Potent antiinflammatory medication with excellent ocular penetration	Predisposes to corneal fungal infection
Dexamethasone HCl 0.5%-1%	q1-6h	Potent antiinflammatory medication with excellent ocular penetration	Predisposes to corneal fungal infection
0.03% Flurbiprofen, 0.1% diclofenac (or other topical NSAIDs)	q1-6h	Antiinflammatory medications with good ocular penetration	Decreases corneal epithelialization
Cyclosporine A 0.02%-2%	q6-12h	Strong immunosuppressant	Poor eye penetration, weak antiinflammatory effect
Atropine HCl 1%	q6-48h	Cycloplegic, mydriatics (pain relief and minimize synechia formation)	May decrease gut motility and predispose to colic
Phenylephrine HCl 10%	q6-12h	Use with atropine as primarily a mydriatic	
SYSTEMIC MEDICATIONS			
Flunixin meglumine	0.5 mg/kg PO, IV, or IM for 5 days then 0.25 mg/kg PO	Potent ocular antiinflammatory medication	Long-term use may predispose to gastric and renal toxicity
Phenylbutazone	4.4 mg/kg PO or IV	Antiinflammatory medication	Long-term use may predispose to gastric and renal toxicity
Prednisone	100-300 mg/day PO or IM	Potent antiinflammatory medication	Frequent side effects, laminitis formation (use with caution and only as a last resort); must taper off dose
Dexamethasone (Azium)	5-10 mg/day po or 2.5-5 mg/day IM	Potent antiinflammatory medication	Frequent side effects, laminitis formation; use with caution and only as a last resort; must taper off dose
Subconjunctival triamcinolone	1-2 mg	Potent antiinflammatory medication with a 7-10 duration of action	Severe predisposition for bacterial or fungal keratitis; cannot remove therapy once given

NSAIDs, Nonsteroidal antiinflammatory drugs.

Topical NSAIDS (e.g., 0.03% flurbiprofen , 0.09% bromfenac sodium, or 0.1% diclofenac sodium) can also be used. Their main advantages are that they can be administered without concern for potentiating infections, but they do delay epithelialization of corneal ulcers. Although bromfenac is a very potent NSAID compared to the others, in general, the antiinflammatory effect of topical NSAIDs is much less than topical dexamethasone and prednisolone.

Systemic therapy is the most potent therapy for management of ERU. Oral, intramuscular, or IV flunixin meglumine is one of the most potent antiinflammatory medications for the eye (see Table 8-4). Phenylbutazone and aspirin are much less effective. Systemic dexamethasone or prednisolone are also effective but generally are only recommended in severe cases that will not respond to other antiinflammatory medication (see Table 8-4).

Initial therapy is instituted for at least 1 to 2 weeks and should be tapered off over an additional 2 weeks after the resolution of clinical signs. Tapering of medication is VERY important to prevent a rebound bout of inflammation from sudden withdrawal of medications. Owners should be warned about this and told not to discontinue medications despite resolution of clinical signs. In severe cases of ERU, local subconjunctival injections of corticosteroids may be indicated as an adjunct to therapy. The steroid of choice subconjunctivally is 2 mg of triamcinolone acetamide (0.2 mL of 10 mg/mL solution). Triamcinolone injections will deliver medication for 7 to 10 days and will not result in granuloma or abscess formation that other steroids, such as methylprednisolone acetate, will cause. However, once the injections are given, the steroid treatment cannot be withdrawn. The chronic presence of corticosteroids may delay healing of corneal ulcers and substantially predispose the eye to fungal keratitis. Therefore, subconjunctival injection of corticosteroids should be initiated with caution. See Chapter 2 for more information and the technique for subconjunctival injection.

RESPONSE TO MEDICAL TREATMENT

Response to treatment of clinical cases of ERU is variable and difficult to predict. Acute attacks of inflammation may last a few days or several weeks. Some recurrences are mild and respond quickly to simple treatment with mydriatics, topical corticosteroids, and systemic NSAIDs, while other episodes are severe and highly refractive to treatment. Subsequent bouts of inflammation may not show the same response to therapy as the initial episode. If a subsequent bout of uveitis does not respond to therapy as in previous episodes and the cornea is edematous, secondary glaucoma (Fig. 8-30) may have developed and should be diagnosed and monitored by tonometry.

Repeat episodes of ocular inflammation may be progressively more severe and refractive to therapy in some horses. These horses usually go blind in the affected eye(s) despite therapy. Other horses experience a few mild relapses then never suffer another episode. Still others (primarily Appaloosas and horses of Draft breeding) experience insidious disease that progresses quietly but relentlessly regardless of treatment. The multiple factors that contribute to the onset of the syndrome in a particular horse (inciting etiology, the specific immune system and genetics of the host) probably play a key role in determining susceptibility to recurrence, response to therapy, and eventual visual outcome.

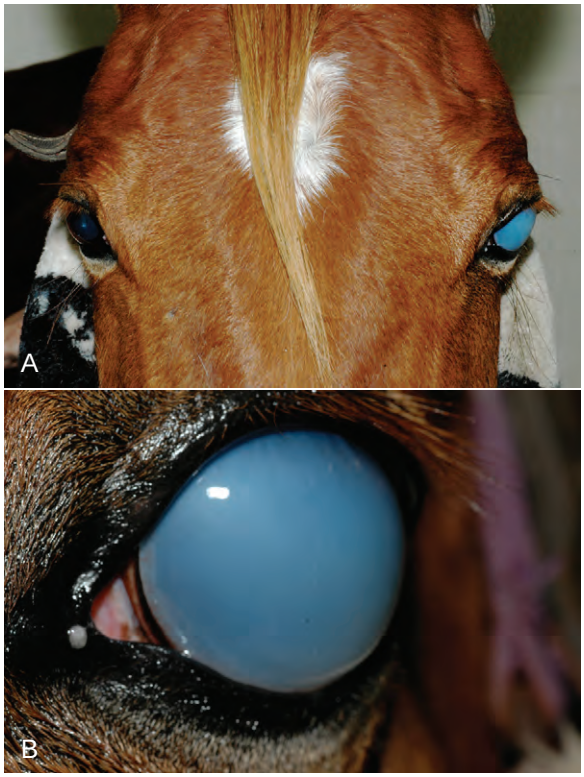


Figure 8-30. **A,** Horse with chronic recurrent uveitis that has developed secondary glaucoma in the left eye. **B,** The most common clinical sign of glaucoma in horses is diffuse corneal edema.

ANTIBIOTIC THERAPIES FOR EQUINE RECURRENT UVEITIS

Traditional treatments used for ERU (i.e., corticosteroids, mydriatics, and NSAIDs) are aimed at reducing inflammation and minimizing permanent ocular damage at each active episode. These treatments are not likely effective in preventing recurrence of disease. Other medications used to prevent or decrease severity of recurrent episodes, such as aspirin, phenylbutazone, and various herbal treatments, have limited efficacy and potential detrimental effects on the gastrointestinal and hematologic systems when used chronically in the horse.

However, several anecdotal reports of benefit have emerged using antibiotics as a primary treatment of ERU. In cases of suspected leptospiral infections (e.g., an elevated leptospiral serum or ocular fluid titer), a 4-week course of oral doxycycline (12 mg/kg PO every 12 hours) or enrofloxacin (7.5 mg/kg PO every 24 hours)[138] is proposed to minimize or eliminate recurrent episodes of uveitis.[57] It is thought that these therapies may kill residual organisms that may be responsible for recurrent uveitis episodes, but no studies have been done to determine if this is the mode of action or if these medications are having another effect. Furthermore, with the strong evidence that ERU is an immune-mediated disease, the use of antibiotics is unlikely to be successful.[37-40,68,74,96,101] Additionally, in one study, oral administration of doxycycline failed to achieve therapeutic

drug concentration in the aqueous or vitreous humor of normal horses.[139] Single injections of 4 mg of gentamicin into the vitreous cavity have also been reported anecdotally to help minimize or eliminate recurrent episodes of uveitis in cases of leptospiral-associated ERU. However, the effectiveness of these treatments has not been reported, and the mode of action, complications, and long-term results of these therapies have not been determined. Until studies are reported, it is recommended these treatments be used with caution and only as a last resort. Acupuncture, herbal, MSM, and holistic therapies may be worth an attempt as long as their use is concurrent with traditional medications or in cases where traditional medication is poorly effective.

SURGICAL TREATMENT OF EQUINE RECURRENT UVEITIS

SUPRACHOROIDAL CYCLOSPORINE SUSTAINED-RELEASE DEVICES

Ocular sustained-release medication devices or implants have many advantages over more traditional methods of drug administration to the eye.[140] These advantages include delivery of constant therapeutic levels of drug directly to the site of action, bypassing some of the blood-ocular barriers, and eliminating the need to rely on owners to treat their horse. Release rates are typically well below toxic levels of the drug, therefore higher concentrations of the drug are achieved in the eye without any systemic side effects. Devices also have the benefit of being more convenient for the patient and reducing the risk involved with frequent intravitreal injections.[140]

Cyclosporine A (CsA) is a 1.2-kD cyclic peptide that blocks the transcription of IL-2 production and the responsiveness of the T cell[141,142]; it may be the ideal drug to prevent the activation of T lymphocytes and recurrence of uveitis. However, CsA is hydrophobic and does not penetrate into the eye when applied topically,[143-145] and systemic treatment may promote serious side effects such as renal, hepatic, and neurologic toxicity.[146] CsA is also very costly to administer to a horse.

Originally, a polyvinyl alcohol silicone-coated intravitreal CsA sustained-delivery device that had been shown previously to produce a sustained level of CsA in rabbit ocular tissues[147,148] was evaluated for use in horses. A CsA device was implanted into normal horse eyes for up to 1 year and was not associated with ocular inflammation or complications.[149] In equine eyes with experimentally induced uveitis, the CsA decreased the duration and severity of inflammation, cellular infiltration, tissue destruction, and level of transcription of proinflammatory cytokines.[56] In a study using CsA devices in horses with naturally occurring ERU,[58] horses with frequent recurrence of uveitis without vision-threatening ocular changes (i.e., cataracts, retinal degeneration) or systemic illnesses were selected to receive the device. Although the device prevented the development of recurrent episodes in 81% of horses, complications were noted after surgery that included intraocular hemorrhage, progression of cataract, and retinal detachment.[58] The surgical intervention in fragile ERU eyes was thought to be the source of the observed complications, so less invasive methods were evaluated for the constant release of cyclosporine.

A device (Fig. 8-31) was developed to be inserted into the suprachoroidal space and allow constant release of cyclosporine (or other selected immunosuppressive medications) directly to the ciliary body. Horses with chronic documented ERU (as determined after complete ophthalmic examination) that have little or no active inflammation but are experiencing frequent recurrences or early relapse of active ERU after stopping medications are appropriate candidates for surgical placement of a CsA implant. Horses with active inflamed eyes that cannot be controlled with antiinflammatory medications are *not* candidates for CsA implantation because CsA has poor antiinflammatory properties (its immunosuppressive properties help prevent new recurrent episodes), and inflamed eyes are prone to postsurgical complications. Control of active inflammation with traditional antiinflammatory medications is critical for success of the CsA implantation technique. Evidence of significant cataract formation or other ocular condition (e.g., glaucoma) make the animal a poor candidate for surgery.

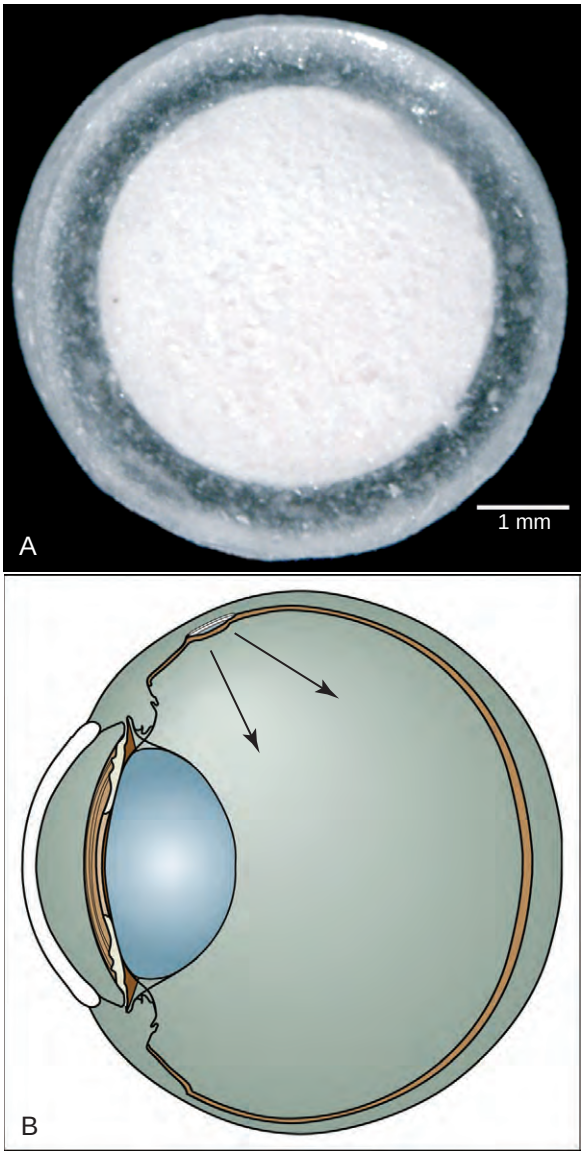


Figure 8-31. **A,** A reservoir/matrix device designed for long-term release of cyclosporine to the eye. **B,** Schematic of the placement of a suprachoroidal drug-delivery device. Drug delivery is in direction of arrows. (**A,** Courtesy Dr. Mike Robinson.)

The suprachoroidal implant surgical technique requires that the horse be placed under general anesthesia. A 1-cm conjunctival incision is made in the dorsolateral bulbar conjunctiva. A 7-mm wide scleral flap is made exposing the uveal tract (the black uvea is just visible through the sclera) approximately 8 mm posterior to the limbus and just lateral to the insertion of the dorsal rectus muscle (Fig. 8-32, *A*). The CsA-containing device is placed into the incision, in contact with the uveal tract (see Fig. 8-32, *B*). The scleral flap and incision is closed with 6-0 Vicryl (see Fig. 8-32, *C*). Postoperative medications include flunixin meglumine (500 mg PO every 24 hours) for 5 days, topical triple antibiotic ophthalmic ointment every 12 hours for 10 days, and topical atropine ointment every 24 hours for 7 days. Approximately 25% of the horses have had a mild flare-up following discontinuation of the flunixin meglumine.

Data from clinical patients suggest that it takes 30 to 45 days after implantation of the device to get adequate ocular levels of CsA. If recurrent episodes occur, traditional treatment with systemic NSAIDS, topical steroids, and atropine is recommended. Approximately 25% of horses have had recurrent episodes after surgery, but subjectively, less medication is required to control the active inflammation, and the duration of the inflammatory episodes are shorter. More importantly, early results suggest that the suprachoroidal implant is not associated with any vision-threatening complications such as retinal detachment. The duration of delivery of medication from the current devices is approximately 36 months.

Use of suprachoroidal placement of a CsA device for the treatment of clinical cases of ERU has been reported.[55] Using this device, mean vitreous CsA concentrations were 0.20 ± 0.14 µg/mL at 4 weeks and 0.14 ±0.04 µg/mL at 9 weeks. CsA was not detected in the cornea, aqueous humor, or peripheral blood at either 4 or 9 weeks after implantation.

Sixty-seven horses received implants in one or both eyes in the 2006 study,[55] and mean follow-up was 14.2 months. The number of uveitis flare-ups was significantly decreased after surgery ($P < 0.0001$). The percentage of eyes with vision at 6 months after surgery was 98% (68/69), after 12 months was 93% (43/46), after 18 months was 90% (28/31), and after 24 months was 96% (22/23). Overall, 85% (68/80) of eyes had vision after surgery.[55]

Recently, data from 186 eyes of 156 horses that had CsA devices implanted for ERU were reviewed.[54] Horses with ERU from six centers in the United States and two in Europe had the CsA device implanted. Mean follow-up was 29 months (1 to 7 years). Horses with implants had significantly fewer flares after surgery (mean 0.05 flares/mo) than prior to implantation. Overall, 79.9% were visual at the last follow-up time. Only three eyes required a repeat implant, all 4 years or longer after the first implant. These results suggested that the suprachoroidal placement of the CsA device resulted in excellent long-term control of ERU.[54] Because recurrences of inflammation did not increase after the theoretical depletion of the CsA (approximately 3 years), it is possible that autoreactive T cells may undergo anergy after a period of time in the presence of CsA, after which recurrence of disease will not occur.

Other immunosuppressive medications may also be evaluated in similar devices, such as tacrolimus (FK506) or rapamycin.[150,151] Intravitreal injection of rapamycin in normal horses was well tolerated without signs of toxicity.[152] A clinical trial

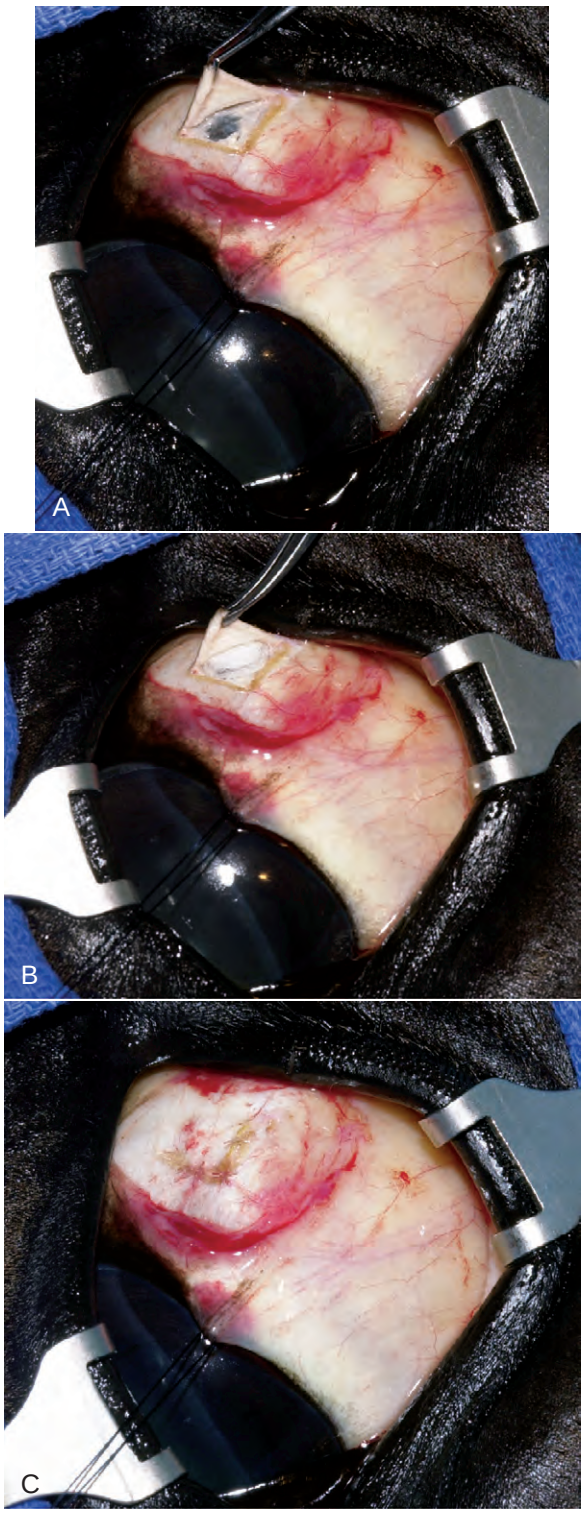


Figure 8-32. Suprachoroidal cyclosporine-releasing device implantation. **A,** A 7-mm wide scleral flap is made, exposing the uveal tract (the black uvea is just visible through the sclera) approximately 8 mm posterior to the limbus and just lateral to the insertion of the dorsal rectus muscle. **B,** The cyclosporine-containing device is placed into the incision, in contact with the uveal tract. **C,** The scleral flap and conjunctival incision are closed with 6-0 polyglactin 910 sutures.

of its use is underway in horses with ERU, with the hope that a single sustained-release injection of rapamycin will induce T cells to undergo anergy.

PARS PLANA VITRECTOMY

Dr. Bernhard Spiess

For more than 25 years, pars plana vitrectomy (PPV) has been used in the management of chronic endogenous uveitis in humans.[153-156] The main goal was to improve vision by clearing the media or removing membranes. However, PPV in eyes with chronic uveitis also altered or diminished the severity as well as the frequency of uveitis relapses.[155] There is evidence that PPV has a beneficial effect on the clinical course of chronic endogenous posterior uveitis in humans, possibly by physically removing any resident inflammatory cells with the vitreous.[157] Despite the reported complications (i.e., vitreal hemorrhage, cataract formation, retinal detachment) following PPV, the majority of the patients were able to switch from rigorous systemic preoperative medication to simple eye drops or no treatment at all.[156]

Vitrectomy has been studied in experimental, protein-induced uveitis in rabbits,[158,159] but it was not until 1991 that PPV was described in the management of ERU.[160] PPV has since been used in the treatment of ERU primarily in Europe.[91,161,162] Similar to the human counterpart, the most common complications reported in horses are transient hypopyon, vitreal and/or retinal hemorrhage, retinal detachment, and cataract formation.[161]

PATIENT SELECTION

Because of the possible serious complications of PPV, patient selection is of great importance. All patients are examined by slit-lamp biomicroscopy, indirect and direct ophthalmoscopy, and applanation tonometry. Ultrasonography is performed in cases with opaque media. The diagnosis of ERU must be confirmed and is based on the description earlier in this chapter, but there must be characteristic signs of acute or chronic uveitis and a documented history of recurrent episodes of acute uveitis. Horses with dense vitreal opacity may benefit most from vitrectomy, not only by decreasing recurrent episodes, but also from improving vision by removal of vitreal debris.

Horses ideally are operated on when in the quiescent stage of the disease. Because of the transpupillary visualization of the vitrectomy probe during the procedure, the optical media (i.e., cornea, anterior chamber, lens) should be as transparent as possible. The pupil should dilate maximally with no or few posterior synechiae. Preexisting focal cataracts are likely to progress following PPV and should be taken into consideration when selecting patients. In patients with secondary glaucoma, phthisis bulbi, or preexisting retinal detachment, PPV should not be recommended. Owners should be carefully informed on the surgery, as well as the possible intra- and postoperative complications.

PREOPERATIVE AND POSTOPERATIVE MEDICATION

Topical 0.1% dexamethasone drops in combination with neomycin and polymyxin B are administered 4 times daily beginning 1 week prior to surgery. Systemic NSAIDs (i.e., flunixin meglumine) are administered beginning 3 days preoperatively. The pupil is dilated with 1% atropine drops on the day of surgery. Postoperatively, topical dexamethasone/neomycin/polymyxin B eye drops are continued 3 times daily for 2 weeks, and then tapered over another 4 weeks. Systemic NSAIDs are continued for 1 week.

SURGICAL TECHNIQUE

A standard two-port PPV is performed in lateral recumbence under general inhalation anesthesia. The eye is prepared for intraocular surgery. After draping, an eyelid speculum is inserted. A lateral canthotomy may improve exposure of the globe, but this is usually not necessary. A limbal stay-suture in the 12 o'clock position is placed for globe manipulation. A limbal-based conjunctival flap is prepared and the sclera exposed medially and laterally to the dorsal rectus muscle. Using a CO_2 laser, a first sclerotomy is performed 10 mm posterior to the limbus. A right-handed surgeon will place this first entry to the left of the rectus muscle. A double-ended lacrimal dilator may be used to enlarge the sclerotomy if necessary. The irrigation port is inserted and its footplate secured to the sclera with two sutures (4-0 polyglactin 910 [Fig. 8-33]). With the vitrectomy unit in continuous irrigation mode and the fluid-containing bottle positioned 85 cm higher than the surgical site, the IOP will be around 40 mm Hg. Balanced salt solution with 40 mg of gentamicin added per 500 mL is used as irrigation fluid. A second laser sclerotomy is performed, again 10 mm posterior to the limbus and to the right of the rectus muscle. The vitrectomy probe is carefully inserted and advanced in the direction of the center of the vitreous (see Fig. 8-33). Again, the sclerotomy may be enlarged with a lacrimal dilator if necessary. Both sclerotomies should be tight enough to prevent leakage of irrigation fluid, which would make maintenance of IOP difficult. The vitrectomy probe should be held at an approximately 70-degree angle and passed toward the optic nerve, taking care to avoid touching the lens when inserting the probe. The probe tip should be held with the aspiration port facing the surgeon. The central and anterior parts of the vitreous can be removed by direct visualization through the dilated

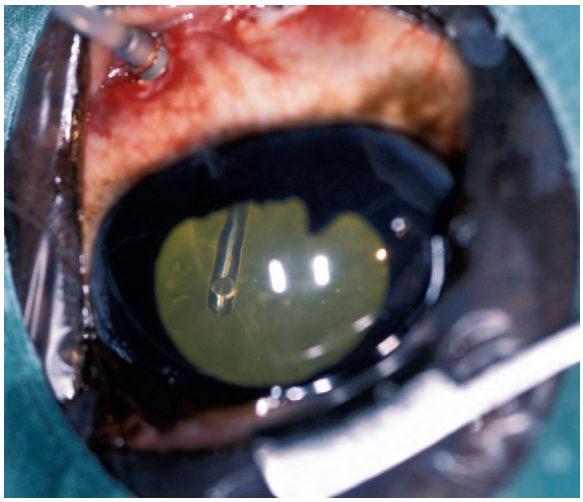


Figure 8-33. Surgeon's view during vitrectomy surgery. The infusion tip is fixed in the sclera at the 11 o'clock position; the cutter is introduced at the 1 o'clock position and observed through the pupil. (Photograph courtesy Hartmut Gerhards and Bettina Wollanke.)

pupil. Indirect ophthalmoscopy using a 20-D lens is used to visualize posterior and peripheral parts of the vitreous. Alternatively, a custom-made equine vitrectomy contact lens (Acrivet, Berlin, Germany) can be used to visualize the posterior segment through the operating microscope (Fig. 8-34). Aspiration of vitreous can easily be observed, especially if there are inflammatory materials. Estimating the distance between the probe and its shadow cast onto the retina will help the surgeon to avoid touching the retina. Throughout the entire procedure, the IOP should be maintained at approximately 40 mm Hg. Slight wrinkling of the retina, seen with the aid of the ophthalmoscope, indicates that the IOP may be too low. Vitrectomy should be interrupted until a normal IOP is restored. The procedure is continued until all turbid vitreal material has been removed. Under continuous irrigation, the vitrectomy probe is removed and the sclerotomy closed with one or two single interrupted sutures using 4-0 polyglactin 910. Subsequently the irrigation port is removed. Remaining peripheral vitreous will usually prevent fluid from escaping through this sclerotomy, which is closed with 4-0 polyglactin 910. The conjunctiva is closed with polyglactin 910 in a continuous pattern. A canthotomy is closed with a figure-of-eight suture using 4-0 nonabsorbable suture materials. At the end of surgery, 20 mg of methylprednisolone may be injected subconjunctivally in the inferior bulbar conjunctiva.

Some differences in performing this procedure in the horse have been established. To avoid uveal hemorrhage, both sclerotomies are performed using a CO_2 laser in continuous mode at 50 W. Commercially available standard vitrectomy probes are too short for use in horses. A 55-mm oscillating vitrectomy with a guillotine-like chopping blade probe is used at 12 Hz, an aspiration vacuum of 400 mm Hg, and a flow rate of 15 mL/min. High oscillation frequency, moderate suction, and low flow are used to minimize vitreoretinal traction and decrease the incidence of iatrogenic retinal breaks.

COMPLICATIONS

Intraoperative complications include lens trauma, vitreal/retinal hemorrhage, and retinal detachment. Maintaining IOP at around 40 mm Hg and using a CO_2 laser instead of surgical blades for the sclerotomies can avoid hemorrhage. Touching the retina should also be avoided as it results in immediate hemorrhage and subsequent detachment.[160,161] Early postoperative complications (less than 3 months) include cataract formation and retinal detachment. Late complications occurring after 3 months include cataract formation as well as recurrence of active uveitis.[157,161]

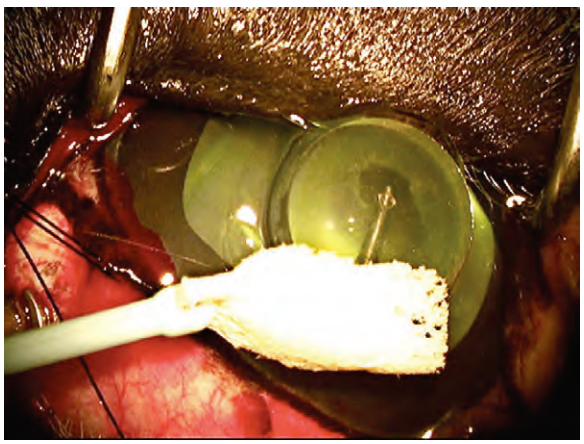


Figure 8-34. A custom-made equine vitrectomy contact lens can be used to visualize the posterior segment through the operating microscope and make vitrectomy more precise by improving visualization. Vitrectomy needle is visualized through the lens.

LONG-TERM RESULTS

Seventy-three percent of horses that underwent pars plana vitrectomy showed no further recurrence of uveitis.[163] Twenty-two continued to suffer from recurrent episodes of uveitis. The remaining horses were reported to have experienced only one more episode of uveitis, which was easily controlled with topical anti-inflammatory therapy.[163]

Vitreous samples of every horse were submitted, and 78% were positive for *Leptospira* spp. MAT serology. The most common serovars were *L.* Grippotyphosa, *L.* Copenhageni, *L.* Bratislava, *L.* Canicola, *L.* Pyogenes, and *L.* Pomona. Of the *Leptospira*-positive horses, 81% showed no further recurrences after vitrectomy, while of the *Leptospira*-negative patients 83% had further recurrences[163] This suggests that pars plana vitrectomy represents a successful surgical therapy for horses suffering from *Leptospira*-related ERU, whereas patients testing negative for *Leptospira* spp. are poorer candidates for this surgery.[163] They may, however, be more suitable candidates for the implantation of cyclosporin-releasing devices.[55]

Clinical experience would suggest that aqueous humor and/or vitreous samples of horses suffering from ERU should be tested for *Leptospira* spp., and that the decision to perform pars plana vitrectomy should based on these results. In another study of 38 cases, five eyes showed recurrence of uveitis between 10 days and 3 years postoperatively.[161] Thirty-three eyes showed no recurrence during a follow-up period of up to 5 years. Vision remained stable in 28 eyes and improved in one eye. The remaining eyes showed marked vision loss as a result of cataracts, phthisis bulbi, or unknown cause. Of the five eyes with recurrent uveitis, two demonstrated marked loss of vision, while three maintained preoperative vision.[161]

In an earlier study of 43 eyes post PPV, 42 remained free of recurrent uveitis during a follow-up period of 67 months.[164] Seventy percent of these eyes retained some vision. The most common complication was cataract formation in 19/43 eyes, followed by phthisis bulbi in 6 eyes, and retinal detachment in 4 eyes.[164]

In selected patients with consenting owners, PPV offers a promising alternative to conventional therapy. With few exceptions, eyes show no recurrence of uveitis after PPV. However, a significant number of postoperative complications cause visual impairment or blindness. The most common long-term postoperative complication appears to be cataract formation (Fig. 8-35). It is unclear whether preexisting lenticular opacities progress despite PPV or if the progression is caused by the procedure. Touching the posterior lens capsule during PPV invariably leads to focal cataracts, which very often progress. Retinal and vitreal hemorrhage is the most common intraoperative complication. Maintaining a high-normal IOP, careful manipulation of the vitrectomy probe, and avoidance of touching the retina usually prevents such complications. Choroidal hemorrhage can be avoided with the use of a CO_2 laser instead

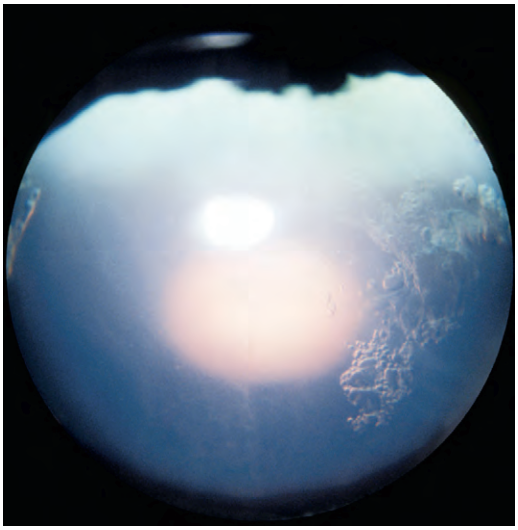


Figure 8-35. Cataract formation after vitrectomy for ERU. (Photograph courtesy Hartmut Gerhards and Bettina Wollanke.)

of a surgical blade. Despite these complications, PPV appears to be a promising method for long-term control of leptospiral-induced equine recurrent uveitis.

FUTURE RESEARCH FOR EQUINE RECURRENT UVEITIS

Future understanding of recurrent uveitis in all species will revolve around the investigation of several key questions[165]:

1. What genetic makeup predisposes individuals to develop disease?
2. If the disease is autoimmune, which autoantigens participate in the initiation and perpetuation of inflammation?
3. What immune mechanisms initiate the immune response and mediate tissue destruction?

In horses, other questions can be added:

1. Is ERU one disease or a symptom/syndrome with many causes?
2. Is the insidious form of ERU a different disease with different etiology and pathogenesis than classic ERU?

Further study is needed to determine the genetic predisposition for ERU. It is not likely to be a monogenetic disease, but research is needed to identify susceptibility factors for ERU.

New immunosuppressive therapies, such as rapamycin, may offer hope in the medical management. Perfecting new and practical sustained-release drug delivery devices or injections are needed. Studies need to be done to determine the role of leptospirosis or other microorganisms in the initiation and pathogenesis of ERU. Effort continues to further quantify the immune events that characterize inflammation and mediate recurrence. Blindness or reduced vision is a common outcome for people or horses, and uveitis is a cause of large economic and humanitarian losses worldwide. Continued research on ERU should provide deeper understanding of the clinicopathologic features of uveitis in all species, and new therapies under development for horses may lead to improved therapy for people, with subsequent reduction in the incidence of blindness in both species worldwide.[165]

Acknowledgment

The authors acknowledge and appreciate the work of Ann Dwyer, who co-authored this chapter in the previous edition, and Jacklyn Salmen, who reviewed this chapter.

References

1. Jones T: Equine periodic ophthalmia, Am J Vet Res 3:45–70, 1942.
2. Barnett KC: Equine periodic ophthalmia: a continuing aetiological riddle, Equine Vet J 19:90–91, 1987.
3. Dwyer AE, Crockett RS, Kalsow CM: Association of leptospiral seroreactivity and breed with uveitis and blindness in horses: 372 cases (1986–1993), J Am Vet Med Assoc 207:1327–1331, 1995.
4. Paglia DT, Miller PE, Dubielzig RR: James Wardrop and equine recurrent uveitis, Arch Ophthalmol 122:1218–1223, 2004.
5. Schwink KL: Equine uveitis, Vet Clin North Am Equine Pract 8:557–574, 1992.
6. Witmer R: Periodic ophthalmia in horses, Am J Ophthalmol 37:243–253, 1954.
7. Deeg CA: Ocular immunology in equine recurrent uveitis, Vet Ophthalmol 11(Suppl 1):61–65, 2008.
8. Deeg CA, Hauck SM, Amann B, et al: Equine recurrent uveitis–a spontaneous horse model of uveitis, Ophthalmic Res 40:151–153, 2008.
9. Roberts SR: Chorioretinitis in a band of horses, J Am Vet Med Assoc 158:2043–2046, 1971.
10. Lavach J: Large animal ophthalmology, St Louis, 1990, Mosby.
11. Schlotthauer C: Recurrent ophthalmia, North Am Vet 14:18–29, 1933.
12. Rimpau W: Leptospirose beim pferde (periodische augenentzundung), Tierarztl Umsch 20:15–16, 1947.
13. Heusser H: Die periodische augenentzundung, eine Leptspirose? Schweiz Arch Tierheilkd 90:288–312, 1948.
14. Brandes K, Wollanke B, Niedermaier G, et al: Recurrent uveitis in horses: vitreal examinations with ultrastructural detection of leptospires, J Vet Med A Physiol Pathol Clin Med 54:270–275, 2007.
15. Brem S, Gerhards H, Wollanke B, et al: [Demonstration of intraocular *Leptospira* in 4 horses suffering from equine recurrent uveitis (ERU)], Berl Munch Tierarztl Wochenschr 111:415–417, 1998.
16. Brem S, Gerhards H, Wollanke B, et al: [*Leptospira* isolated from the vitreous body of 32 horses with recurrent uveitis (ERU)], Berl Munch Tierarztl Wochenschr 112:390–393, 1999.
17. Davidson MG, Nasisse MP, Roberts SM: Immunodiagnosis of leptospiral uveitis in two horses, Equine Vet J 19:155–157, 1987.
18. Faber NA, Crawford M, LeFebvre RB, et al: Detection of *Leptospira* spp. in the aqueous humor of horses with naturally acquired recurrent uveitis, J Clin Microbiol 38:2731–2733, 2000.
19. Halliwell RE, Brim TA, Hines MT, et al: Studies on equine recurrent uveitis. II: The role of infection with *Leptospira interrogans* serovar Pomona, Curr Eye Res 4:1033–1040, 1985.
20. Hartskeerl RA, Goris MG, Brem S, et al: Classification of *Leptospira* from the eyes of horses suffering from recurrent uveitis, J Vet Med B Infect Dis Vet Public Health 51:110–115, 2004.
21. Lucchesi PM, Parma AE: A DNA fragment of *Leptospira interrogans* encodes a protein which shares epitopes with equine cornea, Vet Immunol Immunopathol 71:173–179, 1999.
22. Matthews AG, Waitkins SA, Palmer MF: Serological study of leptospiral infections and endogenous uveitis among horses and ponies in the United Kingdom, Equine Vet J 19:125–128, 1987.
23. Roberts S: Sequela of leptospirosis in horses on a small farm, J Am Vet Med Assoc 133:189–194, 1958.
24. Sillerud CL, Bey RF, Ball M, Bistner SI: Serologic correlation of suspected *Leptospira interrogans* serovar Pomona–induced uveitis in a group of horses, J Am Vet Med Assoc 191:1576–1578, 1987.

25. Wollanke B, Gerhards H, Brem S, et al: [Intraocular and serum antibody titers to *Leptospira* in 150 horses with equine recurrent uveitis (ERU) subjected to vitrectomy], Berl Munch Tierarztl Wochenschr 111:134–139, 1998.
26. Wollanke B, Rohrbach BW, Gerhards H: Serum and vitreous humor antibody titers in and isolation of *Leptospira interrogans* from horses with recurrent uveitis, J Am Vet Med Assoc 219:795–800, 2001.
27. Wood RM, Davis GR: The correlation of periodic ophthalmia with *Leptospira* agglutinins in horses, Am J Ophthalmol 33:961–962, 1950.
28. Yager RH, Gochenour WS, Jr, Wetmore PW: Recurrent iridocyclitis (periodic ophthalmia) of horses; agglutination and lysis of leptospiras by serums deriving from horses affected with recurrent iridocyclitis, J Am Vet Med Assoc 117:207–209, 1950.
29. Abrams K, Brooks D: Equine recurrent uveitis: current concepts in diagnosis and treatment, Equine Pract 12:27–35, 1990.
30. Choyce DP: Ocular onchocerciasis in Central America, Africa and British Isles: (with a note on equine periodic ophthalmia), Trans R Soc Trop Med Hyg 58:11–47, 1964.
31. Evans K, Smith M, McDonough P, et al: Eye infections due to *Listeria monocytogenes* in three cows and one horse, J Vet Diagn Invest 16:464–469, 2004.
32. Gelatt KN: Traumatic hyphema and iridocyclitis in the horse, Mod Vet Pract 56:475–479, 1975.
33. Lavignette AM: Differential diagnosis and treatment of anterior uveitis, Vet Clin North Am 3:503–514, 1973.
34. Moran CT, James ER: Equine ocular pathology ascribed to *Onchocerca cervicalis* infection: a re-examination, Trop Med Parasitol 38:287–288, 1987.
35. Parker JL, White KK: Lyme borreliosis in cattle and horses: a review of the literature, Cornell Vet 82:253–274, 1992.
36. Rebhun WC: Diagnosis and treatment of equine uveitis, J Am Vet Med Assoc 175:803–808, 1979.
37. Deeg CA, Amann B, Raith AJ, et al: Inter- and intramolecular epitope spreading in equine recurrent uveitis, Invest Ophthalmol Vis Sci 47:652–656, 2006.
38. Deeg CA, Ehrenhofer M, Thurau SR, et al: Immunopathology of recurrent uveitis in spontaneously diseased horses, Exp Eye Res 75:127–133, 2002.
39. Deeg CA, Kaspers B, Gerhards H, et al: Immune responses to retinal autoantigens and peptides in equine recurrent uveitis, Invest Ophthalmol Vis Sci 42:393–398, 2001.
40. Gilger BC, Malok E, Cutter KV, et al: Characterization of T-lymphocytes in the anterior uvea of eyes with chronic equine recurrent uveitis, Vet Immunol Immunopathol 71:17–28, 1999.
41. Gilger BC, Yang P, Salmon JH, et al: Expression of a chemokine by ciliary body epithelium in horses with naturally occurring recurrent uveitis and in cultured ciliary body epithelial cells, Am J Vet Res 63:942–947, 2002.
42. Kalsow CM, Dwyer AE: Retinal immunopathology in horses with uveitis, Ocul Immunol Inflamm 6:239–251, 1998.
43. Kalsow CM, Dwyer AE, Smith AW, Nifong TP: Pinealitis coincident with recurrent uveitis: immunohistochemical studies, Curr Eye Res 11(Suppl):147–151, 1992.
44. Romeike A, Brugmann M, Drommer W: Immunohistochemical studies in equine recurrent uveitis (ERU), Vet Pathol 35:515–526, 1998.
45. Verma A, Artiushin S, Matsunaga J, et al: LruA and LruB, novel lipoproteins of pathogenic *Leptospira interrogans* associated with equine recurrent uveitis, Infect Immun 73:7259–7266, 2005.
46. Deeg CA, Marti E, Gaillard C, et al: Equine recurrent uveitis is strongly associated with the MHC class I haplotype ELA-A9, Equine Vet J 36:73–75, 2004.
47. Bellhorn R: An overview of the blood-ocular barriers, Prog Vet Comp Ophthalmol 1:205–217, 1990.
48. Gilger BC, Michau TM, Salmon JH: Immune-mediated keratitis in horses: 19 cases (1998-2004), Vet Ophthalmol 8:233–239, 2005.
49. Hendrix DV, Brooks DE, Smith PJ, et al: Corneal stromal abscesses in the horse: a review of 24 cases, Equine Vet J 27:440–447, 1995.
50. US Horse Council: The economic impact of the horse industry in the United States. http://www.horsecouncil.org/2005.
51. Cook C, Harling D: Equine recurrent uveitis, Equine Vet J 2S:2–15, 1983.
52. Strobel BW, Wilkie DA, Gilger BC: Retinal detachment in horses: 40 cases (1998-2005), Vet Ophthalmol 10:380–385, 2007.
53. Dwyer A: Visual prognosis in horses with uveitis. American Society of Veterinary Ophthalmology annual meeting, Boston, MA, 1998, pp 22–23.
54. Gilger B, Salmon J, Wilkie D, et al: Long-term control of equine recurrent uveitis using a suprachoroidal cyclosporine matrix reservoir drug delivery device. Am Coll Vet Ophthalmol, Chicago, IL; (abstract) November 5, 2009.
55. Gilger BC, Salmon JH, Wilkie DA, et al: A novel bioerodible deep scleral lamellar cyclosporine implant for uveitis, Invest Ophthalmol Vis Sci 47:2596–2605, 2006.
56. Gilger BC, Malok E, Stewart T, et al: Effect of an intravitreal cyclosporine implant on experimental uveitis in horses, Vet Immunol Immunopathol 76:239–255, 2000.
57. Gilger BC, Michau TM: Equine recurrent uveitis: new methods of management, Vet Clin North Am Equine Pract 20:417–427, vii, 2004.
58. Gilger BC, Wilkie DA, Davidson MG, et al: Use of an intravitreal sustained-release cyclosporine delivery device for treatment of equine recurrent uveitis, Am J Vet Res 62:1892–1896, 2001.
59. Lightman S, Greenwood J: Effect of lymphocytic infiltration on the blood-retinal barrier in experimental autoimmune uveoretinitis, Clin Exp Immunol 88:473–477, 1992.
60. Ehrenhofer M, Deeg C, Reese S, et al: Normal structure and age-related changes of the equine retina, Vet Ophthalmol 5:39–47, 2002.
61. Romagnani S: The Th1/Th2 paradigm, Immunol Today 18:263–266, 1997.
62. Aggarwal S, Gurney A: IL-17: prototype member of an emerging cytokine family, J Leukoc Biol 71:1–8, 2002.
63. Martine C, Jean Marc D, Nicolas B, et al: Human interleukin-17: a T cell-derived proinflammatory cytokine produced by the rheumatoid synovium, Arthr Rheum 42:963–970, 1999.
64. Aggarwal S, Ghilardi N, Xie M, et al: Interleukin-23 promotes a distinct CD4 T cell activation state characterized by the production of interleukin-17, J Biol Chem 278:1910–1914, 2003.
65. Ke Y, Liu K, Huang G, et al: Anti-inflammatory role of IL-17 in experimental autoimmune uveitis, J Immunol 182:3183–3190, 2009.
66. Zhang Z, Zhong W, Spencer D, et al: Interleukin-17 causes neutrophil mediated inflammation in ovalbumin-induced uveitis in DO11.10 mice, Cytokine 46:79–91, 2009.
67. Luger D, Caspi R: New perspectives on effector mechanisms in uveitis, Semin Immunopathol 30:135–143, 2008.
68. Deeg CA, Thurau SR, Gerhards H, et al: Uveitis in horses induced by interphotoreceptor retinoid-binding protein is similar to the spontaneous disease, Eur J Immunol 32:2598–2606, 2002.
69. Caspi R, Roberge F, Chan C, et al: A new model of autoimmune disease. Experimental autoimmune uveoretinitis induced in mice with two different retinal antigens, J Immunol 140:1490–1495, 1988.
70. Wacker W: Experimental allergic uveitis. Investigations of retinal autoimmunity and the immunopathologic responses evoked, Invest Ophthalmol Vis Sci 32:3119–3128, 1991.
71. Caspi R, Roberge F, McAllister C, et al: T cell lines mediating experimental autoimmune uveoretinitis (EAU) in the rat, J Immunol 136:928–933, 1986.
72. Hines MT: Immunologically mediated ocular disease in the horse, Vet Clin North Am Large Anim Pract 6:501–512, 1984.
73. Marker-Hermann E, Meyer zum Buschenfelde K, Wildner G: HLA-B27-derived peptides as autoantigens for T lymphocytes in ankylosing spondylitis, Arthr Rheum 40:2047–2204, 1997.
74. Deeg CA, Pompetzki D, Raith AJ, et al: Identification and functional validation of novel autoantigens in equine uveitis, Mol Cell Proteomics 5:1462–1470, 2006.
75. Deeg CA, Raith AJ, Amann B, et al: CRALBP is a highly prevalent autoantigen for human autoimmune uveitis, Clin Dev Immunol 2007:39245, 2007.
76. Kalsow C, Wacker W: Pineal gland involvement in retina-induced experimental allergic uveitis, Invest Ophthalmol Vis Sci 17:77–83, 1978.
77. Kalsow CM, Dubielzig RR, Dwyer AE: Immunopathology of pineal glands from horses with uveitis, Invest Ophthalmol Vis Sci 40:1611–1615, 1999.
78. Kalsow CM, Dwyer AE, Smith AW, et al: Pinealitis accompanying equine recurrent uveitis, Br J Ophthalmol 77:46–48, 1993.
79. Zhao ZS, Granucci F, Yeh L, et al: Molecular mimicry by herpes simplex virus-type 1: autoimmune disease after viral infection, Science 279:1344–1347, 1998.

80. Horwitz MS, Bradley LM, Harbertson J, et al: Diabetes induced by Coxsackievirus: initiation by bystander damage and not molecular mimicry, Nat Med 4:781–785, 1998.
81. Miller SD, Vanderlugt CL, Begolka WS, et al: Persistent infection with Theiler's virus leads to CNS autoimmunity via epitope spreading, Nat Med 3:1133–1136, 1997.
82. Vanderlugt CJ, Miller SD: Epitope spreading, Curr Opin Immunol 8:831–836, 1996.
83. Mackay IR, Rowley MJ: Autoimmune epitopes: autoepitopes, Autoimmun Rev 3:487–492, 2004.
84. Deshmukh US, Gaskin F, Lewis JE, et al: Mechanisms of autoantibody diversification to SLE-related autoantigens, Ann N Y Acad Sci 987:91–98, 2003.
85. Ott PA, Dittrich MT, Herzog BA, et al: T cells recognize multiple GAD65 and proinsulin epitopes in human type 1 diabetes, suggesting determinant spreading, J Clin Immunol 24:327–339, 2004.
86. Sawalha AH, Harley JB: Antinuclear autoantibodies in systemic lupus erythematosus, Curr Opin Rheumatol 16:534–540, 2004.
87. Seissler J, Scherbaum WA: Are we ready to predict and prevent endocrine/organ specific autoimmune diseases? Springer Semin Immunopathol 24:273–295, 2002.
88. Yu M, Johnson JM, Tuohy VK: A predictable sequential determinant spreading cascade invariably accompanies progression of experimental autoimmune encephalomyelitis: a basis for peptide-specific therapy after onset of clinical disease, J Exp Med 183:1777–1788, 1996.
89. Tchernev G, Orfanos C: Antigen mimicry, epitope spreading and the pathogenesis of pemphigus, Tissue Antigens 68:2006.
90. Deeg CA, Reese S, Gerhards H, et al: The uveitogenic potential of retinal S-antigen in horses, Invest Ophthalmol Vis Sci 45:2286–2292, 2004.
91. Werry H, Gerhards H: [The surgical therapy of equine recurrent uveitis], Tierarztl Prax 20:178–186, 1992.
92. de Smet MD, Chan CC: Regulation of ocular inflammation–what experimental and human studies have taught us, Prog Retin Eye Res 20:761–797, 2001.
93. Chiovato L, Latrofa F, Braverman LE, et al: Disappearance of humoral thyroid autoimmunity after complete removal of thyroid antigens, Ann Intern Med 139:346–351, 2003.
94. Pontes de Carvalho LC, Templeman J, Wick G, et al: The role of self-antigen in the development of autoimmunity in obese strain chickens with spontaneous autoallergic thyroiditis, J Exp Med 155:1255–1266, 1982.
95. Hauck SM, Schoeffmann S, Amann B, et al: Retinal Mueller glial cells trigger the hallmark inflammatory process in autoimmune uveitis, J Proteome Res 6:2121–2131, 2007.
96. Deeg CA, Hauck SM, Amann B, et al: Major retinal autoantigens remain stably expressed during all stages of spontaneous uveitis, Mol Immunol 44:3291–3296, 2007.
97. Zipplies JK, Hauck SM, Schoeffmann S, et al: Serum PEDF levels are decreased in a spontaneous animal model for human autoimmune uveitis, J Proteome Res 8:992–998, 2009.
98. Jha P, Sohn JH, Xu Q, et al: The complement system plays a critical role in the development of experimental autoimmune anterior uveitis, Invest Ophthalmol Vis Sci 47:1030–1038, 2006.
99. Jha P, Sohn JH, Xu Q, et al: Suppression of complement regulatory proteins (CRPs) exacerbates experimental autoimmune anterior uveitis (EAAU), J Immunol 176:7221–7231, 2006.
100. Steele FR, Chader GJ, Johnson LV, et al: Pigment epithelium-derived factor: neurotrophic activity and identification as a member of the serine protease inhibitor gene family, Proc Natl Acad Sci U S A 90:1526–1530, 1993.
101. Deeg CA, Altmann F, Hauck SM, et al: Down-regulation of pigment epithelium-derived factor in uveitic lesion associates with focal vascular endothelial growth factor expression and breakdown of the blood-retinal barrier, Proteomics 7:1540–1548, 2007.
102. Zhang SX, Wang JJ, Gao G, et al: Pigment epithelium-derived factor (PEDF) is an endogenous antiinflammatory factor, FASEB J 20:323–325, 2006.
103. Hauck SM, Suppmann S, Ueffing M: Proteomic profiling of primary retinal Muller glia cells reveals a shift in expression patterns upon adaptation to in vitro conditions, Glia 44:251–263, 2003.
104. Petersen SV, Valnickova Z, Enghild JJ: Pigment-epithelium-derived factor (PEDF) occurs at a physiologically relevant concentration in human blood: purification and characterization, Biochem J 374:199–206, 2003.
105. Cooley PL, Wyman M, Kindig O: Pars plicata in equine recurrent uveitis, Vet Pathol 27:138–140, 1990.
106. Dubielzig R, Render J, Morreale R: Distinctive morphologic features of the ciliary body in equine recurrent uveitis, Vet Comp Ophthalmol 7:163–167, 1997.
107. Gilger BC, Salmon JH, Yi NY, et al: Role of bacteria in the pathogenesis of recurrent uveitis in horses from the southeastern United States, Am J Vet Res 69:1329–1335, 2008.
108. Morter RL, Herschler RC, Fessler JF, et al: Experimental equine leptospirosis (*Leptospira* Pomona), Proc Annu Meet U S Anim Health Assoc 68:147–152, 1964.
109. Myers DM: Serological studies and isolations of serotype Hardjo and *Leptospira biflexa* strains from horses of Argentina, J Clin Microbiol 3:548–555, 1976.
110. Ellis TM, Robertson GM, Hustas L, et al: Detection of leptospires in tissue using an immunoperoxidase staining procedure, Aust Vet J 60:364–367, 1983.
111. Bernard WV, Bolin C, Riddle T, et al: Leptospiral abortion and leptospiruria in horses from the same farm, J Am Vet Med Assoc 202:1285–1286, 1993.
112. Divers TJ, Byars TD, Shin SJ: Renal dysfunction associated with infection of *Leptospira interrogans* in a horse, J Am Vet Med Assoc 201:1391–1392, 1992.
113. Giles RC, Donahue JM, Hong CB, et al: Causes of abortion, stillbirth, and perinatal death in horses: 3,527 cases (1986-1991), J Am Vet Med Assoc 203:1170–1175, 1993.
114. Poonacha KB, Donahue JM, Giles RC, et al: Leptospirosis in equine fetuses, stillborn foals, and placentas, Vet Pathol 30:362–369, 1993.
115. Yager RH, Gochenour WS, Jr: Leptospirosis in North America, Am J Trop Med Hyg 1:457–461, 1952.
116. Smith RE, Williams IA, Kingsbury ET: Serologic evidence of equine leptospirosis in the northeast United States, Cornell Vet 66:105–109, 1976.
117. Roberts SJ: Comments on equine leptospirosis, J Am Vet Med Assoc 155:442–445, 1969.
118. Verma BB, Biberstein EL, Meyer ME: Serologic survey of leptospiral antibodies in horses in California, Am J Vet Res 38:1443–1444, 1977.
119. Pearce JW, Galle LE, Kleiboeker SB, et al: Detection of *Leptospira interrogans* DNA and antigen in fixed equine eyes affected with end-stage equine recurrent uveitis, J Vet Diagn Invest 19:686–690, 2007.
120. Roberts S, York C, Robinson J: An outbreak of leptospirosis in horses on a small farm, J Am Vet Med Assoc 121:237–242, 1952.
121. Roberts SR: Etiology of equine periodic ophthalmia, Am J Ophthalmol 55:1049–1055, 1963.
122. Morter RL, Williams RD, Bolte H, et al: Equine leptospirosis, J Am Vet Med Assoc 155:436–442, 1969.
123. Williams RD, Morter RL, Freeman MJ, et al: Experimental chronic uveitis. Ophthalmic signs following equine leptospirosis, Invest Ophthalmol 10:948–954, 1971.
124. Halliwell RE, Hines MT: Studies on equine recurrent uveitis. I: Levels of immunoglobulin and albumin in the aqueous humor of horses with and without intraocular disease, Curr Eye Res 4:1023–1031, 1985.
125. Eule JC, Wagner B, Leibold W, et al: [Occurrence of various immunoglobulin isotopes in horses with equine recurrent uveitis (ERU)], Berl Munch Tierarztl Wochenschr 113:253–257, 2000.
126. Parma AE, Santisteban CG, Villalba JS, et al: Experimental demonstration of an antigenic relationship between *Leptospira* and equine cornea, Vet Immunol Immunopathol 10:215–224, 1985.
127. Parma AE, Fernandez AS, Santisteban CG, et al: Tears and aqueous humor from horses inoculated with *Leptospira* contain antibodies which bind to cornea, Vet Immunol Immunopathol 14:181–185, 1987.
128. Parma AE, Cerone SI, Sansinanea SA, et al: C3 fixed in vivo to cornea from horses inoculated with *Leptospira interrogans*, Vet Immunol Immunopathol 34:181–187, 1992.
129. Verma A, Rathinam SR, Priya CG, et al: LruA and LruB antibodies in sera of humans with leptospiral uveitis, Clin Vaccine Immunol 15:1019–1023, 2008.
130. Gelatt K: The status of equine ophthalmology, J Equine Med Surg 1:13–19, 1977.
131. Angelos J, Oppenheim Y, Rebhun W, et al: Evaluation of breed as a risk factor for sarcoid and uveitis in horses, Anim Genet 19:417–425, 1988.

132. Sandmeyer LS, Breaux CB, Archer S, et al: Clinical and electroretinographic characteristics of congenital stationary night blindness in the Appaloosa and the association with the leopard complex, Vet Ophthalmol 10:368–375, 2007.
133. Antczak DF: Unpublished data, 1989.
134. Rohrbach BW, Ward DA, Hendrix DV, Cawrse-Foss M, Moyers TD: Effect of vaccination against leptospirosis on the frequency, days to recurrence and progression of disease in horses with equine recurrent uveitis, Vet Ophthalmol 8:171–179, 2005.
135. Dwyer AE: Personal communication, 2004.
136. Hacker DV, Buyukmihci NC, Franti CE, et al: Effect of topical phenylephrine on the equine pupil, Am J Vet Res 48:320–322, 1987.
137. Williams MM, Spiess BM, Pascoe PJ, et al: Systemic effects of topical and subconjunctival ophthalmic atropine in the horse, Vet Ophthalmol 3:193–199, 2000.
138. Divers TJ, Irby NL, Mohammed HO, et al: Ocular penetration of intravenously administered enrofloxacin in the horse, Equine Vet J 40:167–170, 2008.
139. Gilmour MA, Clarke CR, Macallister CG, et al: Ocular penetration of oral doxycycline in the horse, Vet Ophthalmol 8:331–335, 2005.
140. Davis JL, Gilger BC, Robinson MR: Novel approaches to ocular drug delivery, Curr Opin Mol Ther 6:195–205, 2004.
141. Kay J: Inhibitory effects of cyclosporin A on lymphocyte activation. In Thomson A, editor: Cyclosporine: mode of action and clinical application, Dordrecht, 1989, Kluwer Academic Publishers, pp 1–23.
142. Granelli-Piperno A: Cellular mode of action of cyclosporin A. In Bach J, editor, T-cell directed immunointervention, Oxford, 1993, Blackwell Scientific Publishers, pp 3–24.
143. BenEzra D, Maftzir G: Ocular penetration of cyclosporine A in the rat eye, Arch Ophthalmol 108:584–587, 1990.
144. BenEzra D, Maftzir G: Ocular penetration of cyclosporin A, the rabbit eye, Invest Ophthalmol Vis Sci 31:1362–1366, 1990.
145. BenEzra D: Ocular penetration of cyclosporin A. III. The human eye, Br J Ophthalmol 74:350–352, 1990.
146. Svenson K, Bohman S, Hallgren R: Renal interstitial fibrosis and vascular changes. Occurrence in patients with autoimmune diseases treated with cyclosporine, Arch Intern Med 146:2007–2010, 1986.
147. Jaffe G: Intravitreal sustained-release cyclosporine in the treatment of experimental uveitis, Ophthalmology 105:46–56, 1998.
148. Enyedi L, Pearson P, Ashton P: An intravitreal device providing sustained release of cyclosporine and dexamethasone, Curr Eye Res 15:549–557, 1996.
149. Gilger BC, Malok E, Stewart T, et al: Long-term effect on the equine eye of an intravitreal device used for sustained release of cyclosporine A, Vet Ophthalmol 3:105–110, 2000.
150. Kulkarni P: Review: uveitis and immunosuppressive drugs, J Ocul Pharmacol Ther 17:181–187, 2001.
151. Sakurai E, Nozaki M, Okabe K, et al: Scleral plug of biodegradable polymers containing tacrolimus (FK506) for experimental uveitis, Invest Ophthalmol Vis Sci 44:4845–4852, 2003.
152. Douglas LC, Yi NY, Davis JL, et al: Ocular toxicity and distribution of subconjunctival and intravitreal rapamycin in horses, J Vet Pharmacol Ther 31:511–516, 2008.
153. Diamond J, Kaplan H: Lensectomy and vitrectomy for complicated cataract secondary to uveitis, Arch Ophthalmol 96:1798–1804, 1978.
154. Diamond J, Kaplan H: Uveitis: effect of vitrectomy combined with lensectomy, Ophthalmology ;86:1320–1329, 1979.
155. Binder S, Freyler H: Vitrektomie bei entzundlichen Erkrankungen des hinteren Augenabschnittes, Klin Monbl Augenheilkd 183:1983.
156. Kloti R: Pars-plana Vitrektomie bei chronischer Uveitis, Klin Monbl Augenheilkd 192:425–429, 1988.
157. Scott R: Vitreous surgery in the management of chronic endogenous posterior uveitis, Eye 17:221–227, 2003.
158. Kaplan H, Diamond J, Brown S: Vitrectomy in experimental uveitis. I. Operative technique in rabbits, Arch Ophthalmol 97:331–335, 1979.
159. Kaplan H, Diamond J, Brown S: Vitrectomy in experimental uveitis. II. Method in eyes with protein-induced uveitis, Arch Ophthalmol 97:336–339, 1979.
160. Werry H, Gerhards H: Moglichkeiten der und indikationen zur chirurgishen behandlung der euinen rezidivierenden uveitis (ERU), Pferdeheilkunde 7:321–331, 1991.
161. Fruhauf B, Ohnesorge B, Deegen E, et al: Surgical management of equine recurrent uveitis with single port pars plana vitrectomy, Vet Ophthalmol 1:137–151, 1998.
162. Gilger B, Spiess B: Surgical management of equine recurrent uveitis. In Stick J, Auer J, editors: Equine surgery. Philadelphia, 2006, WB Saunders, pp 749–755.
163. Tömördy E: Verlaufsstudie der Vitrektomie bei equiner rezidivierender Uveitis, Vetsuisse Faculty 93:2009.
164. Winterberg A: Langzeitergebnisse der Pars-plana-Vitrektomie bei equiner rezidivierender Uveitis, Chirurgische Tierklinik, München, 1997, Universität München; pp 142.
165. Dick AD: Understanding uveitis through the eyes of a horse: relevance of models of ocular inflammation to human disease, Ocul Immunol Inflamm 6:211–214, 1998.

Chapter 9

Glaucoma

Mary E. Utter
Dennis E. Brooks

Glaucoma is a disorder of aqueous humor outflow that results in phases of elevated intraocular pressure (IOP). It is a common but poorly understood eye disease of horses and is related in many aspects to equine recurrent uveitis (ERU). In this chapter, the clinical signs, pathogenesis, and therapy of equine glaucoma are discussed.

CLINICAL ANATOMY AND PHYSIOLOGY

AQUEOUS HUMOR PRODUCTION AND OUTFLOW

Aqueous humor provides nutrition to the avascular cornea, trabecular meshworks, and lens. Knowledge of aqueous humor formation and the structure of the aqueous humor drainage apparatus are critical to understanding glaucoma in horses. Aqueous humor is formed primarily by active secretion through the ciliary body epithelia into the posterior chamber, utilizing energy and the enzyme, carbonic anhydrase (see Chapter 6, Diseases of the Uvea, for more information). A small portion of aqueous humor production arises from ultrafiltration of blood in the ciliary body circulation. Aqueous humor then flows through the pupil into the anterior chamber and finally exits through the highly specialized tissues of the iridocorneal angle (ICA)—the conventional outflow pathway—or through the more primitive outflow pathways of the iris, ciliary body, and sclera—the unconventional outflow pathway. The ICA or ciliary cleft is bordered anteriorly by the peripheral cornea and perilimbal sclera and posteriorly by the peripheral iris and ciliary body. Stout pectinate ligaments separate the anterior chamber from the ICA in the equine eye, and these are visible at the limbus in many horses.[1-3]

Aqueous humor flows between the pectinate ligaments into and through the cell-lined trabecular beams of the uveal trabecular meshwork (UTM), the corneoscleral trabecular meshwork (CSTM), the angular aqueous plexus (AAP), and then the intrascleral plexus (ISP) in the conventional outflow pathway (Figs. 9-1 and 9-2). The aqueous humor then drains from the ISP into the vortex veins that empty into the choroid. The UTM, CSTM, and AAP compose 74.3%, 21.5%, and 4.2% of the equine ICA area, respectively.[1-3]

Resistance to outflow is focused at the AAP and ISP in the conventional outflow system of the horse. The intertrabecular spaces of the UTM are very wide, and the spaces of the CSTM are very narrow. The CSTM acts as a sieve or filter for large particles, but it may or may not restrict aqueous flow directly. The AAP is a plexus of radially oriented, narrow-diameter vessels. The ISP consists of an extensive network of anastomosing circumferential channels that drain aqueous humor to the vortex venous system (Fig. 9-3). The ISP and vortex systems have a rich collateralization. Aqueous humor thus follows a path of low resistance in the UTM and CSTM, high resistance to outflow in the narrow tributaries of the AAP and ISP, and low resistance to outflow again in the vortex systems.[1-3]

Microsphere perfusion studies have shown the suprachoroidal and supraciliary spaces provide an extensive unconventional outflow pathway to the sclera and choroid in the horse (Fig. 9-4). The intertrabecular spaces of the equine ICA provide a large area of aqueous humor contact with the iris and ciliary body. Aqueous humor can enter the anterior iris face to drain into the vortex veins, and it also leaves the UTM through the interstitial spaces of the ciliary body musculature to drain into the supraciliary and suprachoroidal spaces and choroid.[1-3]

RETINAL GANGLION CELLS

The horse has a very large retinal sensory surface area, vast numbers of photoreceptors, a massive population of retinal ganglion cells (RGCs) with large cell bodies, a large optic disc area and optic nerve cross-sectional area (15.7 mm^2 versus

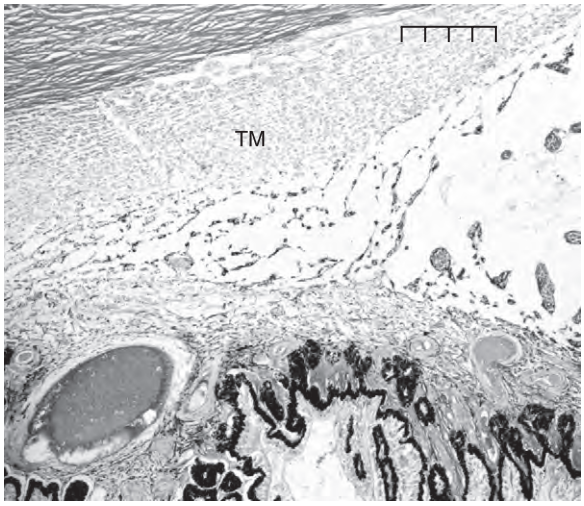


Figure 9-1. The trabecular meshworks (TM) of the iridocorneal angle of the horse are very large, wide, and open for the conventional outflow of aqueous humor (periodic acid-Schiff stain; bar = 70 mm).

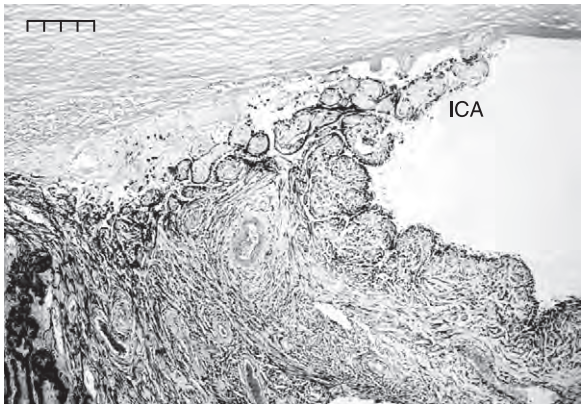


Figure 9-2. The iridocorneal angle (ICA) and trabecular meshworks of this horse with glaucoma have collapsed (periodic acid-Schiff stain; bar = 80 mm).

Figure 9-3. This vascular cast of an equine eye reveals the tremendous plexiform nature of the intrascleral plexus (ISP) and its extensive connections to the posterior vortex veins (VV) (bar = 330 mm).

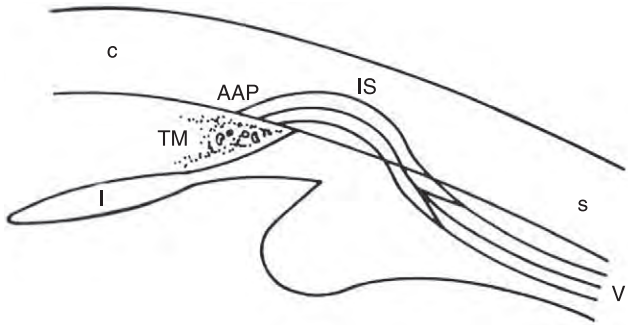


Figure 9-4. Aqueous humor outflow pathways in the horse. Aqueous humor moves through the trabecular meshworks (TM), to the angular aqueous plexus (AAP), to the intrascleral plexus (IS), and then drains into the vortex veins. The lumen diameter of the vessels through which the aqueous humor passes increases along the path.

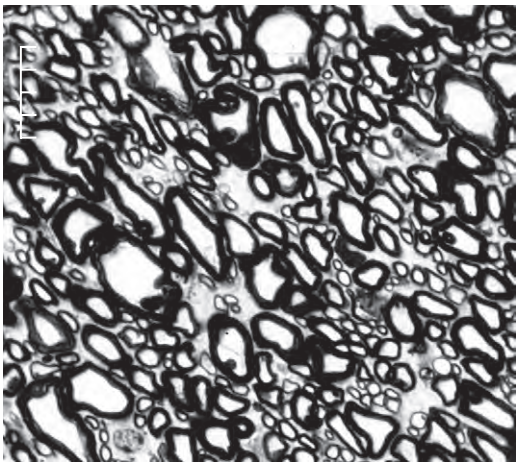


Figure 9-5. Large myelinated axons predominate in the optic nerve of the healthy horse (toluidine blue stain; bar = 2 mm).

5.17 mm^2 in humans), high total optic nerve axon counts (1.076 × 106 versus 1.159 × 106 in humans), large mean individual optic nerve axon cross-sectional areas (3.11 mm^2 versus 1.75 mm^2 in humans), and 4.4 times the percentage of optic nerve axons larger than 2 mm in diameter compared with humans (35.5% in horses versus 8% in humans).[4] The comparatively low density of axons in the horse optic nerve (62,800 axons/mm^2 in horses versus 175,000 axons/mm^2 in humans) undoubtedly reflects a low tissue density of RGCs, because the ratio of ganglion cells to optic nerve axons is 1:1 (Figs. 9-5 and 9-6). The marked proportion of large-diameter ganglion cells in the horse retina may be an adaptation to cover a large retinal sensory surface area with a relatively low population density of ganglion cells.[4]

OPTIC NERVE AND OPTIC NERVE HEAD CUPPING

RGC axons of the retinal nerve fiber layer become arranged into optic nerve fiber bundles by astrocytes in the choroidal lamina cribrosa. The scleral lamina cribrosa is a specialized extracellular matrix of the central nervous system that spans the scleral canal as a complex, multilayered set of collagenous plates (Fig. 9-7).[5] The multiple plates of the scleral lamina

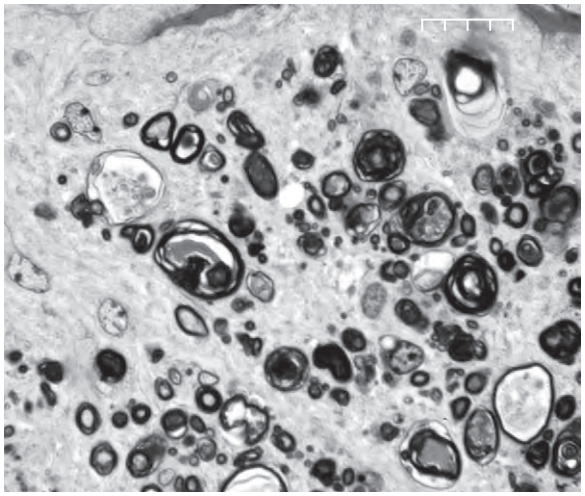


Figure 9-6. Few axons remain in the optic nerve of a horse with chronic glaucoma. (toluidine blue stain; bar = 2 mm).

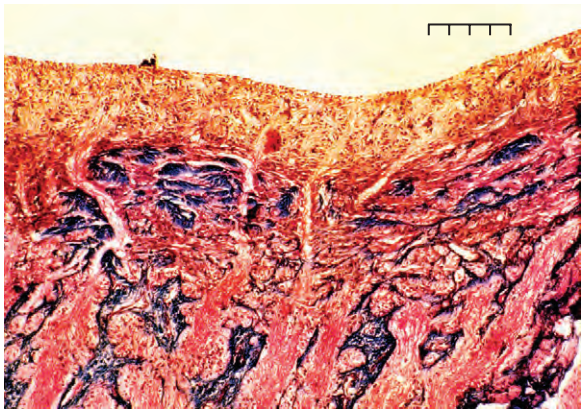


Figure 9-7. This histologic section of an equine optic nerve has the neural axon bundles *(pink)* passing through the plates of the scleral lamina cribrosa (collagen is *blue*) (Gomori's trichrome stain; bar = 2.3 mm).

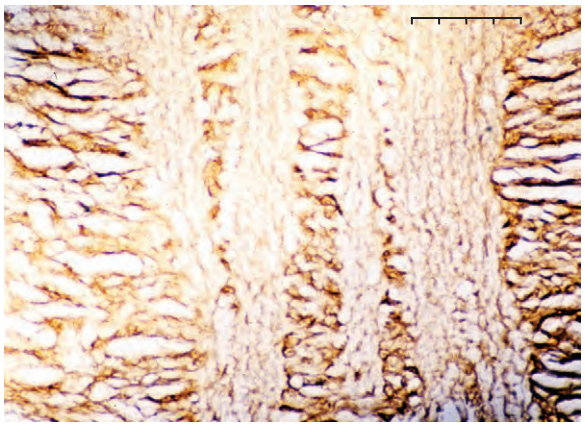


Figure 9-8. The laminar beams of the horse lamina cribrosa stain for collagen type I in this histologic section (bar = 15 mm).

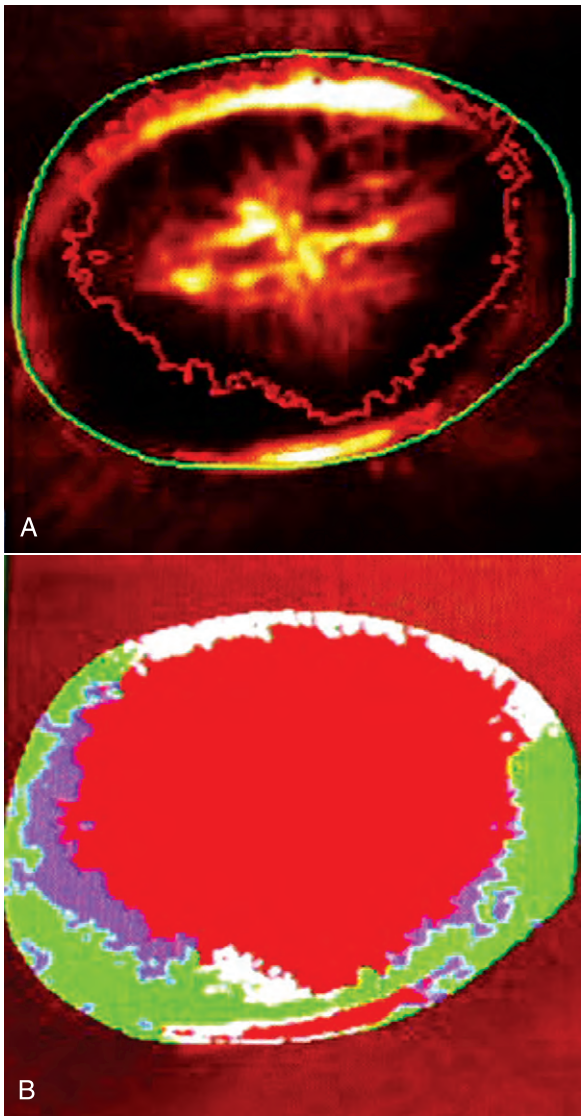


Figure 9-9. Scanning laser tomography of the oval optic nerve head (ONH) of this healthy horse consists of a confocal laser tomographic, extended focus, reflectance/intensity image **(A)** and a stereometric topography analysis image in pseudocolor **(B).** Red indicates areas below the retinal surface, and green, areas above the retinal surface. White areas are caused by irregularities in the disc surface. Note posterior excavation of neuroretinal rim at the 6 o'clock position. Scanning laser tomographic measurements indicate that the equine neuroretinal rim area is smallest at the superior and inferior rims and largest at the nasal and temporal rims. Disc area is 17.6 mm^2, cup area is 14.6 mm^2, and cup-to-disc area ratio is 0.83 in this horse.

cribrosa contain a hydrodynamic extracellular matrix of elastic and collagen fibers (types I, III, and VI), astrocytes, and capillaries (Fig. 9-8).

The prelaminar optic nerve is known as the optic disc, optic nerve head (ONH), or optic papilla and is surrounded by the white peripapillary scleral ring of Elschnig noted at the 6 o'clock position in the horse ONH. Myelin extends anterior to the equine lamina cribrosa to cover the surface of the optic disc. The myelinated axons generally stop at the edge of the scleral canal, although myelinated axons in the retinal nerve fiber layer are noted in the horizontal retinal quadrants of some horses. Scanning laser ophthalmoscopy of the equine ONH indicates that the neuroretinal rim area is smallest at the superior and inferior rims of the horse optic disc and larger at the nasal and temporal rims (Fig. 9-9). The intrapapillary region of the ONH

is the area inside Bruch's membrane at the scleral canal and consists of the neuroretinal rim and the optic cup (Figs. 9-10 and 9-11).

ONH cup enlargement or "cupping" is associated with advanced glaucoma in the horse (Fig. 9-12) and occurs as a result of axonal loss, laminar plate compression (Fig. 9-13), rotation of the scleral insertion zone posteriorly, outward bowing of the lamina cribrosa, and a widening of the scleral canal behind Bruch's membrane. The associated enlargement of the ONH cup with these laminar and axonal changes is unique to glaucoma and not found in other optic neuropathies. The ratio of the cup-to-disc area is used to evaluate progression of glaucomatous optic nerve damage in humans. Enlargement of the cup-to-disc ratio indicates optic nerve axonal loss and is associated with deterioration in visual fields.

The intralaminar optic nerve of horses with glaucoma contains a significantly larger total number of laminar pores, pores of significantly smaller individual area, and pores that are rounder than those in the intralaminar optic nerve of healthy horses.[5] The intralaminar optic nerves of horses with glaucoma contain a higher percentage of connective tissue (74%) than the optic nerves of healthy horses (67%). These differences may represent an anatomic variation found in horses predisposed to develop glaucoma, as well as changes resulting from IOP-induced radial stress forces causing stretching of the scleral lamina cribrosa.

The scleral lamina cribrosa is a transition zone of high to low hydrostatic tissue pressure caused by the prominent pressure gradient formed by the IOP and intraorbital pressure. The axoplasmic flow in the optic nerve axons is subjected to this abrupt change in tissue pressure.[6] The elevated IOP found in glaucoma exacerbates this pressure gradient and is associated with posterior displacement of the lamina cribrosa and disruption of optic nerve axon axoplasmic flow (see Figs. 9-11, 9-12, and 9-13). Disruption of axoplasmic flow may be exacerbated by the sharp edge of Bruch's membrane at the edge of the scleral canal. The lamina cribrosa is thus an active and compliant structure in the horse; its movement during normal and abnormal fluctuations in IOP can both protect and obstruct optic nerve axoplasmic flow.[5]

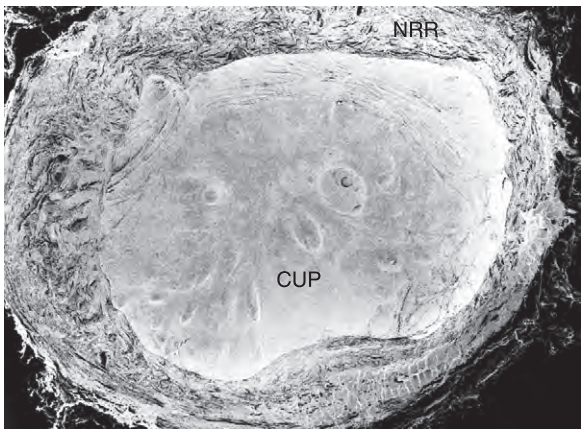


Figure 9-10. The prelaminar optic nerve is known as the *optic disc*, *optic nerve head* (ONH), or *optic papilla*. The equine ONH is oval, with the horizontal axis longer. The intrapapillary region of the ONH consists of the narrow neuroretinal rim (NRR) and the large central optic cup. This scanning electron micrograph illustrates the NRR and optic cup (CUP).

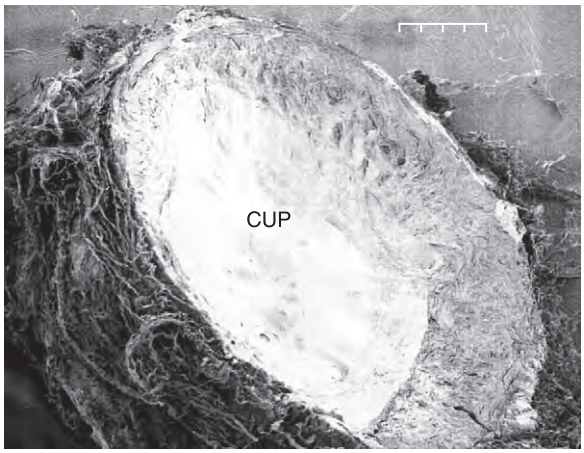


Figure 9-12. This scanning electron micrograph demonstrates optic nerve head cup (CUP) enlargement associated with advanced glaucoma in the horse. Optic nerve "cupping" occurs as a result of axonal loss, laminar plate compression, and posterior bowing of the lamina cribrosa. The neuroretinal rim narrows because retinal ganglion cells and axons are lost in glaucoma. The ratio of the cup-to-disc area is used to evaluate progression of glaucomatous optic nerve damage (bar = 690 mm.)

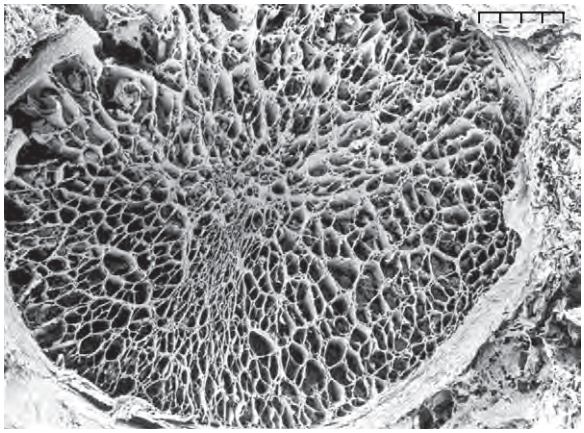


Figure 9-11. This trypsin digest of the scleral lamina cribrosa of a horse reveals the many laminar pores through which optic nerve axon bundles exit the eye to go to the brain (bar = 690 mm).

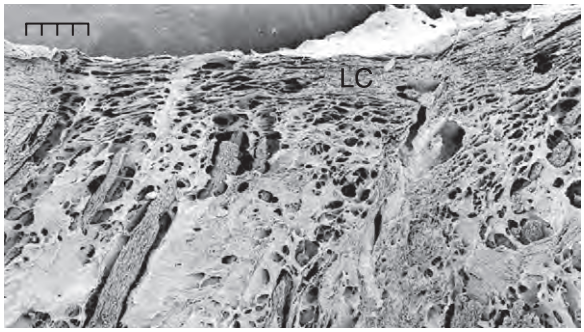


Figure 9-13. Glaucoma causes compression of the anterior laminar beams of the lamina cribrosa (LC) in this trypsin digest of the optic nerve head of a horse with glaucoma (bar = 500 mm).

INTRAOCULAR PRESSURE

The balance between the rate of production and the rate of exit of aqueous humor from the eye results in the tissue pressure of the eye, the IOP. Obstruction to the outflow of aqueous humor causes an elevation in IOP, and persistent IOP elevation reduces blood flow in the eye and induces degeneration of optical and neural structures. If RGC death occurs, this elevation in IOP is termed *glaucoma*. Elevation in IOP with no detectable loss of RGCs is called *ocular hypertension*.

IOP measured with a Tono-Pen applanation tonometer (Reichert, Inc, Depew, NY) in normal horses had a mean of 23.3 ± 6.9 mm Hg with a range from 7 to 37 mm Hg in one study (Fig. 9-14).[7] Other studies have identified a similar normal range.[8-11] Rebound tonometers appear to provide accurate estimate of IOP in horses, although values tend to be 1 mm Hg higher with the rebound compared to the applanation tonometer (Fig. 9-15).[11] The TonoVet rebound tonometer (Icare Finland OY, Helsinki, Finland) may be easier to use in horses than the Tono-Pen applanation tonometer. No topical anesthetic is needed with the TonoVet, and the TonoVet instrument is held quietly relative to the Tono-Pen (Fig. 9-16).

A consistent technique for measuring IOP should be utilized in the horse. The IOP should be measured with the same amount of sedation, the use of a motor lid nerve block, touching the same area of the cornea, by the same person, and at the same time of day. Failure to use auriculopalpebral nerve blocks during tonometry may result in slight overestimates of IOP and is recommended in most horses but especially fractious ones. Horses who require sedation for ocular examination may show dramatic decreases in IOP, as illustrated by a study in which xylazine decreased IOP by 23% to 27%.[12] Head position effects IOP in horses such that IOP is increased when measured with the head below the heart, as with heavy sedation.[13] Head position should be consistent between consecutive IOP measurements to prevent variation in IOP caused by head position alone. Although the horse does not seem to experience significant diurnal changes in IOP, in one study the IOP in the afternoon was slightly higher than the IOP in the morning.[12] Horses appear more tolerant of ocular hypertension than other species. Some anecdotal reports indicate that IOP can remain high (>50 mm Hg) for several days and horses can retain vision, unlike dogs and other species. See Chapter 1 for more information regarding tonometry and tonography in the horse.

PATHOPHYSIOLOGY OF GLAUCOMA

Pathologic elevation of IOP is always an outflow obstructive phenomenon. Physical obstruction of the aqueous humor outflow pathways can occur as result of contraction of pre-iridal postinflammatory membranes, obstruction of the ICA with inflammatory debris, and posterior synechia causing pupillary block, iris bombe, and trabecular compression and angle closure.[14] Postinflammatory uveal atrophy may predispose the

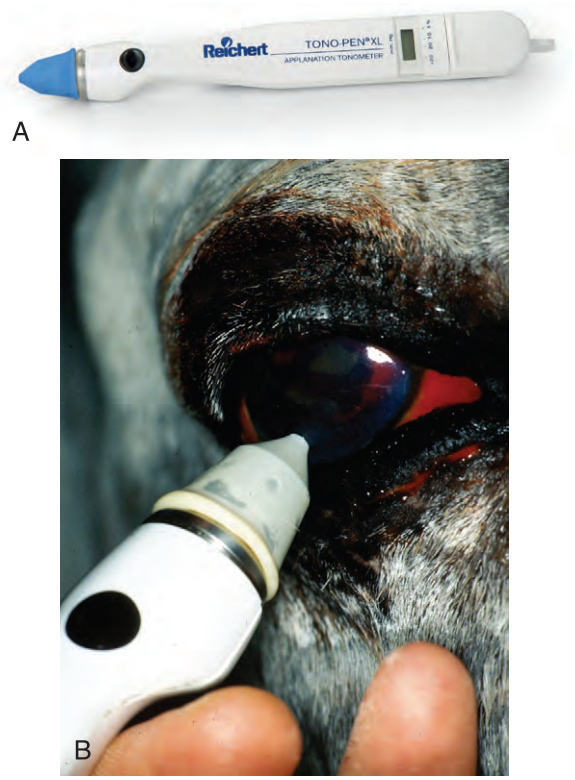


Figure 9-14. The Tono-Pen applanation tonometer is necessary for the diagnosis of elevated intraocular pressure (IOP) and serial measurements of IOP in response to therapy. **A,** Tono-Pen XL tonometer. **B,** Tono-Pen tonometer in use on a horse. (**A,** Courtesy Reichert Technologies, Depew, New York.)

Figure 9-15. TonoVet rebound tonometer can provide an accurate estimate of IOP in horses.

Figure 9-16. TonoVet rebound tonometer does not require topical anesthetic and involves less instrument movement near the eye.

ICA to collapse. Anterior lens luxation and vitreal prolapse appear common in Appaloosas and Rocky Mountain horses and may obstruct the pupil or the ICA. ICA obstruction by melanoma or other tumor cells can also occur.[14,15] Infectious endophthalmitis can cause secondary glaucoma.

IOP-induced compressive conformational distortion within the scleral lamina cribrosa in glaucoma results in rotation, misalignment, and collapse of the laminar pores and laminar channels such that optic nerve axoplasmic flow is reduced and eventually blocked to cause RGC death. Glaucoma in the horse results in extensive and diffuse optic nerve damage, and the optic nerve axon density in horses with glaucoma is reduced by 65%.[4] Gliosis is dramatic, with primarily glial cells remaining in the severely atrophied optic nerves. The median individual optic nerve axon cross-sectional areas were smaller in glaucomatous eyes than in normal eyes (1.60 mm^2 versus 1.35 mm^2), indicating that horses with glaucoma lose optic nerve axons of large individual cross-sectional area more rapidly than medium- and small-sized axons.[4] Axons of all sizes are eventually injured by elevated IOP, but some RGCs and their axons appear to be IOP resistant; vision can often be retained for substantial periods in horses, despite extreme elevations in IOP.

DIAGNOSIS AND CLINICAL SIGNS OF GLAUCOMA

TYPES OF GLAUCOMA

The glaucomas are a group of diseases resulting from reductions in aqueous humor outflow that cause an IOP increase above that which is compatible with normal function of the retina and optic nerve. All glaucomas consist of five stages: (1) an initial event or series of events that progressively reduce function of the aqueous humor outflow system, (2) morphologic alterations of the aqueous outflow system that eventually lead to obstruction of aqueous humor outflow and IOP elevation, (3) elevated IOP that is too high for normal RGC and optic nerve axon function, (4) RGC and optic nerve axon degeneration, and (5) progressive visual deterioration that eventually leads to blindness.[16]

True glaucoma was once thought to be a variant of ERU and an uncommon ocular problem in horses. Glaucoma is still an infrequently diagnosed disease in the horse. This is due in part to the limited availability of tonometers in equine practice but also to the fact that diurnal fluctuations in IOP, even in chronic ERU cases, may make documentation of elevated IOP difficult. Equine glaucoma may not be easily recognized in the early stages of the disease because of the subtle nature of the clinical signs. This may be explained by the prominent role of uveoscleral aqueous humor outflow in the horse, which may be higher than that in other species, and by microanatomic differences in the aqueous humor outflow pathways in horses compared with those in other species.[1-3]

Equine glaucoma is frequently categorized into primary, secondary, and congenital types. The terms may not be completely relevant, because all glaucomas are secondary to some causative mechanism. Primary glaucomas have a bilateral and heritable potential, have no overt ocular abnormality to account for the increase in IOP, and have not been conclusively reported in the horse. Secondary glaucomas in horses have an identifiable cause such as iridocyclitis, lens luxation, or intraocular neoplasia. Iris and ciliary body neoplasms can obstruct aqueous humor outflow to cause secondary glaucoma. Congenital glaucoma caused by developmental anomalies of the ICA (goniodysgenesis) has been reported in foals (Box 9-1).[17,18]

Horses with active or quiescent uveitis, aged horses (>15 years old), and Appaloosas are at increased risk for the development of glaucoma. Glaucoma has also been reported in the American paint, Standardbred, Morgan, Trakehner, Percheron, mule, Paso Fino, Quarter Horse, Tennessee Walking horse, Thoroughbred, Arabian, pony (Americas, Connemara, Shetland), American Saddlebred, and Warmbloods.[4,6,8,15,19] Congenital glaucoma has been reported in Thoroughbred, Arabian, and Standardbred foals.[17,18,20] Elevated IOP is clearly the primary risk factor for rapid progression of optic nerve damage and blindness in the horse, but iridocyclitis is the primary risk factor for development of glaucoma.[14,19,20]

DIAGNOSIS

The diagnosis of equine glaucoma is made with the documentation of elevated IOP and the presence of clinical signs specific to glaucoma (Table 9-1). The IOP in horses with glaucoma and horses with ERU does not remain consistently elevated; large, asynchronous, diurnal fluctuations in IOP can occur in diseased globes.[19] Frequent tonometric IOP measurements during the

Box 9-1 | Types of Equine Glaucoma and Causes

Primary

Possibly heritable

Secondary

Severe iridocyclitis
Lens luxation
Intraocular neoplasia
Intraocular infection

Congenital

Goniodysgenesis

Table 9-1 | Clinical Signs of Glaucoma

SIGN	ACUTE/ACTIVE GLAUCOMA	CHRONIC GLAUCOMA
Corneal edema	Typically mild	May be permanent, severe
Corneal band opacities	May see	Often see
Aqueous flare	May be present	Inconsistent
Pupil	Mydriasis	Extensive synechia
Iridocyclitis	Often concurrent	May be "quiet"
Lens	May see subluxation	May see luxation, often posterior
Posterior segment changes	Not typical	Optic nerve atrophy, lamina cribrosa exposed
Blepharospasm	Mild to severe	Not typical
Hydrophthalmos	Not typical	Typical
Blindness	Not typical	Typical

day may be necessary to initially detect transient acute IOP elevation (i.e., "spikes"). This wide variation in IOP not only interferes with the diagnosis of glaucoma but also complicates monitoring the response to therapy. The IOP will eventually decrease in enlarged globes as the ciliary body atrophies. Once elevated IOP is detected, subsequent IOP measurements should be evaluated at the same time of day.

Equine glaucoma may not be easily recognized in the early stages of the disease because of the subtle initial clinical signs. Veterinarians generally have a low index of suspicion of glaucoma in horses with eye problems, because the pupils are often only slightly dilated and overt discomfort is uncommon. The predominant clinical sign may be partial or complete corneal edema. The iridocorneal angles should be routinely examined for alterations in width and degree of obstruction (Fig. 9-17). Afferent pupillary light reflex deficits, linear band opacities, mild generalized corneal edema (Fig. 9-18), decreased vision, lens luxations, mild iridocyclitis, and optic nerve atrophy/cupping may also be found in eyes of horses with glaucoma (see Table 9-1). Vertical corneal edema may result from aqueous humor convection current irregularities and is a cardinal sign of early glaucoma in horses (Fig. 9-19). Linear *band opacities* are thinned areas of Descemet's membrane that resemble Haab striae but do not display the typical curling of the ruptured elastic basement membrane on histologic examination.[14] Band opacities in horses may be associated with edema in early stages and with fibrosis if glaucoma is chronic. They may also be found in normotensive eyes after traumatic corneal injury and in apparently "normal" eyes. Congenital glaucoma of foals may be bilateral. Corneal edema, corneal stria, mild hydrophthalmos (i.e., buphthalmos), lens luxation, lens coloboma, absent corpora nigra, iris hypoplasia, retinal degeneration, and optic nerve cupping may also be found (Figs. 9-20 to 9-34; see Figs. 9-18 and 9-19).[14,17,18,20] *Hydrophthalmos* refers to an unusually enlarged globe, which is associated with chronically increased intraocular pressure secondary to glau-

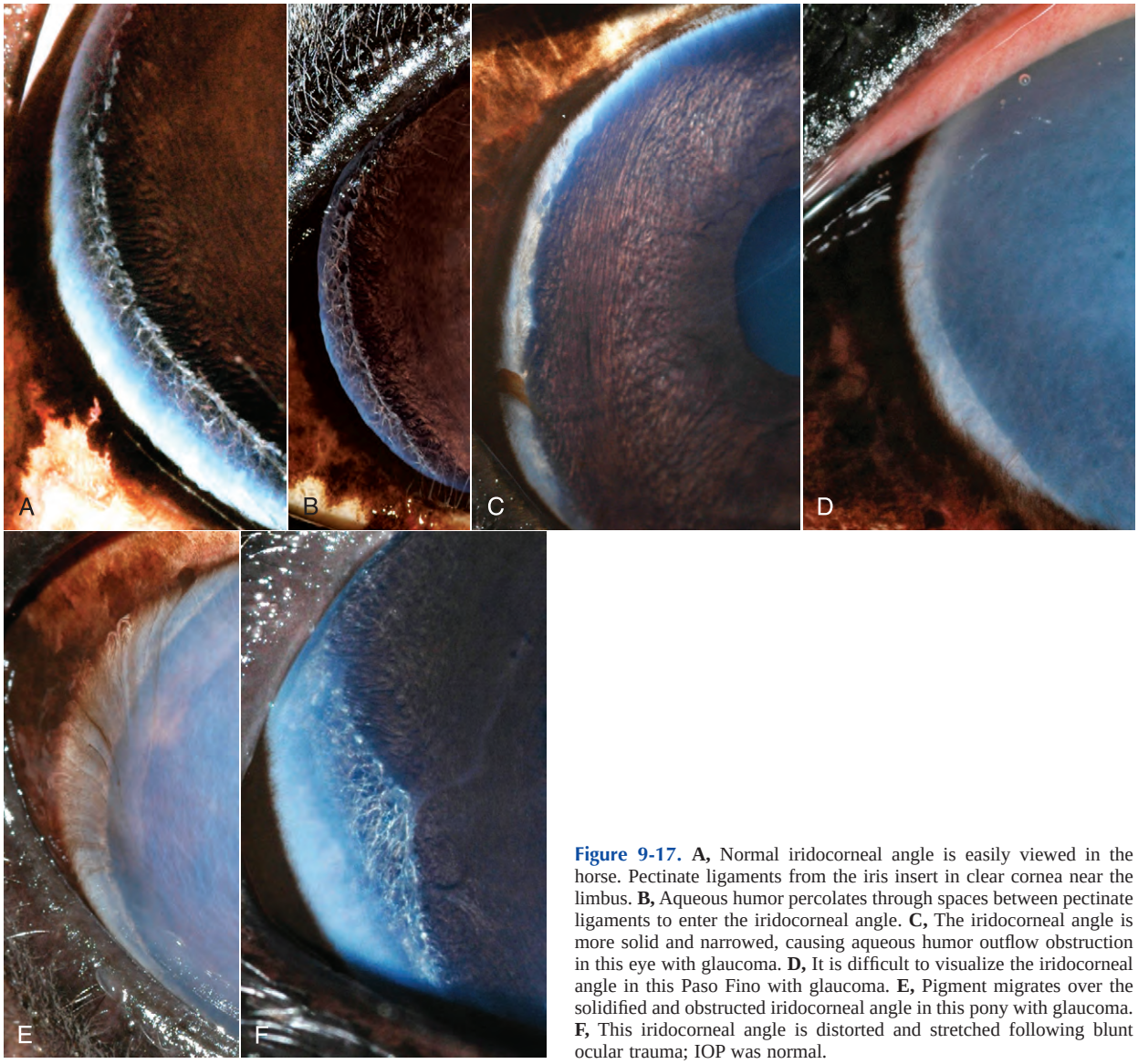


Figure 9-17. A, Normal iridocorneal angle is easily viewed in the horse. Pectinate ligaments from the iris insert in clear cornea near the limbus. **B,** Aqueous humor percolates through spaces between pectinate ligaments to enter the iridocorneal angle. **C,** The iridocorneal angle is more solid and narrowed, causing aqueous humor outflow obstruction in this eye with glaucoma. **D,** It is difficult to visualize the iridocorneal angle in this Paso Fino with glaucoma. **E,** Pigment migrates over the solidified and obstructed iridocorneal angle in this pony with glaucoma. **F,** This iridocorneal angle is distorted and stretched following blunt ocular trauma; IOP was normal.

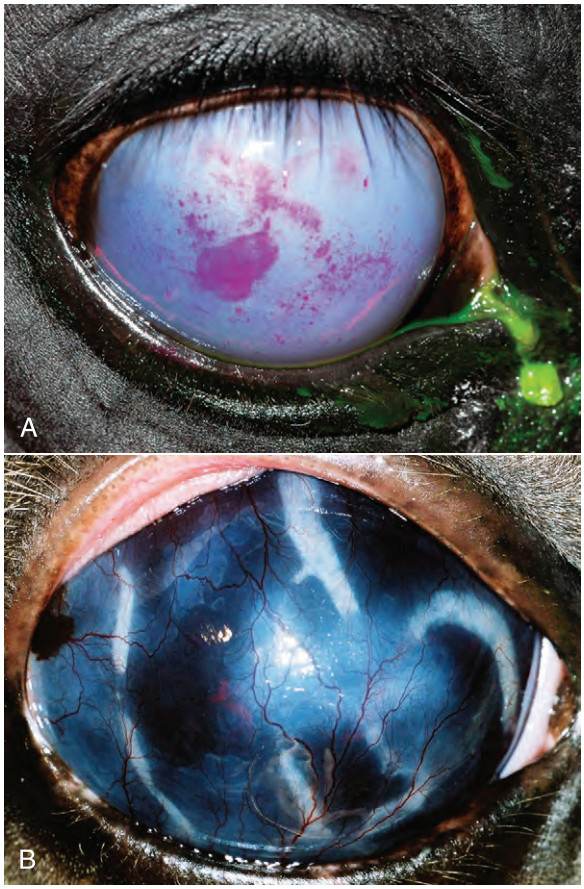


Figure 9-18. **A,** Rose bengal retention in a glaucoma eye following tonometry. The persistent corneal edema must prevent normal tear film adherence. **B,** Large band opacities and corneal edema with vascularization are present in this eye with chronic glaucoma.

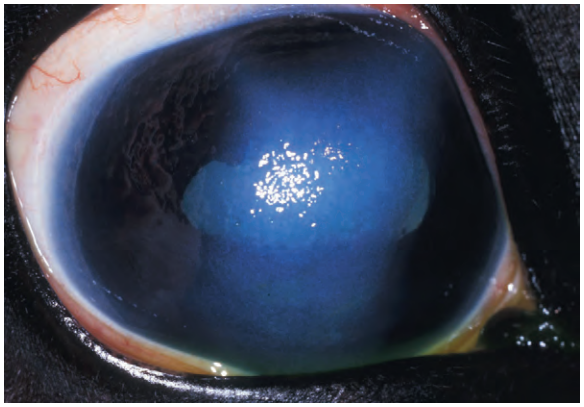


Figure 9-19. Vertical corneal edema is an early warning sign of glaucoma in the horse. This may result from abnormal aqueous humor convection currents.

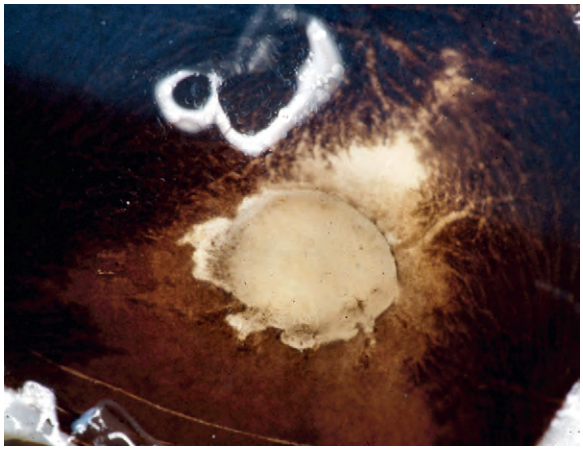


Figure 9-20. This tissue photograph is of a pale, glaucomatous optic nerve and nontapetal depigmentation in a horse.

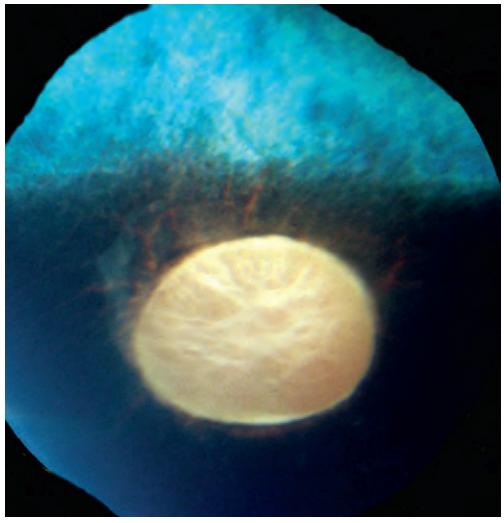


Figure 9-21. This fundus photograph shows optic nerve atrophy caused by glaucoma. The anterior lamina cribrosa is seen as reticulated lines caused by loss of myelin and axons.

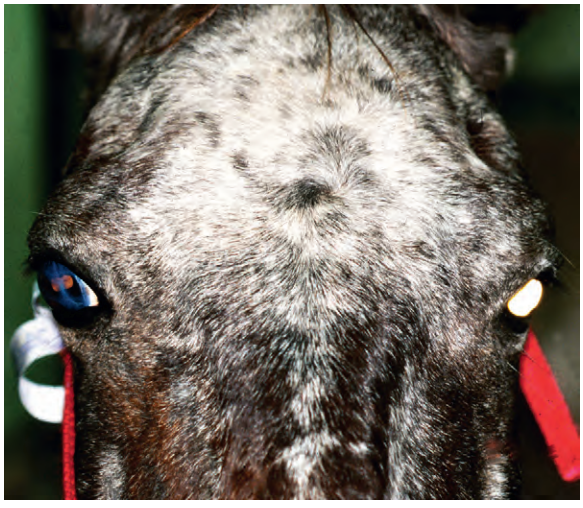


Figure 9-22. Striate keratopathy and slight hydrophthalmos are present in the right eye of this Appaloosa with glaucoma.

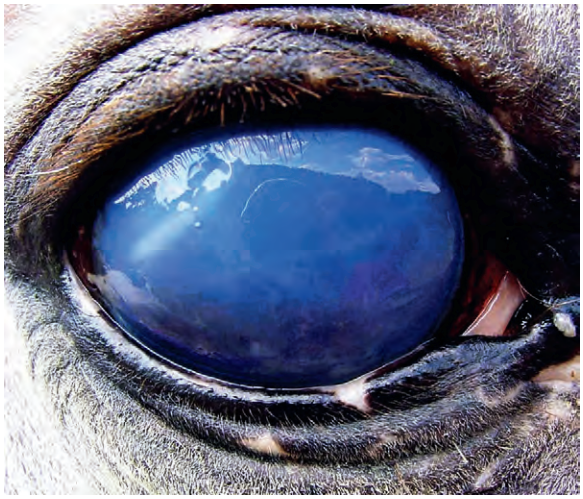


Figure 9-23. Generalized corneal edema is present in this glaucomatous equine eye.

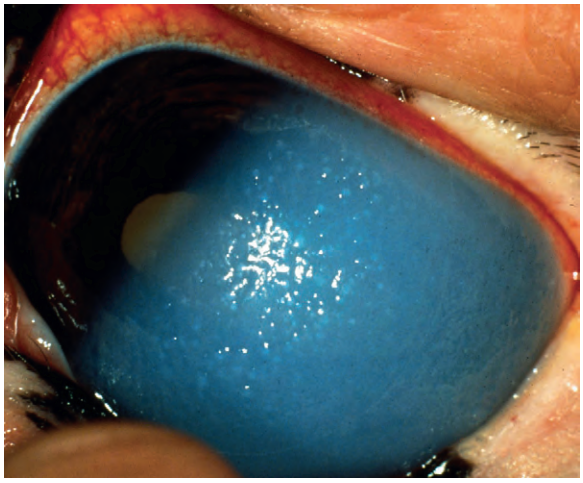


Figure 9-24. Bullous keratopathy from profound edema is present in this glaucomatous globe in a horse.

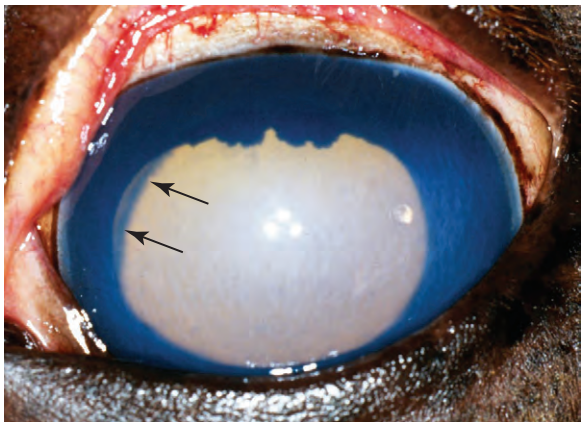


Figure 9-25. The pupil is dilated and the cornea slightly edematous in this Thoroughbred mare with an intraocular pressure of 80 mm Hg. An aphakic crescent is noted nasally *(arrows)*.

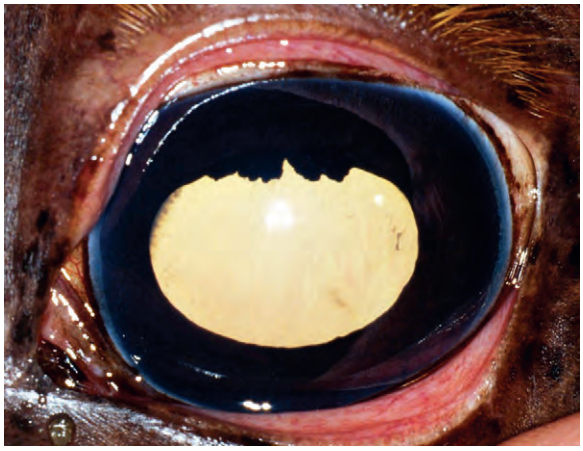


Figure 9-26. The intraocular pressure is 20 mm Hg 1 month after transscleral cyclophotocoagulation in the eye shown in Fig. 9-25.

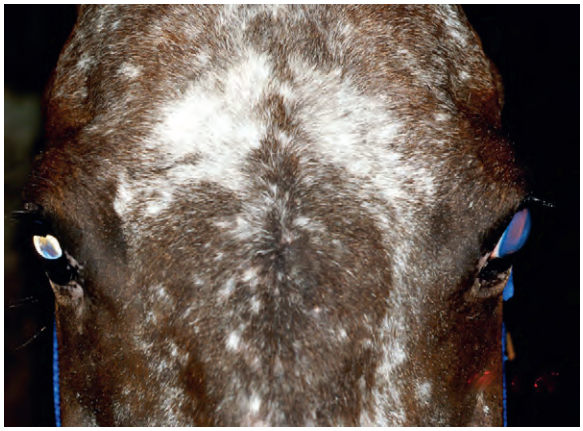


Figure 9-27. The intraocular pressure is 65 mm Hg, the pupil is fixed and dilated, and the cornea is edematous in this enlarged left eye of an Appaloosa mare.

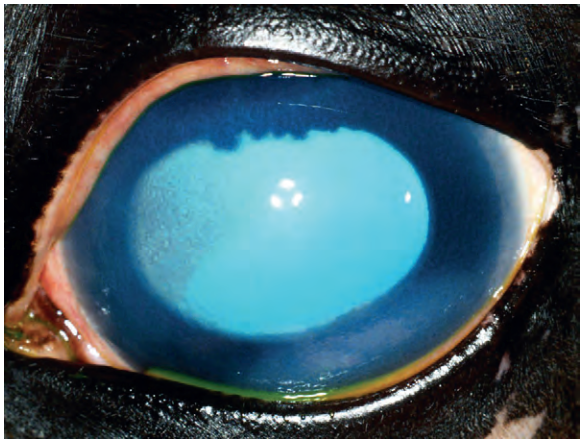


Figure 9-28. Close-up of the left eye shown in Fig. 9-27.

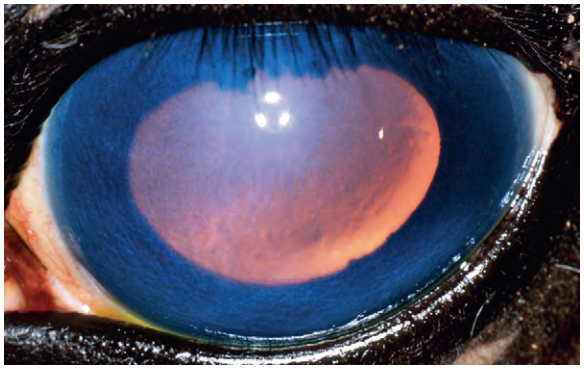


Figure 9-29. Elevated intraocular pressure, edema, and mydriasis persist 10 days after initiation of medical therapy in the horse from Fig. 9-27.

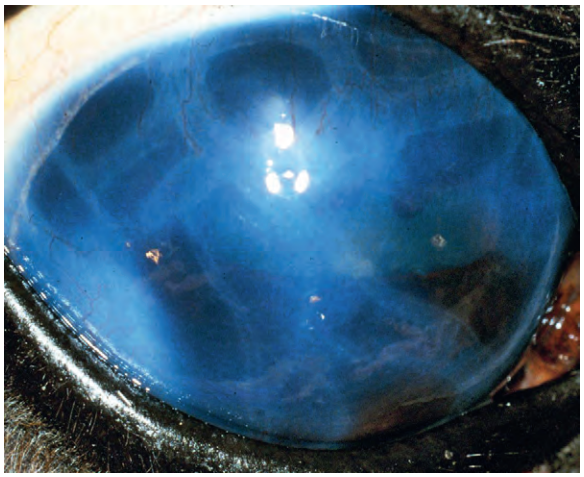


Figure 9-30. Large band opacities or striae are present in this glaucomatous equine eye.

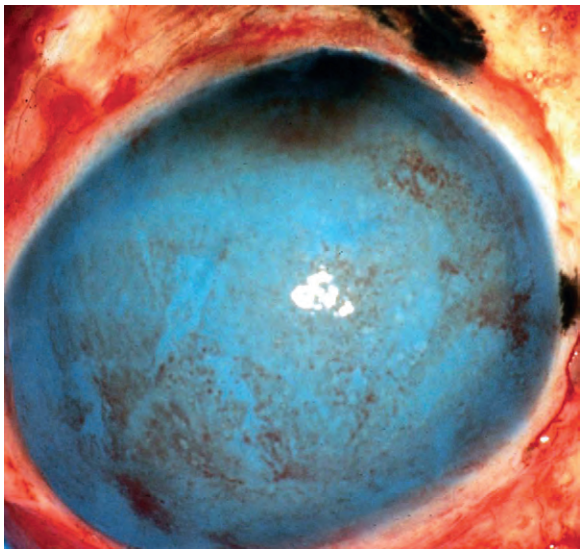


Figure 9-31. Pigmentation of the dorsal cornea and sclera and generalized corneal edema are found in an eye with glaucoma caused by an intraocular melanoma.

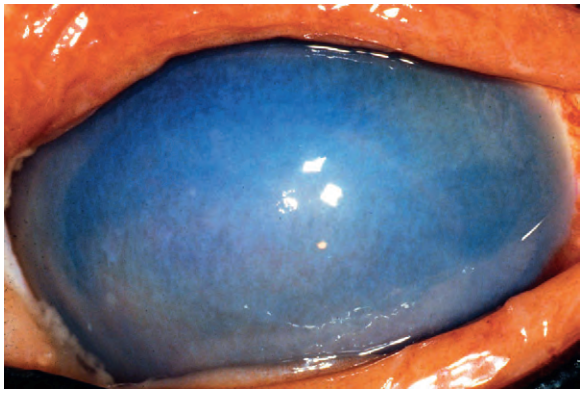


Figure 9-32. Generalized corneal edema and glaucoma are present in an eye that had some unknown "trauma."

Figure 9-33. Suppurative endophthalmitis from a gram-negative rod infection caused the glaucoma in the eye from Fig. 9-32.

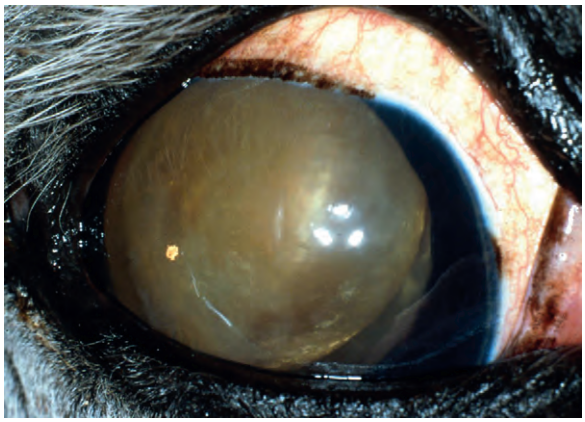


Figure 9-34. Anterior lens luxation and secondary glaucoma in a 21-year-old Arabian mare.

coma. Technically, the term *buphthalmos* indicates a globe typical of a bovine, which is generally smaller than that of the horse. *Hydrophthalmos* indicates that the globe is larger than on previous examinations and may be the preferred term in the horse.

Fixed and dilated pupils are observed in horses with glaucoma. Positive dazzle and menace reflexes may remain in many eyes with chronic glaucoma. The pupils may be miotic, and posterior synechia and iris bombe may be present in ERU cases. Some eyes may have subluxated or luxated lenses (see Fig. 9-25). ONH cupping/degeneration will be present in advanced

cases of equine glaucoma (see Figs. 9-19 and 9-21). Areas of retinal degeneration may be present in some cases (see Fig. 9-21). Hydrophthalmos, or buphthalmos, will occur in eyes with end-stage glaucoma (see Figs. 9-18 and 9-30), and enucleation may be necessary. Corneal edema and vascularization, blindness caused by optic nerve atrophy, and pain in some cases characterize chronic glaucoma in the horse. An ulcerative exposure keratitis may also develop.

Glaucoma in the horse results in early peripheral retinal and optic nerve damage with progression to generalized retinal and optic nerve atrophy (see Figs. 9-5 and 9-6). The equine eye seems to tolerate elevations in IOP that would quickly blind a dog, but blindness is eventually the result. The marked number of axons in the optic nerve of the horse may act as an anatomic reservoir of axons that provide some early protection against total loss of vision despite very high IOP. Some RGCs may actually be IOP resistant. Horses with glaucoma also appear to lose large optic nerve axons more rapidly than medium and small axons. Large RGCs are involved in motion detection, stereopsis, and sensitivity to dim light, but the consequences of the loss of such axons to the visual capabilities of the horse in early glaucoma are not known. The progressive sustained elevation in IOP found in equine glaucoma is still associated with optic nerve cupping, atrophy, and blindness (see Figs. 9-6, 9-17, and 9-18).

TREATMENT FOR GLAUCOMA

MEDICAL TREATMENT

The events and mechanisms that lead to obstruction of aqueous humor outflow and increased IOP in the horse are not well understood, which makes it very difficult to institute effective therapy. Medical management of equine glaucoma follows the same general guidelines as that for glaucoma in other species, with the aims of therapy being reduction of IOP and suppression of iridocyclitis (Table 9-2). The initial response to IOP-reducing medical therapy in early cases of equine glaucoma is usually good, but the long-term prognosis for maintaining vision with medical therapy alone is guarded. However, despite dramatically high IOP, partial vision may be retained for extended periods in some horses. Glaucoma is particularly aggressive and difficult to control in the Appaloosa.

The goals of therapy in glaucoma are to reduce IOP to levels compatible with the health of the retina and optic nerve by decreasing production of aqueous humor by the ciliary body and increasing outflow of aqueous humor through the conventional and unconventional outflow systems. Iridocyclitis must be vigorously suppressed if it is present. Various combinations of drugs and surgery may be needed to reduce IOP to selected target levels compatible with preservation of vision in horses with glaucoma. A target IOP of less than 20 mm Hg is a reasonable goal in the glaucomatous equine eye. Control of IOP can improve vision in horses with decreased vision through resolution of marked corneal edema and improvement of vascular perfusion.

Table 9-2 | **Topically Applied Medications for Equine Glaucoma**

MEDICATION	TYPE	DOSE
Timolol maleate 0.5%	β-Blocker	0.2 mL bid
Dorzolamide 2%*	CAI	0.2 mL bid
Prednisolone	Corticosteroid	0.2 mL tid acetate 1%

bid, Twice a day; *tid*, 3 times a day.
*Cosopt (combination of timolol and dorzolamide), Merck & Co., Whitehouse Station, NJ.

TOPICAL β-ADRENERGIC BLOCKER

The β-adrenergic blocker, timolol maleate (0.5%), was shown to decrease IOP in normal horses by 17% (4.2 mm Hg) with twice-daily topical administration.[21] β-Blockers interfere with the production of cyclic adenosine monophosphate by the enzyme adenylcyclase to reduce aqueous humor production. The maximum effect was in the afternoon and occurred 4.5 days after administration. A decrease in pupil size was observed in another study with normal horses, but there were no other adverse effects.[21] Experimental data from horses with glaucoma are not currently available.

TOPICAL OR ORAL CARBONIC ANHYDRASE INHIBITOR

Aqueous humor production can also be reduced if 99% of the carbonic anhydrase enzyme in the ciliary body is inhibited. The carbonic anhydrase inhibitor, dorzolamide (2%), alone or in combination with timolol maleate was effective in lowering IOP by 10% (2 mm Hg) when administered topically twice a day in normal horses.[22] Once-a-day use increased IOP in normal horses in another study.[21] Brinzolamide, a carbonic anhydrase inhibitor associated with fewer side effects in people, most likely due to a physiologic pH (relative to dorzolamide, which is acidic), has been shown to decrease IOP following once- and twice-daily topical administration of a 1% solution in normal horses.[23] Neither topical carbonic anhydrase inhibitor has been used in a controlled study with glaucomatous horses.

Acetazolamide, dichlorphenamide, and methazolamide are systemically administered carbonic anhydrase inhibitors that have been used to reduce IOP in other species, but the pharmacokinetics have been studied only for acetazolamide in horses. In horses, when acetazolamide is given orally, it is absorbed rapidly and has somewhat lower bioavailability, but it is eliminated more slowly than when it is administered intravenously.[24] Acetazolamide has been shown to reduce clinical signs of hyperkalemia in horses with hyperkalemic periodic paralysis when given at 4.4 mg/kg twice daily, but no studies have evaluated the effect of acetazolamide on IOP in either normal or glaucomatous horses. Administration of systemic carbonic anhydrase inhibitors should be accompanied by electrolyte supplementation because of presumed potassium loss.

TOPICAL DIRECT- AND INDIRECT-ACTING PARASYMPATHOMIMETIC DRUGS

Direct- and indirect-acting parasympathomimetic drugs increase the facility of aqueous outflow in many mammals by constricting the ciliary muscles to open the trabecular meshworks. These drugs also inhibit unconventional outflow. In a study with normal horses, pilocarpine did not decrease IOP, and actually trended toward increasing IOP after multiple twice-daily applications. Pilocarpine decreased vertical pupil size after multiple twice-daily applications.[9] Acetylcholinester-

ase inhibitors such as demecarium bromide have effects similar to those of pilocarpine. Demecarium bromide has been used in dogs with glaucoma to reduce intraocular pressure,[25] as well as to delay the onset of glaucoma in the second eye of dogs with primary closed-angle glaucoma.[26] The use of these drugs in horses with glaucoma has not been tested and is not recommended.

TOPICAL PROSTAGLANDIN ANALOGS

Prostaglandin analogs have revolutionized the treatment of glaucoma in dogs[27,28] but have not proven as promising for horses. Latanoprost (0.005%) is an analog of prostaglandin F2a that increases uveoscleral outflow and induces miosis. In one study, latanoprost had no effect on IOP or pupil size in the normal equine eye when administered once a day.[29] In another study, latanoprost lowered IOP by 1 mm Hg in geldings (5%) and 3 mm Hg in mares (17%), but it was associated with a high frequency of prostaglandin-induced adverse effects that included conjunctival hyperemia, epiphora, and blepharospasm.[30] Synthetic prostaglandins dramatically potentiate the clinical signs of uveitis and therefore should be used cautiously, if at all, in horses with glaucoma.

TOPICAL MYDRIATICS/ATROPINE

Atropine has been recommended as possible therapy for equine glaucoma.[2] It was once thought to reduce the incidence of glaucoma in horses with uveitis. However, atropine should be used cautiously in horses with glaucoma because it may cause acute IOP elevations and does not appear to have the benefit of lowering IOP as once proposed. Atropine administered once a day had no effect on IOP but caused mydriasis in one study.[31] In another study, atropine administered twice a day caused an 11% reduction in IOP in treated eyes of 10 horses and an increase in IOP in one horse.[32] Use of topically administered atropine for the specific purpose of IOP reduction is not recommended unless daily tonometric IOP measuring is available.

ANTIINFLAMMATORY THERAPY

Antiinflammatory therapy consisting of topically administered corticosteroids, such as prednisolone acetate, and systemically administered nonsteroidal antiinflammatory drugs (NSAIDs), such as phenylbutazone and flunixin meglumine, are beneficial in the control of the iridocyclitis that may be contributing to the elevation of IOP. Chronic use of systemic NSAIDs can be associated with complications such as kidney disease and right dorsal colitis; cautious use and close monitoring for clinical signs associated with these complications is essential.[33] A topical NSAID such as diclofenamic acid and systemically administered dexamethasone may also be used.

SURGICAL TREATMENT

When medical therapy is inadequate, surgery should be performed to control IOP and preserve vision in the horse with glaucoma (Table 9-3). Currently available surgical options for horses with a glaucomatous but still visual eye include laser cyclophotoablation and gonioimplant filtration. Cyclocryoablation, ciliary body ablation, placement of intrascleral prostheses, and enucleation are indicated for blind, chronically painful, and buphthalmic eyes.

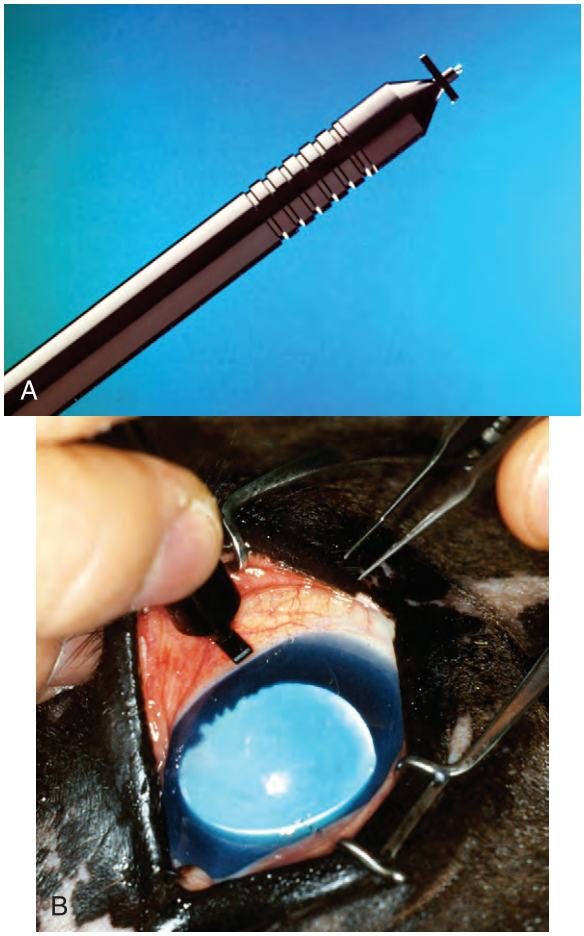


Figure 9-35. A diode laser is used for transscleral cyclophotocoagulation of the eye shown in Fig. 9-28.

Table 9-3 | **Surgical Interventions for Equine Glaucoma**

GOAL	SURGERY	MECHANISM
Preserve/restore vision	Transscleral cyclophotoablation (TSCP)	Reduce aqueous production
	Gonioimplant	Increase aqueous production
Control IOP, relieve pain	Chemical ciliary body ablation (gentamicin injection)	Reduce aqueous production
	Intrascleral prosthesis	Remove eye
	Enucleation	Remove eye

LASER CYCLOPHOTOCOAGULATION

When IOP cannot be controlled with medical therapy, neodymium-doped yttrium aluminum garnet (Nd:YAG) or diode laser cyclophotocoagulation or ablation may be a viable alternative for long-term IOP control (Fig. 9-35). Laser cyclophotoablation involves the use of laser energy to preferentially destroy the ciliary body epithelium and stroma of the pars plicata, thereby reducing aqueous humor production. Of the various laser sources available, the semiconductor diode laser has been used most commonly for cyclophotoablation in veterinary ophthalmology. The diode laser emits light with a wavelength of 810 nm, which interacts with melanin in pigmented tissues.

Contact transscleral laser cyclophotocoagulation (TSCP) has been shown to be effective in controlling IOP and maintaining vision in the horse (Figs. 9-36 to 9-38; see Fig. 9-35).[34,35] After Nd:YAG laser TSCP in the glaucomatous equine eye, a mean drop of 17 mm Hg can be expected during the first few days, with a decrease of 25 mm Hg at 20 weeks postoperatively. The settings for the Nd:YAG laser are 10 W, 0.4 seconds.[35] After diode laser cyclophotocoagulation, the IOP-lowering effects occur in 2 to 4 weeks. At least 40 to 60 sites, 4 to 6 mm posterior to the limbus (except nasally) should be targeted with the laser (Fig. 9-39). Accurate anatomic positioning of TSCP optimizes therapeutic outcomes. The settings for the diode laser are 1500 mW power, 1500 msec duration (2.25 J/site).[36,37] Too little laser energy (0.75 J/site) does not cause sufficient coagulative necrosis to the pars plicata, whereas too much laser energy (4 J/site) will cause too much collateral normal tissue damage.[37] The horse eye with glaucoma is very responsive to TSCP treatment, and this is the therapy of choice for long-term IOP control.

Uveitis and corneal edema will increase initially after TSCP. Medical therapy must be maintained until the iridocyclitis is reduced and the IOP diminished after laser cyclophotocoagulation. Laser therapy should not be performed until any uveitis or corneal edema present is controlled with corticosteroids. The corneal edema of the horse with glaucoma may be the result of uveitis rather than increased IOP, and this corneal edema may become permanent after laser cyclophotocoagulation as a result of increased post-laser damage to the corneal endothelium. Superficial corneal ulcers may develop as a result of corneal desensitization from the TSCP or exposure during the procedure.

Endoscopic cyclophotocoagulation (ECP) has been used with increasing success to control refractory glaucoma in humans[38] and dogs.[39,40] We have used ECP to treat horses with glaucoma (Figs. 9-40 to 9-43). With this procedure, an endoscopic system is used to provide a direct view of the ciliary processes, the target of cyclophotocoagulation, thereby mini-

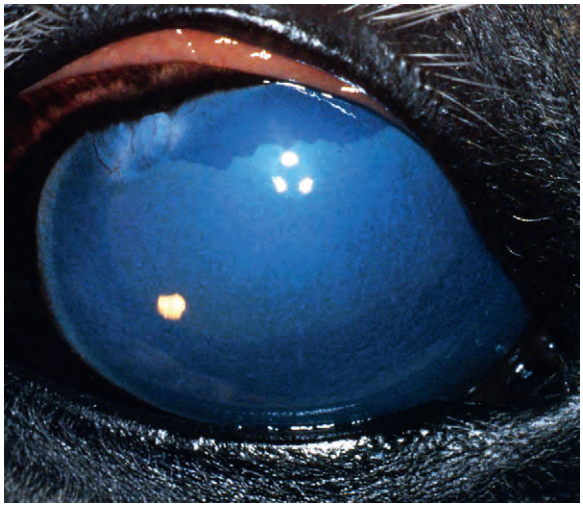


Figure 9-36. Generalized corneal edema and mydriasis are present in the glaucomatous eye of a Paso Fino stallion. Intraocular pressure is 55 mm Hg.

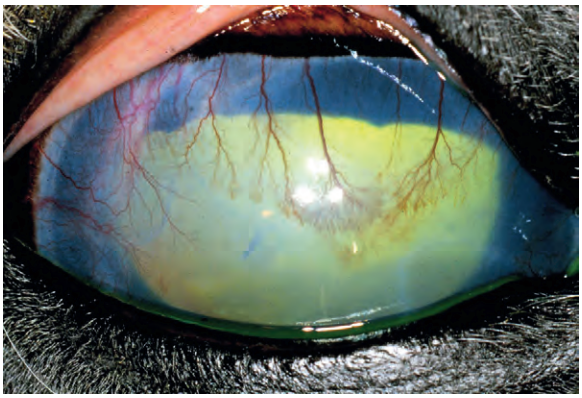


Figure 9-38. The intraocular pressure is 20 mm Hg, and the eye is stable and quiet 5 months after laser cyclophotocoagulation in the eye shown in Figure 9-36.

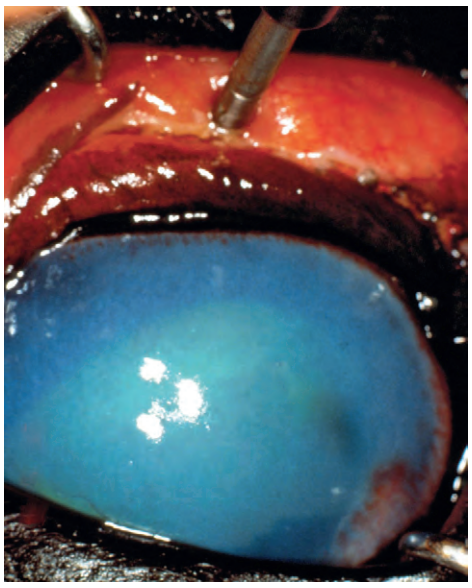


Figure 9-37. Neodymium-doped yttrium aluminum garnet (Nd:YAG) laser transscleral cyclophotocoagulation is performed on the eye shown in Fig. 9-36.

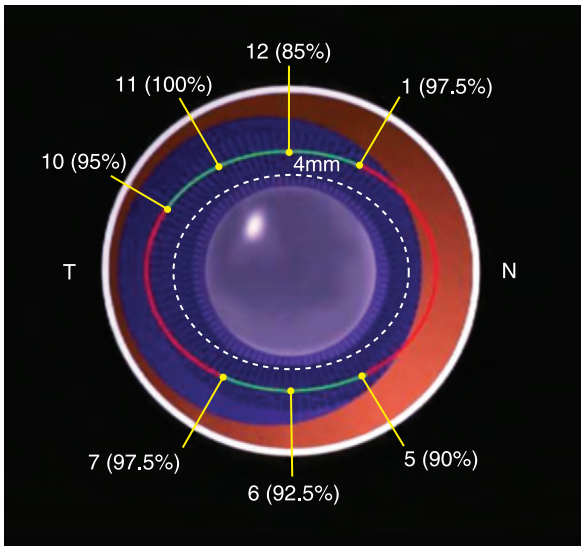


Figure 9-39. Sites for transscleral cyclophotocoagulation. (Photograph courtesy Dr. Tammy Miller.)

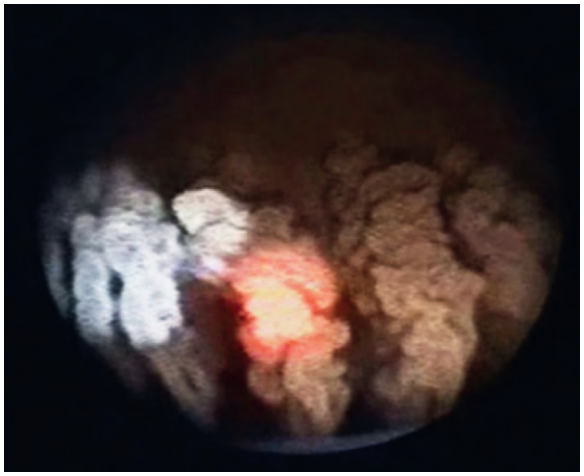


Figure 9-40. Endocyclophotocoagulation of the ciliary processes is utilized to deliver laser energy directly to the ciliary processes. The white areas were just photocoagulated with the red aiming beam of the laser.

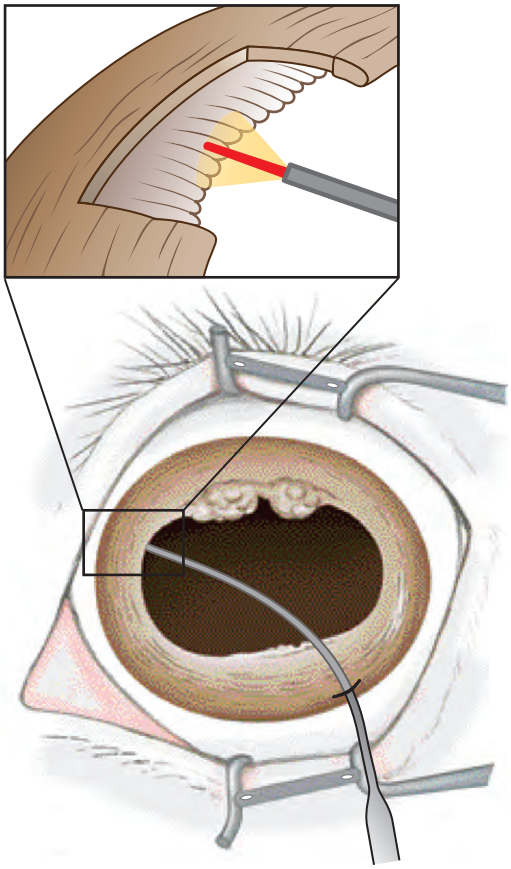


Figure 9-41. An equine globe with the curved, equine specific, endolaser probe inserted through a ventrolateral 3 mm trilaminar clear corneal incision. The exploded box represents the dorsomedial section of the globe with the ciliary processes exposed, for illustration purposes, by partial removal of the iris. The tip of the endolaser probe is visible with the red beam representing the laser energy (targeting the central ciliary process in view) and the yellow color fan representing the number of processes visualized "on screen" during laser application. (Original drawing courtesy Dr. Richard McMullen.)

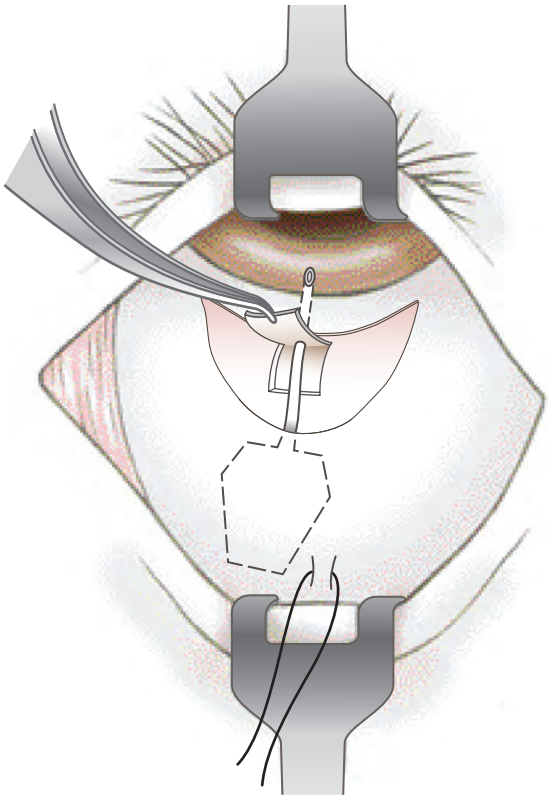


Figure 9-42. Schematic of gonioimplant.

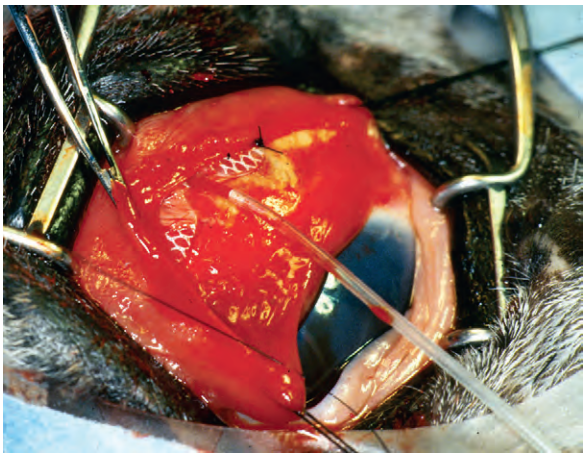


Figure 9-43. A gonioimplant is placed in the eye of an Appaloosa with glaucoma unresponsive to medical therapy.

mizing the risk of collateral tissue damage. Reported efficacy for lowering IOP and preserving vision in dogs is 80% to 90%.[41] Complications may be less frequent with ECP than TSCP, but ECP requires intraocular placement of the laser and general anesthesia. Further studies are needed to determine the long-term control of glaucoma in horses using ECP.

CYCLOCRYOSURGERY

Glaucomatous equine eyes can benefit from nitrous oxide–induced cryodestruction of the ciliary body, or cyclocryotherapy. A 3-mm-diameter cryoprobe is placed on the conjunctiva/

sclera 6 mm posterior to the limbus for a 1-minute freeze/thaw cycle in six locations (Fig. 9-44). Cyclocryotherapy is associated with severe postoperative iridocyclitis and may be best limited to use in blind eyes.[42] The IOP-lowering effects may only last 6 weeks, and cyclocryotherapy may need to be repeated.

GONIOIMPLANTS

Gonioimplant filtration surgeries to bypass the obstructed ICA and direct the outflow of aqueous humor to the subconjunctival spaces can be used to reduce IOP in patients with glaucoma. These implants may have a short lifespan owing to fibrosis of the drainage tube and filtration bleb, but they can be particularly effective when combined with laser cycloablation. IOP is controlled in the short term by the implant and long term by laser. These implants are experimental in the horse (see Figs. 9-42 and 9-43) but have been successful in dogs, controlling IOP in 74% to 76% and preserving vision in 41% to 58% of dogs after 12 months.[43-44]

CHEMICAL CILIARY BODY ABLATION

Intravitreal injection of intravenous gentamicin (50 mg with 1 mg of dexamethasone) can induce phthisis bulbi in a blind equine eye to result in varying degrees of pain and hydrophthalmos reduction (see Fig. 9-44). A single injection is typically sufficient for pain reduction, but a second may be necessary in some cases. After sedation, frontal nerve block, instillation of topical anesthetic and phenylephrine (2.5% to vasoconstrict conjunctival vessels), and with appropriate restraint, the ciliary body ablation is performed with a 20-gauge needle attached to a 3-mL syringe (Fig. 9-45). The needle is positioned dorsolaterally, approximately 7 mm posterior to the limbus at a 45-degree angle, toward the optic nerve and away from the lens (Fig. 9-46). Before the gentamicin/dexamethasone is injected, an equal volume (or greater) of vitreous is aspirated. If no vitreous can be aspirated, an aqueous paracentesis can be performed to decrease the intraocular volume and thereby temporarily decrease IOP. Progressive increases in globe size (hydrophthalmos) may be prevented. Equal volumes of dexamethasone may minimize discomfort from the injection.

SALVAGE PROCEDURES

Eyes with glaucoma caused by infection or intraocular tumors and eyes with painful lens luxations should be enucleated. Chronically painful and blind eyes and severely buphthalmic globes should be enucleated or have intrascleral prostheses implanted. A 34- to 44-mm-diameter intrascleral silicone implant can provide a cosmetic alternative to enucleation (Fig. 9-47).[45] Intraorbital silicone implants can minimize the pitting of the skin after enucleation. See Chapter 3, Diseases and Surgery of the Globe and Orbit, for more information on these procedures.

FUTURE STUDY: WHY IS EQUINE GLAUCOMA AN "ENIGMA"?

Despite a large population of large-diameter optic nerve axons, the horse can maintain functional vision in spite of elevated IOP. This occurs even though the critical collapsing pressure of large-diameter axons is lower than that of small-diameter axons.[4] Such large axons must be under severe stresses during glaucomatous episodes. Does the equine eye have a reservoir of RGCs and axons that allows for some vision despite the progressive glaucoma damage, or do these axons not collapse until late in the disease? It may be that a relatively large popula-

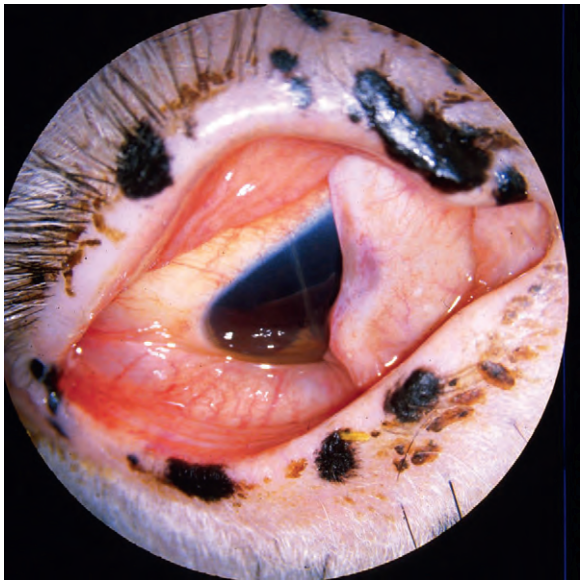


Figure 9-44. Gentamicin injection, end result, phthisis bulbi.

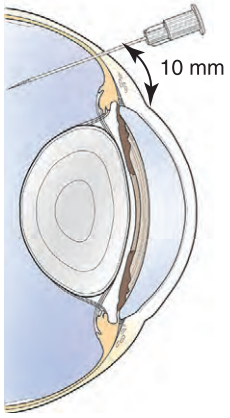


Figure 9-45. Gentamicin injection schematic.

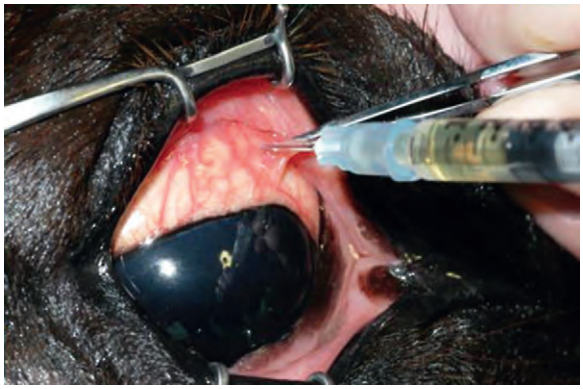


Figure 9-46. Gentamicin injection being performed.

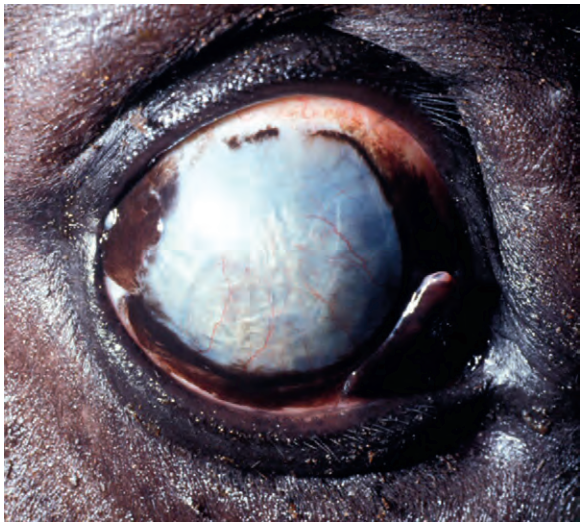


Figure 9-47. An intraocular silicone prosthesis after evisceration of the eye due to chronic glaucoma. Although the cornea was scarred, the horse appeared comfortable and received no therapy.

tion of equine RGCs are glaucoma resistant and able to function even in the presence of elevated IOP.

Tonographic values indicate a large functioning conventional outflow system, and the structure of the ICA indicates an apparent prominence of the unconventional outflow system. It thus appears that the equine eye has both outflow pathways available. Is this why glaucoma is rarely diagnosed in the early stages? Uveoscleral outflow is independent of IOP and morphologically prominent in the horse. Does this correlate to a safety mechanism for preventing complete aqueous humor obstruction? Or does the unconventional outflow system not work in the horse, as suggested by the microanatomy? The optic nerve axons can only tolerate high IOP if the IOP is balanced by an increase in the ophthalmic artery pressure. Is this ocular perfusion pressure gradient elevated in the equine eye and thus more important than IOP?

Pilocarpine contracts the weak ciliary muscles and reduces the intercellular spaces in the supraciliary space of the horse but does not lower IOP.[2,9] Pilocarpine acts by inducing the ciliary musculature to contract and pull on the "scleral spur" in human eyes. In horses, neither of these structures is well developed, so it makes sense that pilocarpine would have little effect on aqueous outflow. The IOP is not responsive to atropine in most equine glaucomatous eyes, although it may decrease IOP by a small percentage in healthy horses.[32] Considering the prominence of the two types of aqueous drainage pathways in the horse, these results are surprising and somewhat confusing.

Many equine eyes diagnosed with glaucoma may actually be eyes with hypertension associated with ERU, thus displaying less RGC degeneration and able to maintain sight once the IOP and uveitis are controlled. Eyes with hypertensive uveitis can have a resolution of their clinical signs, but eyes with true glaucoma will progress to blindness. Glaucomatous globes in horses respond to TSCP better than those in other species.[36] TSCP damages the supraciliary spaces and ciliary body, but the IOP eventually declines in most horses.

There is much that is not understood in the pathogenesis of equine glaucoma. Until better knowledge of the disease processes is available, controlling the disease will be difficult. Understanding why the horse maintains vision despite chronically high IOP may also assist in the management of canine glaucoma. Furthermore, the relationship between ERU and glaucoma remains poorly understood.

References

1. Samuelson D, Smith P, Brooks D: Morphologic features of the aqueous humor drainage pathways in horses, Am J Vet Res 50(5):720–727, 1989.
2. Smith PJ, Samuelson DA, Brooks DE, et al: Unconventional aqueous humor outflow of microspheres perfused into the equine eye, Am J Vet Res 47(11):2445–2453, 1986.
3. De Geest JP, Lauwers H, Simoens P, et al: The morphology of the equine iridocorneal angle: a light and scanning electron microscopic study, Equine Vet J Suppl (10):30–35, 1990.
4. Brooks DE, Blocker TL, Samuelson DA, et al: Histomorphometry of the optic nerves of normal horses and horses with glaucoma, Vet Comp Ophthal 5:193–210, 1995.
5. Brooks DE, Komaromy AM, Garcia-Fernandez MC, et al: Immunohistochemistry of the extracellular matrix of the normal equine lamina cribrosa, Vet Ophthalmol 3(2–3):127–132, 2000.
6. Yablonski ME, Asamoto A: Hypothesis concerning the pathophysiology of optic nerve damage in open angle glaucoma, J Glaucoma 2:119–127, 1993.
7. Miller PE, Pickett JP, Majors LJ: Evaluation of two applanation tonometers in horses, Am J Vet Res 51(6):935–937, 1990.
8. Smith PJ, Gum GG, Whitley RD, et al: Tonometric and tonographic studies in the normal pony eye, Equine Vet J Suppl (10):36–38, 1990.
9. van der Woerdt A, Gilger BC, Wilkie DA, et al: Normal variation in, and effect of 2% pilocarpine on, intraocular pressure and pupil size in female horses, Am J Vet Res 59(11):1459–1462, 1998.
10. Ramsey DT, Hauptman JG, Petersen-Jones SM: Corneal thickness, intraocular pressure, and optical corneal diameter in Rocky Mountain horses with cornea globosa or clinically normal corneas, Am J Vet Res 60(10):1317–1321, 1999.
11. Knollinger AM, La Croix NC, Barrett PM, et al: Evaluation of a rebound tonometer for measuring intraocular pressure in dogs and horses, J Am Vet Med Assoc 227(2):244–248, 2005.
12. van der Woerdt A, Gilger BC, Wilkie DA, et al: Effect of auriculopalpebral nerve block and intravenous administration of xylazine on intraocular pressure and corneal thickness in horses, Am J Vet Res 56(2):155–158, 1995.
13. Komaromy AM, Garg CD, Ying GS, et al: Effect of head position on intraocular pressure in horses, Am J Vet Res 67(7):1232–1235, 2006.
14. Wilcock BP, Brooks DE, Latimer CA: Glaucoma in horses, Vet Pathol 28(1):74–78, 1991.
15. Brooks DE: Equine glaucoma. In Robinson NE, editor: Current therapy in equine medicine, ed 5, Philadelphia, 2003, W.B. Saunders, pp 486–488.
16. Brooks DE, Komaromy AM, Kallberg ME: Comparative optic nerve physiology: implications for glaucoma, neuroprotection, and neuroregeneration, Vet Ophthalmol 2(1):13–25, 1999.
17. Gelatt KN: Glaucoma and lens luxation in a foal, Vet Med Small Anim Clin 68(3):261, 1973.
18. Barnett KC, Cottrell BD, Paterson BW, et al: Buphthalmos in a Thoroughbred foal, Equine Vet J 20(2):132–135, 1988.
19. Miller TR, Brooks DE, Gelatt KN, et al: Equine glaucoma: clinical findings and response to treatment in 14 horses, Vet Comp Ophthal 5:170–182, 1995.
20. Halenda RM, Grahn BH, Sorden SD, et al: Congenital equine glaucoma: clinical and light microscopic findings in two cases, Vet Comp Ophthal 7:105–116, 1997.

21. Van Der Woerdt A, Wilkie DA, Gilger BC, et al: Effect of single- and multiple-dose 0.5% timolol maleate on intraocular pressure and pupil size in female horses, Vet Ophthalmol 3(2–3):165–168, 2000.
22. Willis AM, Robbin TE, Hoshaw-Woodard S, et al: Effect of topical administration of 2% dorzolamide hydrochloride or 2% dorzolamide hydrochloride-0.5% timolol maleate on intraocular pressure in clinically normal horses, Am J Vet Res 62(5):709–713, 2001.
23. Germann SE, Matheis FL, Rampazzo A, et al: Effects of topical administration of 1% brinzolamide on intraocular pressure in clinically normal horses, Equine Vet J 40(7):662–665, 2008.
24. Alberts MK, Clarke CR, MacAllister CG, et al: Pharmacokinetics of acetazolamide after intravenous and oral administration in horses, Am J Vet Res 61(8):965–968, 2000.
25. Gum GG, Gelatt KN, Gelatt JK, et al: Effect of topically applied demecarium bromide and echothiophate iodide on intraocular pressure and pupil size in beagles with normotensive eyes and beagles with inherited glaucoma, Am J Vet Res 54(2):287–293, 1993.
26. Miller PE, Schmidt GM, Vainisi SJ, et al: The efficacy of topical prophylactic antiglaucoma therapy in primary closed angle glaucoma in dogs: a multicenter clinical trial, J Am Anim Hosp Assoc 36(5):431–438, 2000.
27. Gelatt KN, MacKay EO: Effect of different dose schedules of latanoprost on intraocular pressure and pupil size in the glaucomatous Beagle, Vet Ophthalmol 4(4):283–288, 2001.
28. Studer ME, Martin CL, Stiles J: Effects of 0.005% latanoprost solution on intraocular pressure in healthy dogs and cats. Am J Vet Res 61(10):1220–1224, 2000.
29. Davidson HJ, Pinard CL, Keil SM, et al: Effect of topical ophthalmic latanoprost on intraocular pressure in normal horses, Vet Ther 3(1):72–80, 2002.
30. Willis AM, Diehl KA, Hoshaw-Woodard S, et al: Effects of topical administration of 0.005% latanoprost solution on eyes of clinically normal horses, Am J Vet Res 62(12):1945–1951, 2001.
31. Mughannam AJ, Buyukmihci NC, Kass PH: Effect of topical atropine on intraocular pressure and pupil diameter in the normal horse eye, Vet Ophthalmol 2(4):213–215, 1999.
32. Herring IP, Pickett JP, Champagne ES, et al: Effect of topical 1% atropine sulfate on intraocular pressure in normal horses, Vet Ophthalmol 3(2–3):139–143, 2000.
33. Utter ME, Wotman KL: Complications of chronic ocular disease. In Robinson NE, Sprayberry KA, editors. Current therapy in equine medicine, ed 6, 2009, Saunders.
34. Annear MI, Wilkie DA, Gemensky-Metzler AJ: Diode laser transscleral cyclophotocoagulation for treatment of equine glaucoma: A retrospective study of 42 eyes of 36 horses. Abstracts: 39th Annual Meeting of the American College of Veterinary Ophthalmologists, Boston, MA, October 2008, p 86.
35. Whigham HM, Brooks DE, Andrew SE, et al: Treatment of equine glaucoma by transscleral neodymium:yttrium aluminum garnet laser cyclophotocoagulation: a retrospective study of 23 eyes of 16 horses, Vet Ophthalmol 2(4):243–250, 1999.
36. Miller TL, Willis AM, Wilkie DA, et al: Description of ciliary body anatomy and identification of sites for transscleral cyclophotocoagulation in the equine eye, Vet Ophthalmol 4(3):183–190, 2001.
37. Morreale RJ, Wilkie DA, Gemensky-Metzler AJ, et al: Histologic effect of semiconductor diode laser transscleral cyclophotocoagulation on the normal equine eye, Vet Ophthalmol 10(2):84–92, 2007.
38. Lin SC: Endoscopic and transscleral cyclophotocoagulation for the treatment of refractory glaucoma, J Glaucoma 17(3):238–247, 2008.
39. McLellan G: What's new in the management of glaucoma? Proc Brit Assoc Vet Ophthalmolgists, Birmingham, UK, 2005, November 11–13, pp 13–18.
40. Grahn BH, Barnes LD, Breaux CB, et al: Chronic retinal detachment and giant retinal tears in 34 dogs: outcome comparison of no treatment, topical medical therapy, and retinal reattachment after vitrectomy, Can Vet J 48(10):1031–1039, 2007.
41. Palmer LE, Byers CG, Caruso K: Acute glaucoma, Stand of Care: ECC Med 10(6):1–8, 2008.
42. Frauenfelder HC, Vestre WA: Cryosurgical treatment of glaucoma in a horse, Vet Med Small Anim Clin 76(2):183–186, 1981.
43. Sapienza JS, van der Woerdt A: Combined transscleral diode laser cyclophotocoagulation and Ahmed gonioimplantation in dogs with primary glaucoma: 51 cases (1996–2004), Vet Ophthalmol 8(2):121–127, 2005.
44. Bentley E, Miller PE, Murphy CJ, et al: Combined cycloablation and gonioimplantation for treatment of glaucoma in dogs: 18 cases (1992–1998), J Am Vet Med Assoc 215(10):1469–1472, 1999.
45. Meek LA: Intraocular silicone prosthesis in a horse, J Am Vet Med Assoc 193(3):343–345, 1988.

Chapter 10

Diseases of the Ocular Posterior Segment

David A. Wilkie

Evaluation of the posterior segment of the equine eye is an essential part of an ophthalmic, prepurchase, and general physical examination. Initial examination includes a history with respect to vision, determination of menace response and pupillary light reflex (PLR), and evaluation of clarity of transmitting media (cornea, aqueous, lens, vitreous). The resting pupil size and direct and consensual PLRs are evaluated. Menace response should be evaluated in various visual fields: anterior, central, and posterior. Although it is possible to examine portions of the fundus without dilation, for proper examination of the posterior segment of the equine eye, mydriasis, a darkened environment, and proper equipment are essential. Diagnostic mydriasis is achieved by using topical 1% tropicamide (Mydriacyl), which has an onset of action of 15 to 25 minutes and a duration of action of 8 to 12 hours. As a solution, 0.2 mL of tropicamide is easily sprayed on the cornea with a tuberculin syringe and the hub of a 25-gauge needle. If required, sedation and nerve blocks can be performed to facilitate examination. Blocking the auriculopalpebral nerve will facilitate examination by allowing the clinician to elevate the superior eyelid (see Chapter 1).

Posterior segment abnormalities can be congenital or acquired and include both primary ophthalmic and systemic diseases. When present, posterior segment abnormalities must be assessed with respect to current and future visual impact and importance with respect to usefulness and safety of the horse. The clinician should remember that much of what is examined by ophthalmoscopy is a direct extension of the brain and central nervous system (CNS). In addition, it is the only area where arterioles and venules can be viewed directly. This is, in reality, clinical histopathology. Lesions adjacent to the optic nerve or involving the area centralis will have a greater impact on vision than those that are more peripheral. The menace response in various visual fields and maze testing can be used to assess current vision. In addition, evidence of anterior segment disease or inflammation and the possibility of progression and future inflammatory episodes should be considered. Use of the animal must also be considered. A barrel horse or competitive jumper requires greater vision than a brood mare or halter show horse. The possibility that a lesion is inherited or breed-related should also be considered if the animal is to be used for breeding.

Despite the significance of the retina and choroid to vision, little is known about posterior segment diseases in the horse as compared with diseases of the anterior or posterior segment in other species. This may be a result of fewer inherited abnormalities and fewer infectious and hematogenous diseases because of the horse's paurangiotic retina, or it may simply

reflect a lack of examination of the equine posterior segment by veterinarians.

EXAMINATION OF THE OCULAR FUNDUS

DIRECT AND INDIRECT OPHTHALMOSCOPY

Both direct and indirect ophthalmoscopy should be used for examination of the equine posterior segment. Indirect examination is performed initially for an overview of the fundus, and direct ophthalmoscopy is preferred for detailed examination of the optic nerve and retinal blood vessels. Indirect examination with a 20-diopter (D) condensing lens and a Finnoff transilluminator will provide a more panoramic but less magnified view of the fundus, with lateral and axial magnifications of ×0.79 and ×0.84, respectively.[1] Indirect examination provides better visualization of the peripheral retina and can also be performed by using an indirect headset that provides stereopsis and leaves the examiner a free hand to elevate the superior eyelid (Figs. 10-1 to 10-3). Indirect examination allows visualization of the fundus through cloudy transmitting media such as aqueous flare or lenticular sclerosis, which is often not possible with direct examination. A virtual, upside down, reversed image is created. If a headset is used, it will provide the examiner with illumination and stereopsis. Alternately, a device called a *PanOptic ophthalmoscope* (Welch Allyn, Skaneateles Falls, NY) can be used. The PanOptic is an indirect monocular ophthalmoscope that provides an erect image with a wider field of view but less magnification than that provided by direct examination (Fig. 10-4) (for more information, see Chapter 1).

Direct examination provides the greatest magnification, with lateral and axial magnifications of ×7.9 and ×8.4, respectively (Fig. 10-5).[1] Direct ophthalmoscopy should be used for detailed examination of the optic nerve, retinal blood vessels, and peripapillary region. For examination of the posterior segment, the direct ophthalmoscope is set to 0 D, and the ophthalmoscope is held approximately 2 cm from the horse's eye (Fig. 10-6). The optic nerve should be in focus for most examiners at this setting. Changing the diopter settings will allow the clinician to focus vitread or more posterior to determine whether an abnormality is elevated or depressed, respectively. The image obtained with a direct ophthalmoscope is upright and magnified

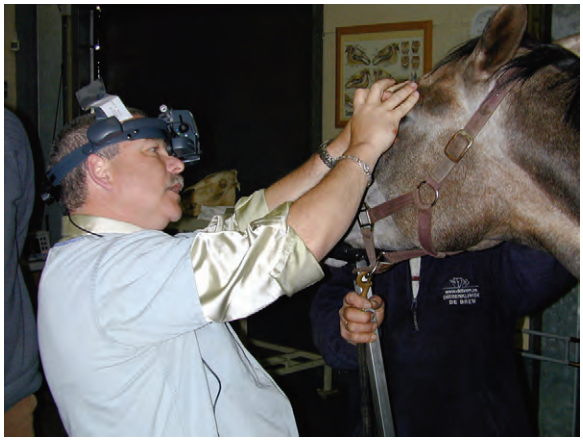


Figure 10-1. Indirect ophthalmoscopic examination with a 20-D condensing lens and a headset.

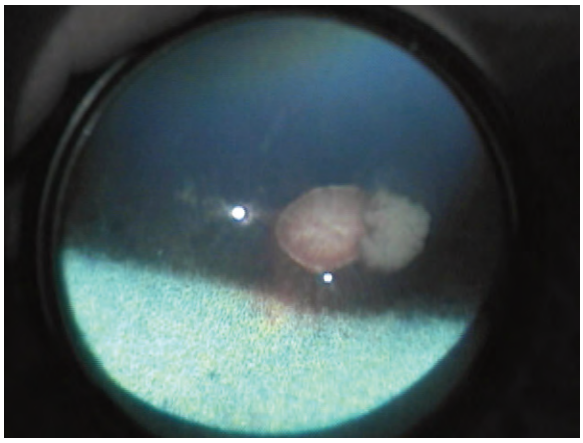


Figure 10-3. View of the equine posterior segment as seen through a 20-D indirect lens. The image is upside down and reversed. A proliferative lesion is present on the optic nerve.

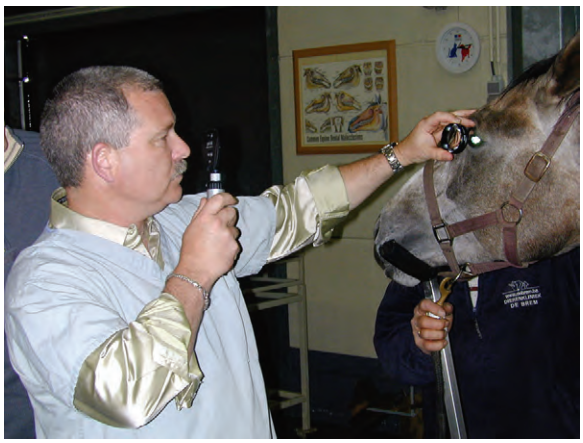


Figure 10-2. Indirect ophthalmoscopic examination using a direct ophthalmoscope as a light source and a 20-D lens. This technique is used when an indirect headset is not available.

Figure 10-4. Examination of the posterior segment, using the Welch-Allyn PanOptic monocular indirect ophthalmoscope. (Photograph courtesy Dr. Dennis Brooks, University of Florida.)

Figure 10-5. Welch-Allyn direct ophthalmoscope.

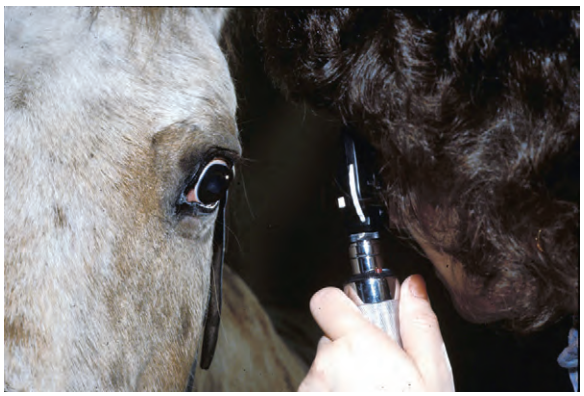


Figure 10-6. Technique of direct ophthalmoscopy in the horse.

(Fig. 10-7). Abnormalities of the cornea, aqueous, lens, and vitreous make direct examination difficult. In such instances, indirect examination should be performed.

BIOMICROSCOPY

Biomicroscopy should also be used for examination of both the anterior segment and the anterior third of the vitreous for vitreous syneresis, asteroid hyalosis, debris, membranes, vascular remnants, and hyalitis (see Chapter 1 for more information). A yellow-green discoloration of the vitreous may be observed and is indicative of serum staining and previous intraocular inflammation.

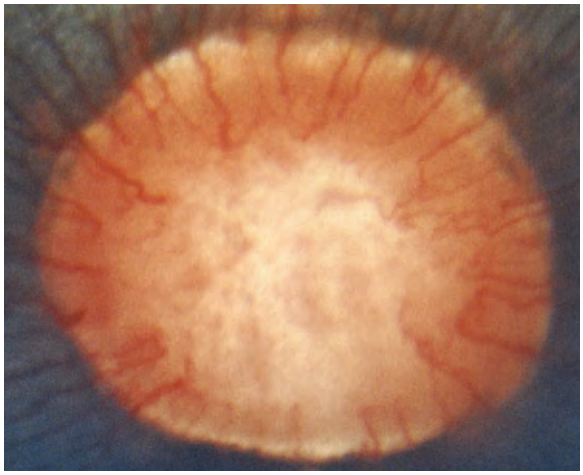


Figure 10-7. Image of an equine optic nerve as seen by direct examination.

During examination of the posterior segment, what the clinician sees is dependent on color and thickness of the three concentric tunics—the retina, choroid, and sclera—that comprise the posterior eye wall. The neurosensory retina (NSR) has the optical consistency of wax or tissue paper, rendering tissues below it less reflective and dull. A loss of retinal tissue will therefore increase the reflectivity and color of the underlying tissue. This is called *hyperreflectivity* in the tapetal fundus. Alternately, thickening of the retina (e.g., edema, cells, dysplasia) will obscure and dull the underlying tissue. The outermost layer of the retina is the monolayer, or retinal pigment epithelium (RPE), which is normally pigmented in the ventral nontapetal retina and nonpigmented over the tapetum in most horses. The choroid or vascular tunic is composed of melanin-containing cells, blood vessels, and dorsally, the fibrous tapetum. The outermost fibrous tunic, the sclera, appears white. The coat color of the horse, amount of melanin, and thickness of the tapetum all influence the normal appearance on fundic examination. Normal variations are common, and the clinician must be familiar with these before being able to interpret and understand abnormalities.

Posterior segment examination should include evaluation of the vitreous, tapetal and nontapetal fundus, retina, retinal blood vessels, and optic nerve. Variations in the normal equine fundus are common, and familiarity with these variations is essential.[2-9] Additional posterior segment diagnostic tests may include ocular ultrasonography,[10] fluorescein angiography,[11] computed tomography (CT), electroretinography (ERG),[12] and visual evoked potential (VEP) (see Chapter 1 for more information).

ULTRASONOGRAPHY

Ultrasonography is indicated when opacities of the transmitting media prevent examination of the posterior segment. Typically, cataracts and hyphema are the most common indications for ultrasound examination of the posterior aspect of the globe.[10] A 5- to 20-MHz ultrasound probe will provide diagnostic images of the posterior globe. The 5-MHz probe provides less near-field resolution and greater penetration of the orbit, whereas the 20-MHz probe provides excellent resolution of the anterior segment, but the posterior eye wall is the limit of its

penetration in the equine eye. Direct corneal contact with the use of methylcellulose gel is the technique of choice, provided the cornea is intact. Imaging can be performed through the eyelid if the cornea is compromised (see Chapter 1 for more information).

ELECTRORETINOGRAPHY

While the ERG has traditionally been performed using general anesthesia, a technique for obtaining a flash photopic and scotopic ERG in a standing sedated horse has been described, making this test more easily obtained and associated with less risk and expense.[12] An ERG is indicated to evaluate retinal function prior to cataract surgery and to assess retinal health and aid in diagnosis in congenital stationary night blindness, glaucoma, equine motor neuron disease, chorioretinitis, optic neuritis, and ocular trauma.

FLUORESCEIN ANGIOGRAPHY

The technique and results of fluorescein angiography have been described in the normal horse.[11] Two successive angiographic phases were described: the choriocapillary phase, starting at 46.95 ± 9.48 seconds, and the retinal vascular phase, starting at 47.79 ± 10.38 seconds. The retinal vascular phase was divided in three parts: filling phase, maximum fluorescence point, and fading phase. During the filling phase, the dye progressed into the retinal vessels, obtaining maximum fluorescence at 59.79 ± 10.39 seconds, termed the *maximum fluorescence point*. The fading phase started immediately following the maximum fluorescence point. During this phase, vascular fluorescence decreased to complete reduction at 74.76 ± 9.81 seconds. Areas of delayed choroidal filling, the presence of short retinal vessels in the ventral region of the optic disc, and a particular filling of the optic disc were also observed.[11] Fluorescein angiography may have value in evaluating diseases of the retina, choroid, retinal pigment epithelium, and optic nerve (see Chapter 1 for more information).

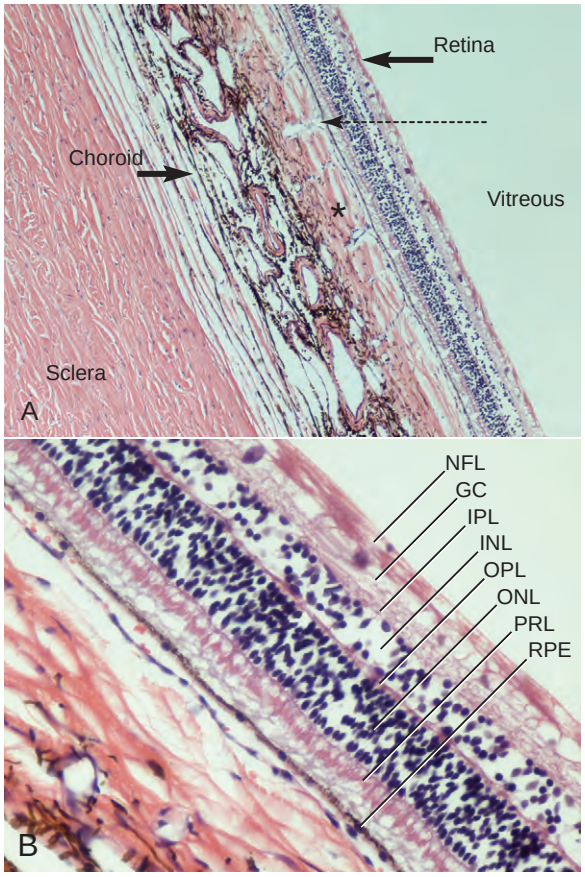


Figure 10-8. **A,** Histologic section of the posterior segment of the equine eye (H&E ×100). *, Tapetum; *dotted arrow*, stars of Winslow. **B,** Histologic section through the nontapetal equine retina (H&E ×200). *GC*, Ganglion cell; *INL*, inner nuclear layer; *IPL*, inner plexiform layer; *NFL*, nerve fiber layer; *ONL*, outer nuclear layer; *OPL*, outer plexiform layer; *PRL*, photoreceptor layer; *RPE*, retinal pigment epithelium.

CLINICAL ANATOMY AND PHYSIOLOGY

The posterior segment of the eye includes the vitreous, retina, choroid, sclera, and optic nerve (Fig. 10-8). The anterior-most extent of the posterior segment is the ora ciliaris retinae where the retina attaches to the pars plana of the ciliary body. The anterior extension of the ora ciliaris varies by quadrant of the eye and is important because it has significance for glaucoma and vitreoretinal surgery.[14] The ora is located more anteriorly in the nasal and ventral quadrants and further posterior in the dorsal and temporal quadrants.[14] This makes the dorsal and temporal locations the areas of choice for surgical approaches to the posterior segment and for transscleral and endocyclophotocoagulation.

The vitreous body is predominately composed of type II collagen fibrils, hyaluronic acid, and water. It is divided into cortical, intermediate, and central zones and has a volume of approximately 28 mL in the adult horse.[15,16] Transrectal ultrasound of the dimensions of the fetal vitreous body has been used to predict parturition date in light horse mares and ponies.[17] Normally the vitreous is transparent and uniform in appearance. Abnormalities of the vitreous generally result in loss of uniformity, with debris, membranes, and collagen fibrils appearing to float and swirl in a liquid medium. In addition, changes in vitreous color are often noted as a result of inflammation with the vitreous and the lens appearing yellow-green in color as a result of chronic inflammation. On ultrasonography, the vitreous is normally anechoic with increased vitreous echogenicity, indicating degeneration, inflammation, hemorrhage, mass lesions, or retinal detachment. This is evidence that the vitreous may have a role as an effector in some instances of equine recurrent uveitis (ERU), and pars plana vitrectomy has been advocated to control recurrent inflammation in ERU.[18]

The horse has a paurangiotic (partially vascularized) retina with 30 to 60 small retinal vessels radiating from the margin of an elliptical optic disc. These vessels are visible for a distance of 1 to 2 disc diameters but are less prominent dorsal and ventral to the optic nerve (Fig. 10-9). The remainder of the equine retina is avascular, being supplied from the underlying choroid. The thickness of the NSR varies from 250 mm medial to the optic disc to 80 mm at the ora ciliaris.[19] The majority of the equine retina is less than 130 mm in thickness to allow for oxygen diffusion from the underlying choroid.[19] The choroidal or vascular tunic is external to the NSR. It is composed of the larger choroidal vessels, the tapetum, choriocapillaris, and

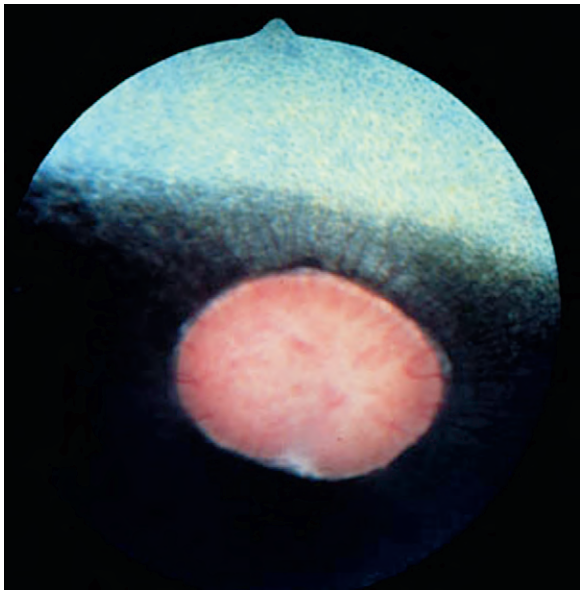


Figure 10-9. Normal optic nerve and peripapillary fundus. Note the normal notch at the 6 o'clock optic nerve and the decreased number of retinal vessels in this region.

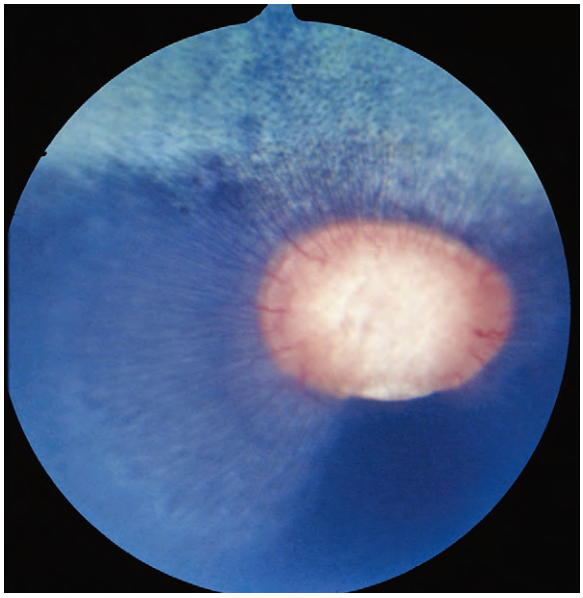


Figure 10-10. Normal fundic photograph of a dark bay horse with a blue tapetum. (Photograph courtesy Drs. Ingo Walde and Barbara Nell, University of Vienna.)

melanocytes. In the equine eye, the choroid is responsible for the majority of retinal nutrition because the retina is paurangiotic.

The fundus is divided into the dorsal tapetal and ventral nontapetal regions. The fibrous tapetum is situated in the dorsal choroid and is responsible for the characteristic yellow-green color of this portion of the fundus. Variations in tapetal color are related to iris and coat color and include yellow, orange, and blue-green.[3,6,8] Dark bay and brown horses usually have a blue-green tapetum with a dark nontapetal region (Figs. 10-10 and 10-11). Lighter chestnuts and palominos may have a yellow tapetum with a less pigmented nontapetal region (Figs. 10-12 and 10-13). Gray and white horses generally have a yellow tapetum with a lightly pigmented or nonpigmented nontapetal fundus. This may allow visualization of the choroidal vasculature and sclera. Finally, in color-dilute horses, the tapetum may be hypoplastic or absent.[21-22] Tapetal hypoplasia can be generalized or confined to a portion of the tapetum, most often immediately dorsal to the optic disc (Figs. 10-14 to 10-16). Color and thickness of the tapetum and choroidal pigment vary not only between horses but also within horses from right to left eyes. Near the periphery of the tapetum, it is not unusual to see focal areas of RPE pigmentation obscuring the underlying tapetum (Fig. 10-17). In addition, random foci of RPE pigmented freckles or nevi may appear throughout the tapetum (Fig. 10-18). These must be differentiated from postinflammatory hyperpigmentation or choroidal melanoma. The tapetum of the horse is penetrated by small choroidal arterioles that serve to supply the retina via the choriocapillaris. These vessels are seen end-on on fundic examination and appear as uniformly distributed dark dots in the tapetum called the *stars of Winslow* (Fig. 10-19). The ultrastructure of the equine RPE and choriocapillaris have been described.[23] The function of the tapetum is to enhance vision in low-light conditions by allowing reflected light the opportunity to stimulate the photoreceptors a second time. However, although the tapetum improves the threshold

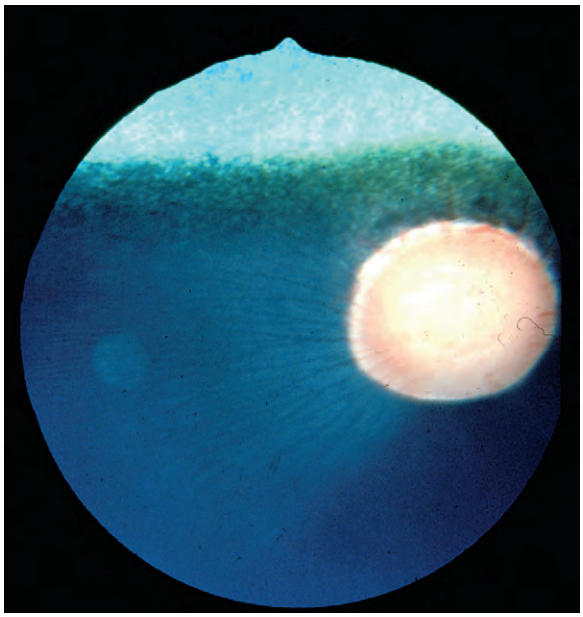


Figure 10-11. Normal fundus with a green tapetum.

of light detection, it also causes glare and thereby decreases visual acuity in bright light.[20]

The ventral nontapetal fundus is generally dark brown or black but can appear lighter or nonpigmented, depending on coat color.[6,8] In color-dilute horses, the tapetum may be hypoplastic or absent, and the choroid and RPE may demonstrate partial or complete albinism. This can affect one or both eyes and can even be observed to vary within an eye. Choroidal vasculature and vortex veins may be visible, especially in association with tapetal hypoplasia and ocular albinism (Figs. 10-20 and 10-21).[3] These vessels may appear as radiating, dark striae seen through a normal tapetum or as red vessels in a subalbinotic to albinotic eye.

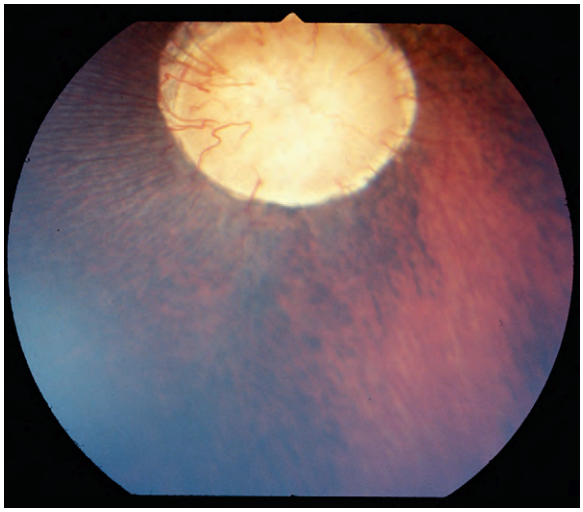


Figure 10-12. Nontapetal fundus of a light-colored horse. An area of choroidal hypopigmentation is present, allowing visualization of the choroidal vasculature.

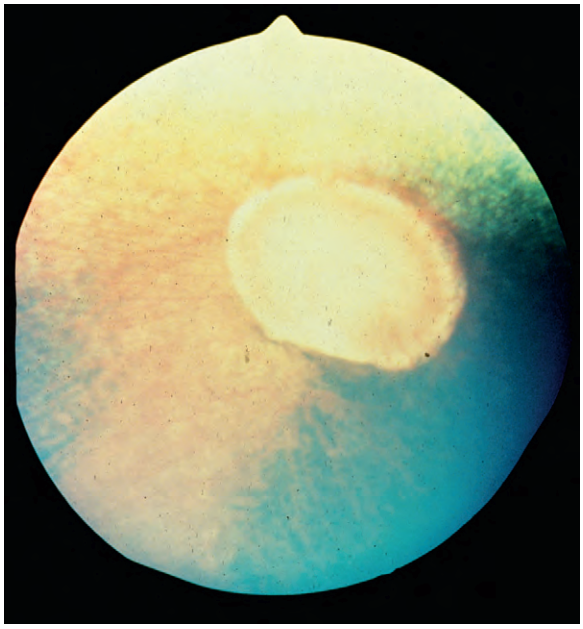


Figure 10-13. Normal fundus of a palomino horse, demonstrating a yellow tapetum and area of choroidal hypopigmentation.

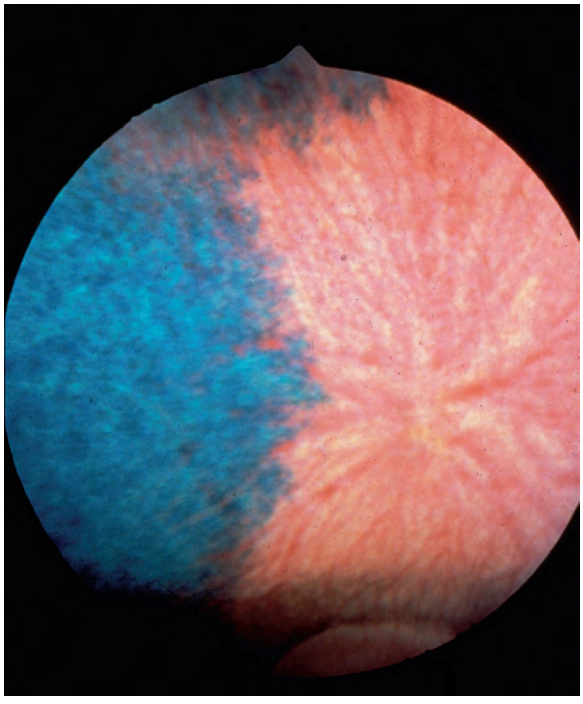


Figure 10-14. Normal fundic photograph of a color-dilute horse. The edge of the optic nerve is visible ventrally. The tapetum is absent in half of the dorsal fundus, allowing visualization of the choroidal vasculature and sclera.

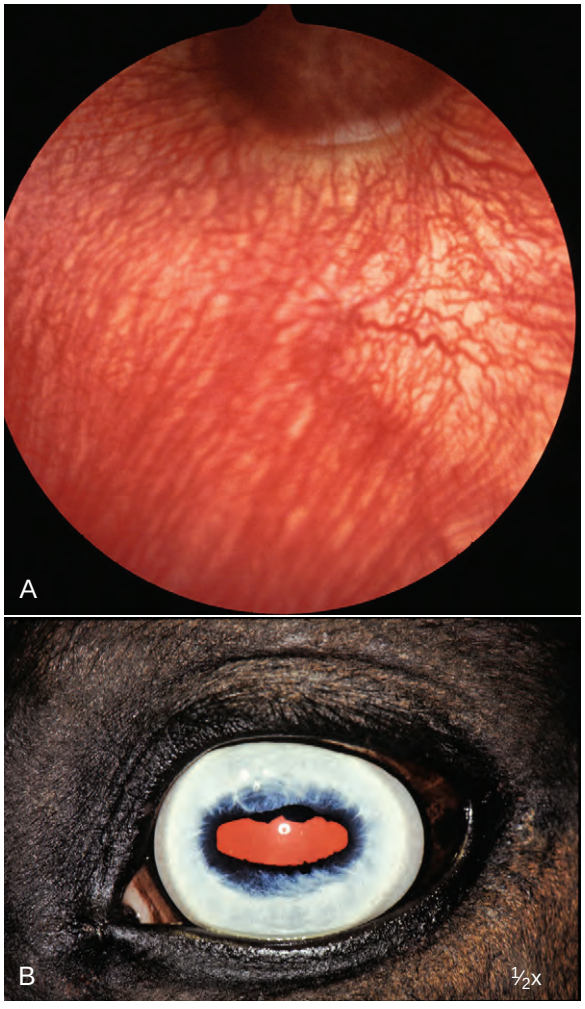


Figure 10-15. **A,** Normal fundic photograph of an albinotic eye. This photo is taken in the ventral nontapetal fundus. **B,** Gross external photograph of same horse, showing a red fundic reflex and a blue iris. (Photographs courtesy Drs. Ingo Walde and Barbara Nell, University of Vienna.)

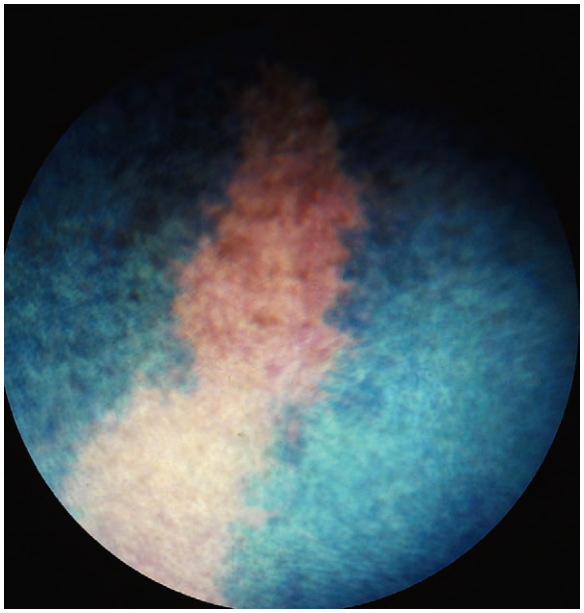


Figure 10-16. Normal fundic photograph with a linear area of tapetal hypoplasia. (Photograph courtesy Drs. Ingo Walde and Barbara Nell, University of Vienna.)

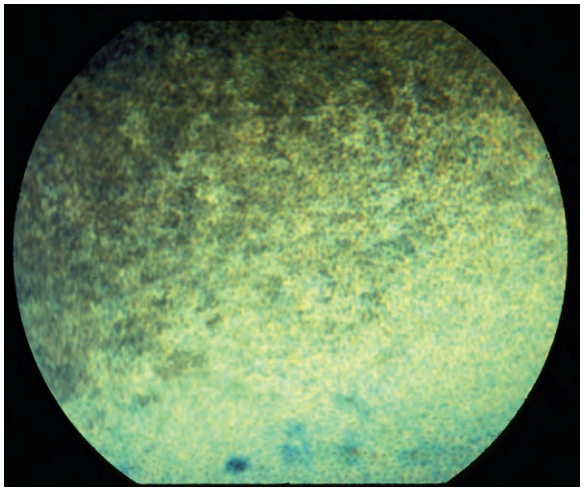


Figure 10-17. Dorsal tapetum with areas of retinal pigment epithelium pigmentation obscuring the underlying green tapetum. This is a normal variation.

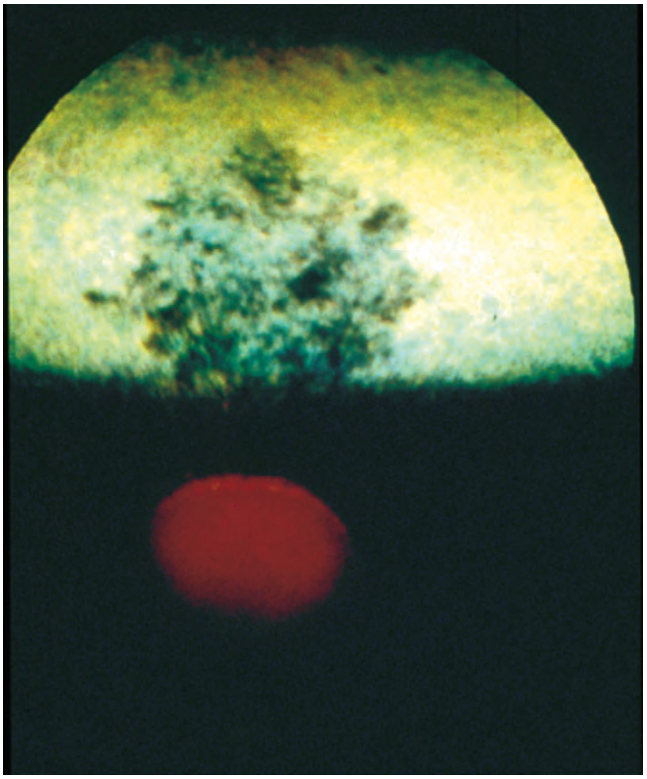


Figure 10-18. Retinal pigment epithelium pigmentation over the tapetal retina dorsal to the optic nerve. This is a normal variation.

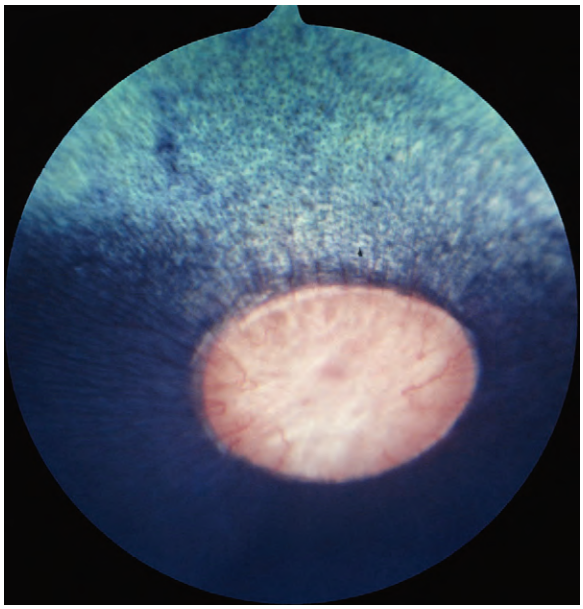


Figure 10-19. Normal equine fundus. The stars of Winslow are apparent dorsal to the optic nerve as multifocal, uniform black dots in the tapetal fundus. (Photograph courtesy Drs. Ingo Walde and Barbara Nell, University of Vienna.)

Focal areas of nonpigmentation or depigmentation are often observed in the peripapillary nontapetal fundus (Fig. 10-22). These are often normal variations, but because previous intraocular inflammation can also result in depigmentation, a complete ophthalmic examination should be performed to rule out prior disease. In addition, infection with equine herpesvirus 1 (EHV-1) has been reported to result in focal white chorioretinal lesions in the nontapetal fundus (see discussion of chorioretinitis).[24]

The retina consists of the NSR and RPE. The photoreceptors, rods and cones, are located in the sensory retina. The rods predominate and are responsible for achromatic low-light vision, whereas the cones are responsible for vision in bright light and color vision. The horse lacks a fovea but has an area centralis, which serves as the area of maximum visual acuity and has an increased density of retinal ganglion cells. The equine area centralis is a horizontal band of 1 mm by 22 mm and is located approximately 3 mm dorsotemporal to the optic nerve.[25,26] The concentration of ganglion cells in the area centralis is 4000 to 6000 cells/mm^2 as compared with less than 500 cells/mm^2 in the dorsal and ventral retina.[27,28] In addition to

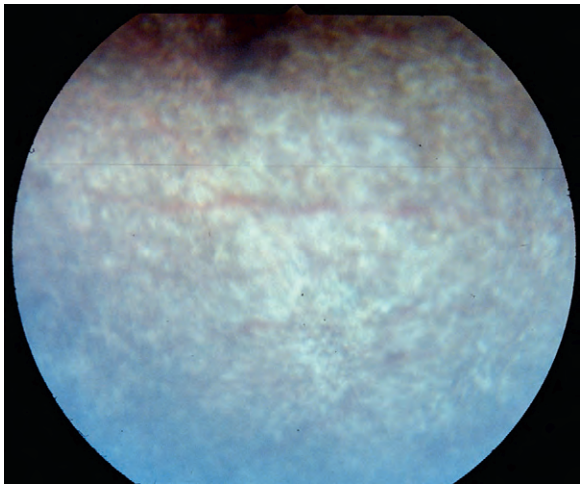


Figure 10-20. Normal nontapetal fundus of a color-dilute horse. The underlying choroidal vasculature can be seen.

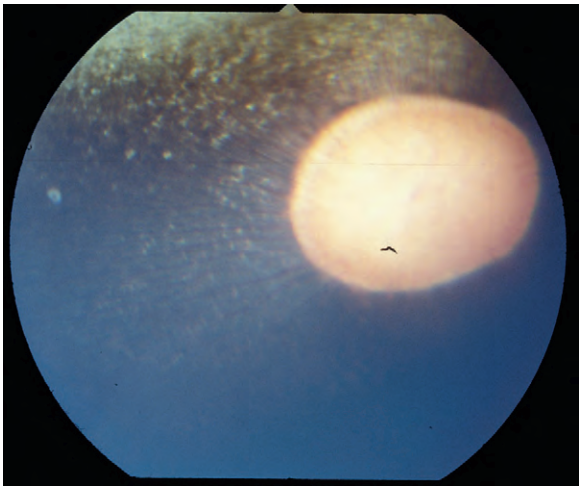


Figure 10-22. Peripapillary pigment variation. Multifocal areas of hypopigmentation are noted. The overlying retinal vessels are normal.

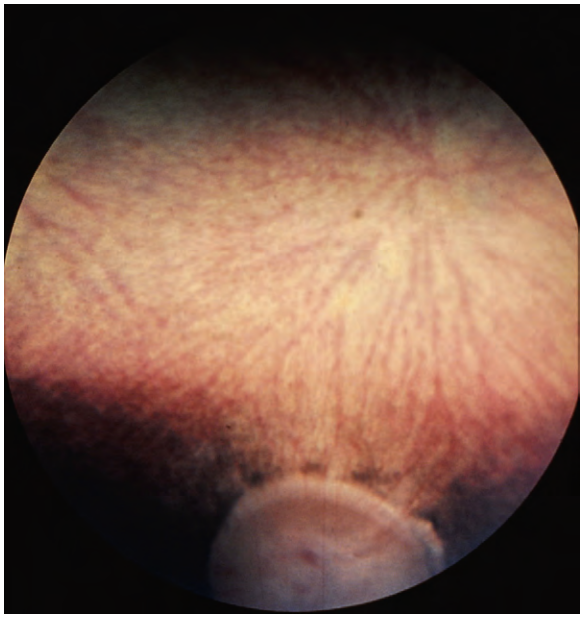


Figure 10-21. Normal fundic photograph of a color-dilute horse with tapetal hypoplasia. (Photograph courtesy Drs. Ingo Walde and Barbara Nell, University of Vienna.)

regional differences in ganglion cell density, it has been shown that variation in ganglion cell density within the area centralis also occurs by breed of horse and skull conformation.[29] Evaluation of the equine inner retina has demonstrated the presence of bipolar, amacrine, horizontal, and Müller cells in percentages of 44%, 24%, 1%, and 29%, respectively.[30] Specific markers for these and other retinal cells have been identified for the equine retina.[31] The horse has dichromatic vision, with a short-wavelength cone (spectral peak of 425 nm) and a middle-wavelength cone (spectral peak of 540 nm).[32,33] This translates into a blue-gray and yellow-green visual spectrum. The horse has been shown to be able to discriminate color from grays and to demonstrate color-discrimination performance behavior.[34] The visual field of the horse is approximately 350 degrees, with a small area—65 to 70 degrees—of binocular overlap.[5] Please see Chapter 11 for more information on equine vision.

The optic disc is normally oval, salmon pink, and situated slightly temporal and ventral in the nontapetal fundus. The optic nerve will fill the view of a direct ophthalmoscope; it measures 3 to 5 mm vertically and has a horizontal diameter of 5 to 8 mm.[20] The optic nerve in foals may appear more round. The surface of the optic nerve is often irregular and honeycombed as a result of the axons exiting at the fibrous lamina cribrosa. Ventrally, the optic nerve may appear notched (see Fig. 10-9). The equine optic nerve is composed of approximately 1 million axons, with larger axons found at the periphery of the optic nerve as compared with the central portion.[26,35] These large axons are preferentially lost in equine glaucoma.[35] Although the optic nerve is myelinated, myelin does not typically extend to the intraocular portion of the nerve. If myelin does extend into the eye, it is most often associated with retinal vessels. Myelin extending along the nerve fiber layer axons appears as light gray striations and is more common in aged horses (Fig. 10-23). Radiating from the margin of the optic nerve are 30 to 60 small arterioles and venules. They cannot be distinguished from one another and may be absent at the 6 o'clock region of the nerve. These retinal vessels travel 1 to 2 optic disc diameters into the retina before they disappear. Occasionally, a small vessel may be seen to emerge from the central optic nerve and course across its surface. The margin of the optic nerve may have a peripapillary ring associated with changes in thickness of the tapetum or pigmentation of the RPE or choroid. This circumpapillary ring can be dark or hypopigmented. This is a normal variation, provided that the overlying retinal vessels do not deviate or attenuate while crossing this region. Changes in vessel direction or thickness suggest a coloboma or degeneration. The axons of the retinal ganglion cells exit the eye through the scleral lamina cribrosa. The adult equine lamina cribrosa is a complex, multilayered structure composed of myelinated optic nerve axons, capillaries, astrocytes, and an extracellular matrix.[36] The immunohistochemistry of the extracellular matrix of the normal equine lamina cribrosa has been described. It has been suggested that this macromolecular structure of the equine lamina cribrosa may make it

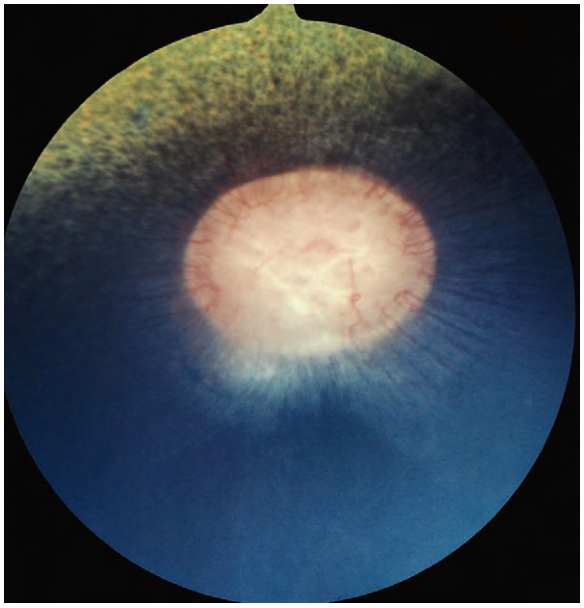


Figure 10-23. Myelin is seen radiating from the optic nerve along the nerve fiber layer axons in an aged horse. (Photograph courtesy Drs. Ingo Walde and Barbara Nell, University of Vienna.)

resistant to changes associated with elevations of intraocular pressure and offer protection to the optic nerve axons.[36] This is supported clinically by the preservation of vision in horses despite often chronic elevations in intraocular pressure.

IMPACT OF DISEASE OF THE OCULAR POSTERIOR SEGMENT ON THE EQUINE INDUSTRY

The significance of posterior segment disease to an individual horse and the equine industry is difficult to quantitate. Equine recurrent uveitis (ERU) affects 5% to 15% of the equine population and is the most common cause of posterior segment abnormalities. As a result of ERU, secondary glaucoma, retinal detachment, and retinal and optic nerve degeneration may affect vision and thus function. These changes are generally observed by owners and can be quantitated. However, more subtle lesions may go unnoticed, resulting in poor performance and affecting use without the owner being aware of the reason. In addition, posterior segment abnormalities noted on a prepurchase examination may result in a loss of value. Finally, horses with posterior segment lesions significant enough to result in visual disturbance may present a safety concern for the owner with respect to riding, driving, or behavior.

The impact of posterior segment disease is significantly greater than has been appreciated, and veterinarians are strongly encouraged to make examination of the posterior segment a routine part of a physical and prepurchase examination. In a recent survey of 204 racing Thoroughbred horses in Australia, ocular abnormalities were observed in 138 (67.6%) of the horses examined. Of these findings, potential vision-threatening abnormalities were noted in 15 horses (7.4%) and non–vision-threatening abnormalities in 117 (57.4%). The most frequent abnormalities involved the retina and lens, with abnormalities of the retina noted in 117 (57.4%) of the horses examined.[13] If a complete examination of the posterior segment is required, the pupil should be pharmacologically dilated. It should be noted on a prepurchase examination whether the pupil was or was not dilated for the ophthalmic examination.

DISEASES OF THE OCULAR FUNDUS

Abnormalities on fundic examination include vitreous degeneration; membranes; inclusions and vascular remnants; changes in size, shape, and color of the optic nerve and retinal vessels; elevation or depression of the optic nerve; retinal dysplasia, detachment, and hemorrhage; changes in tapetal reflectivity (hyperreflective and hyporeflective); and changes in pigmentation. Most abnormalities are identified in the peripapillary region and can be visually significant because this area has a greater concentration of retinal axons. Abnormalities that are hyperreflective indicate thinning or loss of retinal tissue and are observed in the tapetal fundus. Hyperreflective changes include retinal atrophy or degeneration, retinal tears, and retinal detachment. Hyporeflective changes can indicate an increase in tissue thickness resulting from cellular infiltrates, edema, or folding of the retina as seen in retinal dysplasia. Hyporeflective changes appear dull gray or white, depending on the background (tapetal or nontapetal). In addition, the retina may appear elevated. Inflammation can result in depigmentation and pigment clumping in the nontapetal fundus and hyperpigmentation in the tapetal fundus. These changes must be differentiated from normal variations in pigmentation of the RPE.

CONGENITAL DISEASES

Congenital abnormalities of the equine posterior segment are uncommon. They can be seen alone or in association with multiple congenital anomalies such as anterior segment dysgenesis, congenital megaloglobus, the multiple congenital ocular anomalies (MCOA) syndrome (i.e., the Rocky Mountain horse [RMH] syndrome), and other such ocular anomalies. In one study, the incidence of congenital ocular abnormalities was 0.5% of all equine cases presented.[37]

RETINAL HEMORRHAGES

Subretinal and intraretinal hemorrhages may be noted in neonatal foals (Fig. 10-24).[38] In one study of 167 neonatal Thoroughbred foals, 27 (16%) were found to have retinal hemorrhages.[38] Most hemorrhages were bilateral, and females were more commonly affected than males.[38] Hemorrhages were punctate in 36% and "splash-like" in 56%; the number of hemorrhages per eye ranged from 1 to 20.[38] Such hemorrhages may be the result of intraocular vascular hypertension with capillary rupture during parturition.[20] Hemorrhages will resolve over a few weeks with no visual or residual abnormalities.[38]

COLOBOMAS

Colobomas are absences of or defects in normal ocular tissue and typically occur in the area of the embryonic optic fissure, which is ventral to slightly ventronasal; if colobomas are noted elsewhere, they are considered atypical. Colobomas can be unilateral or bilateral and can affect the iris, ciliary body, lens, retina, choroid, optic disc, and sclera.[3,21,22,39-42] They can occur alone or in association with multiple congenital ocular anoma-

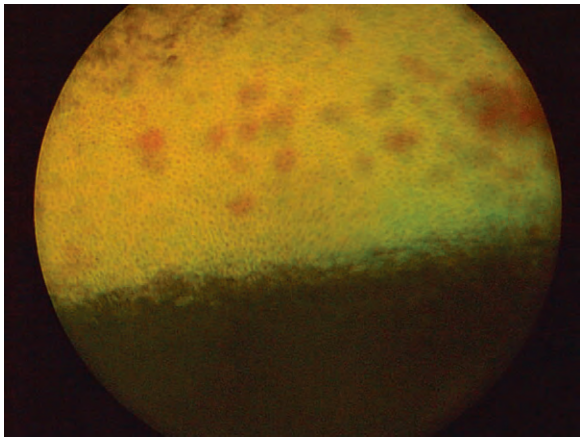


Figure 10-24. Multifocal retinal hemorrhages in a 2-day-old Standardbred foal. (Photograph courtesy Dr. Ralph Hamor, University of Illinois.)

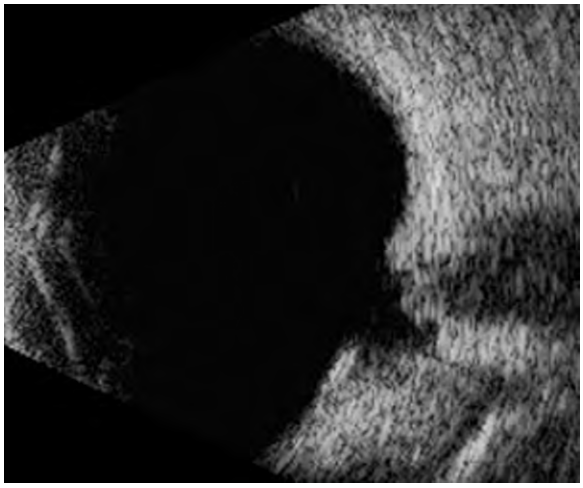


Figure 10-25. Ultrasound examination of a posterior segment coloboma. The posterior eye wall extends posteriorly toward the orbit in the area of the optic nerve.

lies. One report of a Thoroughbred with bilateral optic disc colobomas also included mention of microphthalmos, microcornea, and iris and lens abnormalities.[43] In a survey of 204 Thoroughbred racehorses in Australia, optic nerve coloboma and "unusual optic nerve head anatomy" was described in 2 horses.[13] Bilateral colobomas involving the iris, ciliary body, lens, choroid, retina, and optic nerve have been described clinically and using fluorangiography in a donkey.[42] Posterior segment colobomas have been found to affect the optic disc in horses, most commonly the Quarter Horse.[39-41] Others report a predisposition in the Appaloosa.[20] Optic nerve colobomas accounted for 1.8% of all congenital ocular anomalies in one study.[37] Small colobomas must be distinguished from the small 6 o'clock notch and peripapillary ring that can be normal in some horse optic nerves (see Fig. 10-9).[20] Severe colobomas involving the optic disc have been associated with vision deficits, specifically in the Quarter Horse (Fig. 10-25).[39-41]

CLINICAL APPEARANCE AND DIAGNOSIS

Colobomas can involve other areas of the fundus and appear white (complete absence of choroid) or orange and white (some

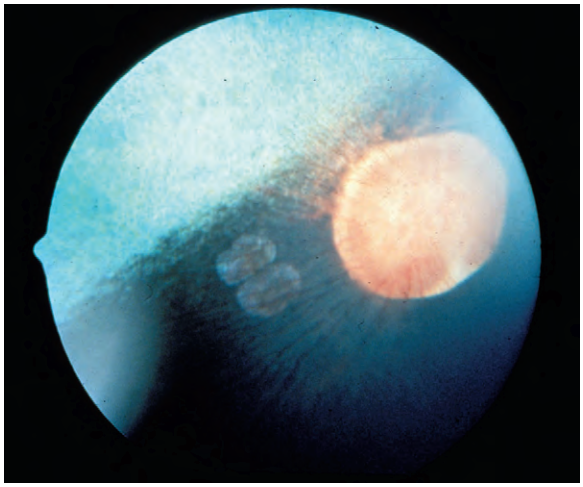


Figure 10-26. Two "window defects," or retinal pigment epithelium colobomas, are noted adjacent to the optic nerve.

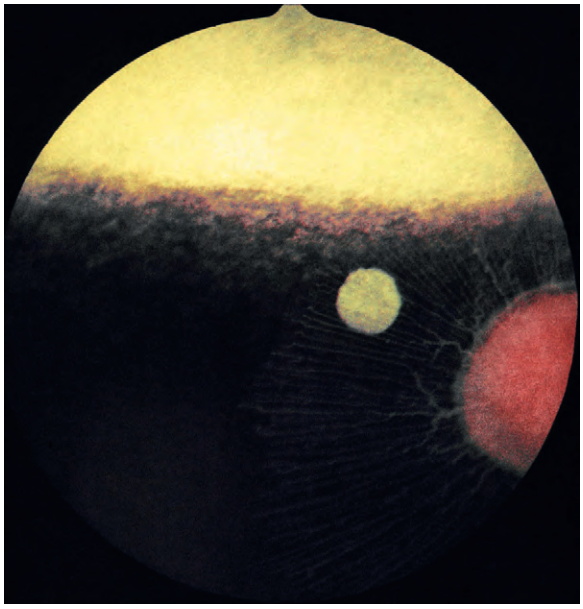


Figure 10-27. Late-phase fluorescein angiogram of a horse with a retinal pigment epithelium coloboma. (Photograph courtesy Drs. Ingo Walde and Barbara Nell, University of Vienna.)

choroidal vasculature present). Involvement of the area centralis will have a more significant impact on vision, although most horses with colobomas are asymptomatic. On ophthalmoscopic examination, the edges of the coloboma may appear recessed below the surrounding tissue.

Additionally, a "window defect" involving the RPE has been described as an RPE coloboma (Figs. 10-26 and 10-27).[3,20] This abnormality occurs most commonly in the nontapetal fundus adjacent to the optic disc and appears as a sharply demarcated focal area of decreased pigmentation. Such an abnormality has no known visual or genetic significance.

TREATMENT

There is no treatment for colobomas.

LONG-TERM PROGNOSIS AND HERITABILITY

Given the predisposition of colobomas in Quarter Horses, breeding of affected animals and their sires and dams should be avoided.

OPTIC NERVE HYPOPLASIA

Optic nerve hypoplasia can be unilateral or bilateral and is a rare congenital abnormality.[44] Optic nerve hypoplasia accounted for 0.9% of all congenital ocular anomalies in one study.[37]

CLINICAL APPEARANCE AND DIAGNOSIS

In optic nerve hypoplasia, the optic nerve appears pale, is smaller than normal, and may be depressed or recessed; retinal vessels are difficult to visualize.[20,45] Numbers of retinal ganglion cells are reduced, the pupil is dilated, and the pupillary light response is reduced or absent.[20] Nystagmus and decreased to absent vision are also observed.

TREATMENT

There is no treatment for optic nerve hypoplasia.

LONG-TERM PROGNOSIS AND HERITABILITY

The cause is not known, visual loss depends on severity, and affected horses should not be used for breeding.

RETINAL DYSPLASIA

Retinal dysplasia is a congenital malformation of the retina, with the formation of folds or rosettes that appear clinically as retinal folds or larger areas of geographic dysplasia. Retinal dysplasia can be developmental or occur as a result of inflammation. Retinal dysplasia accounted for 3.5% of all congenital ocular anomalies in one study.[37]

CLINICAL APPEARANCE AND DIAGNOSIS

On ophthalmoscopic examination, dysplasia can appear as gray or hyperpigmented areas caused by retinal disorganization and RPE proliferation, respectively (Fig. 10-28). Histologically, the NSR is folded and disorganized, often forming rosettes (Fig. 10-29). The rosettes can be single or multiple and unilateral or bilateral. Retinal folds can be associated with in utero infections and have been attributed to various viral infections. In other species, they are also seen in association with multiple congenital ocular anomalies, which are inherited. One example of multiple congenital anomalies with associated retinal dysplasia in the horse is the MCOA syndrome.[46] In addition, congenital megaloglobus has been seen with associated severe retinal dysplasia. The retinal dysplasia in one case was associated with a cartilaginous choristoma of the choroid (D. Wilkie, unpublished data) (Figs. 10-30 to 10-32).

TREATMENT

Retinal folds are nonprogressive, and no treatment is required.

LONG-TERM PROGNOSIS AND HERITABILITY

Although one author states that retinal dysplasia is not inherited,[5] not all veterinarians share this opinion. Others comment that the Thoroughbred may be predisposed to retinal dyspla-

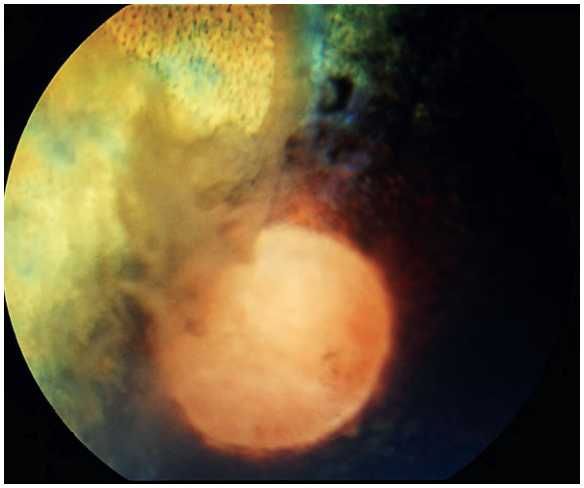


Figure 10-28. Congenital retinal dysplasia and retinal nonattachment in a foal. (Photograph courtesy Drs. Ingo Walde and Barbara Nell, University of Vienna.)

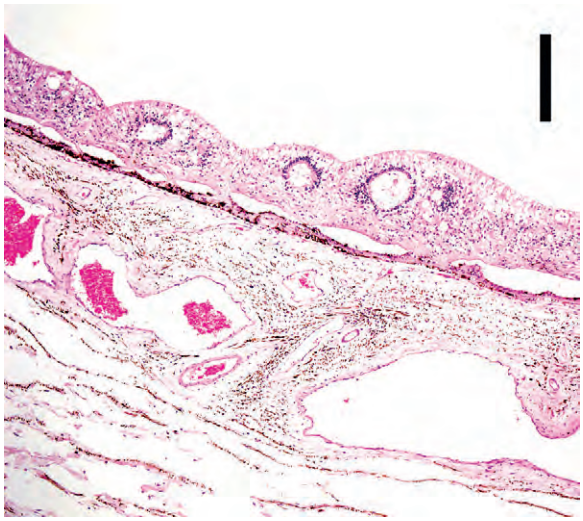


Figure 10-29. Histopathologic examination of the retina of the horse in Fig. 10-28. The retina shows retinal atrophy, disorganization, and rosette formation (H&E; bar = 400 µm). (Photograph courtesy Drs. Ingo Walde and Barbara Nell, University of Vienna.)

Figure 10-30. Gross photograph of a foal with bilateral congenital megaloglobus and corneal opacities.

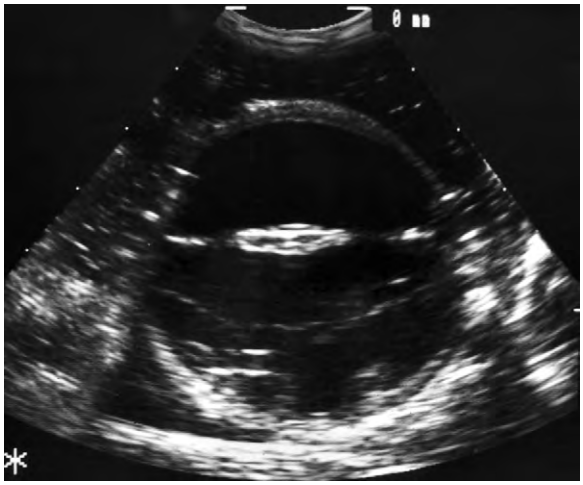


Figure 10-31. Ultrasound examination of the right eye of the foal in Fig. 10-30. Congenital megaloglobus with microphakia, vitreous dysplasia, and retinal detachment are confirmed histologically because retinal dysplasia with nonattachment is present.

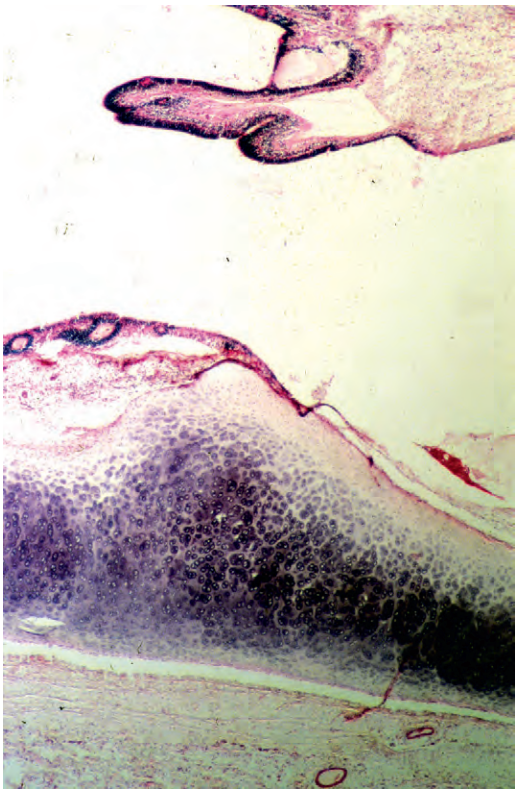


Figure 10-32. Histopathologic examination of the posterior globe of the horse in Fig. 10-30. The retina is nonattached, with retinal dysplasia and a cartilaginous choristoma of the retinal pigment epithelium or choroid.

sia.[20] Breeding of horses with severe retinal dysplasia and/or multiple congenital ocular anomalies should be discouraged.

CONGENITAL RETINAL DETACHMENT

Congenital retinal detachment can be an isolated finding or associated with the anterior segment dysgenesis of MCOA, severe retinal dysplasia, or multiple congenital defects such as coloboma, microphakia, microphthalmos, and lens luxation.[21] Retinal detachment accounted for 6.2% of all congenital ocular anomalies in one study.[37] In a study of 40 horses with retinal detachment, congenital detachment was noted in only two horses (5%).[47] One proposed cause is a failure of attachment of the NSR to the underlying RPE, which occurs as a result of incomplete invagination of the optic vesicle.[20]

CLINICAL APPEARANCE AND DIAGNOSIS

The affected eye is blind with dilated nonresponsive pupils. Clinically, a veil of gray tissue radiating forward from the optic nerve is observed. If the retina is torn from the ora and falls ventral, tapetal hyperreflection will be noted. Hyphema, cataract, and secondary glaucoma may occur as a result of chronic retinal detachment.

TREATMENT

There is no treatment for congenital retinal detachment, and affected animals should not be used for breeding.

LONG-TERM PROGNOSIS AND HERITABILITY

A predilection for the Standardbred and Thoroughbred has been suggested.[20-22] Hyphema, cataract, and secondary glaucoma may occur as a result of chronic retinal detachment.

MULTIPLE CONGENITAL OCULAR ABNORMALITIES OF THE ROCKY MOUNTAIN HORSE

Multiple congenital anterior and posterior segment abnormalities have been described in the Rocky Mountain horse, Kentucky Saddle horse, and Mountain Pleasure horse breeds.[20,46,48] The abnormalities are associated with coat color, and horses with chocolate (also termed *silver*) coat color and a white mane and tail are more severely affected.[46,48,49]

CLINICAL APPEARANCE AND DIAGNOSIS

The abnormalities can affect the cornea, iris, ciliary body, lens, and retina. The anterior segment anomalies include temporal ciliary cysts, iridal hypoplasia, iridocorneal angle abnormalities, corneal globosa, and cataract. With respect to the posterior segment, temporal peripheral retinal cysts, retinal dysplasia, RPE proliferation, focal retinal degeneration, and retinal detachment have been described in affected horses.[46] Cysts can involve the posterior iris, ciliary body, or peripheral retina and are always located temporally. Cysts can be unilateral or bilateral and affect 48% of Rocky Mountain horses examined.[46] Retinal dysplasia appears as linear folds, most commonly in the temporal retina; affects 24% of the horses examined; and is only found in association with retinal or ciliary body cysts (Fig. 10-33).[46] These lesions have been confirmed by histologic examination as retinal dysplasia, hypoplasia, rosette formation, and RPE proliferation. Proliferation of the RPE appears as pigmented, curvilinear streaks that originate and terminate at the ora and extend toward the optic disc. These pigmented streaks are believed to indicate previous retinal detachment (Fig. 10-34).[46] Retinal detachments appear to be associated with peripheral retinal cysts and thus occur temporally. Rhegmatogenous detachments were also observed in 16% of horses examined.[46]

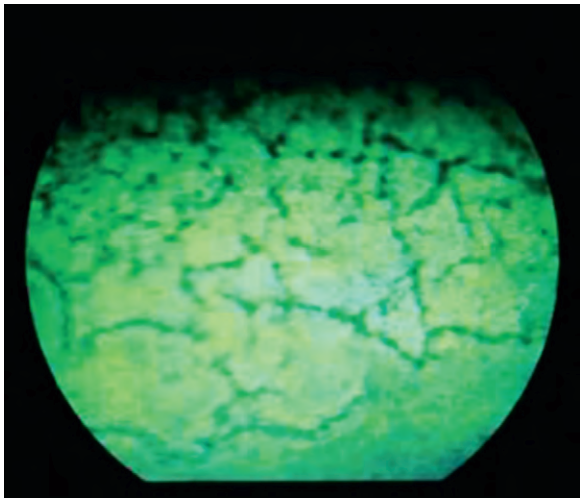


Figure 10-33. Retinal dysplasia as seen in a Rocky Mountain horse. (Photograph courtesy Dr. David Ramsey.)

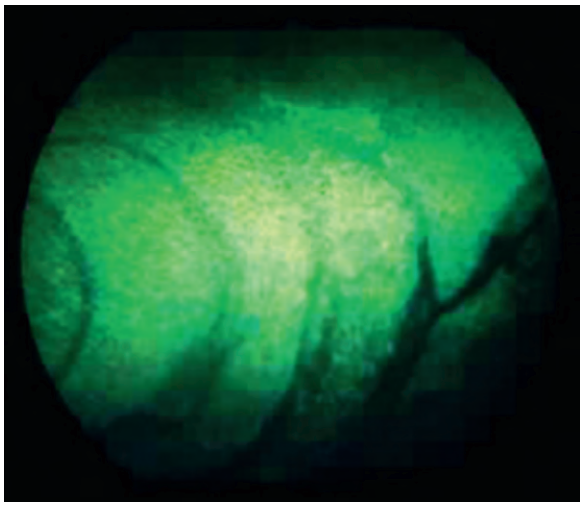


Figure 10-34. Pigment streaks of retinal pigment epithelium extending outward from the ora. These are suggestive of previous retinal detachment. (Photograph courtesy Dr. David Ramsey.)

TREATMENT

There is no treatment, and affected animals should not be used for breeding.

LONG-TERM PROGNOSIS AND HERITABILITY

The MCOA of the Rocky Mountain horse is inherited as a codominant trait with incomplete penetrance.[46,48,49] Affected horses that are heterozygous for the disease-causing allele exhibit ciliary cysts, and those that are homozygous have multiple anterior and posterior segment anomalies. The MCOA anomaly has been shown to map to a 4.9-megabase interval on horse chromosome 6.[49]

CONGENITAL STATIONARY NIGHT BLINDNESS

Congenital stationary night blindness (CSNB) has been reported in the Appaloosa and the Quarter Horse.[50-55] This condition is similar to congenital stationary night blindness in humans.[53] It has also been noted in Thoroughbreds, Paso Finos, and Standardbreds.[22,56] Affected horses have a defect in neural transmission between the photoreceptors and the inner retina, perhaps at the level of the bipolar cells.[53] Congenital stationary night blindness accounted for 3.5% of congenital ocular anomalies in one study.[37] In another study of Appaloosa horses, CSNB was present in one-third of the horses studied, and a significant association was noted between CSNB and the leopard complex gene (Lp).[55] The leopard complex gene (LP) is responsible for the white spotting patterns of the Appaloosa. Homozygosity for LP (LP/LP) is associated with CNSB in the Appaloosa.[57] Examination of candidate genes in the LP region have demonstrated a decrease in TRPM1 gene expression. TRP proteins are believed to play a role in intracellular Ca^{++} concentration, and a decreased TRPM1 expression may alter both retinal bipolar cell signaling and melanocyte function.[57]

CLINICAL APPEARANCE AND DIAGNOSIS

Affected horses have severely compromised vision in low-light conditions (nyctalopia) and may have some decreased function in day vision as well.[51,58] Owners may notice a reluctance to enter darkened areas such as barns or difficulty riding in evening conditions. Findings on posterior segment examination are normal. Some affected horses also exhibit microphthalmia, dorsomedial strabismus, nystagmus, and an unusual gaze associated with head elevation, which has been termed *star gazing* (Fig. 10-35). It has also been suggested that abnormalities in daylight vision, head elevation, and strabismus may relate to concurrent myopia.[10,20]

There are no histologic or ultrastructural differences between affected and normal equine retinas. Diagnosis can be confirmed by ERG in which a normal a wave but a decreased photopic and absent scotopic b wave are noted.[51,53] This is referred to as a *negative ERG*. A differential diagnosis would include a long-standing vitamin A deficiency. Vitamin A deficiency may also lead to complete blindness, dull brittle hair coat, and hyperkeratinization.[54]

TREATMENT

As indicated by the name, the condition is congenital and nonprogressive. There is no treatment, and affected animals should not be used for breeding.

LONG-TERM PROGNOSIS AND HERITABILITY

The abnormality is thought to be inherited in a recessive or sex-linked recessive pattern, with the defect located on the X chromosome.[5,51]

PERSISTENT HYALOID ARTERY

The hyaloid artery travels from the optic nerve anteriorly to the posterior lens capsule, where it connects with the posterior portion of the tunica vasculosa lentis. This vascular network generally disappears before or at the time of birth.[15,22] In one study of the hyaloid apparatus in neonatal thoroughbred foals, some portion of the hyaloid was present in over 80% of 169 foals examined. The entire hyaloid artery was observed in approximately 60% of foals examined. In general, the presence of the hyaloid apparatus was bilateral, symmetrical, correlated with the presence of the posterior pupillary membrane, and was

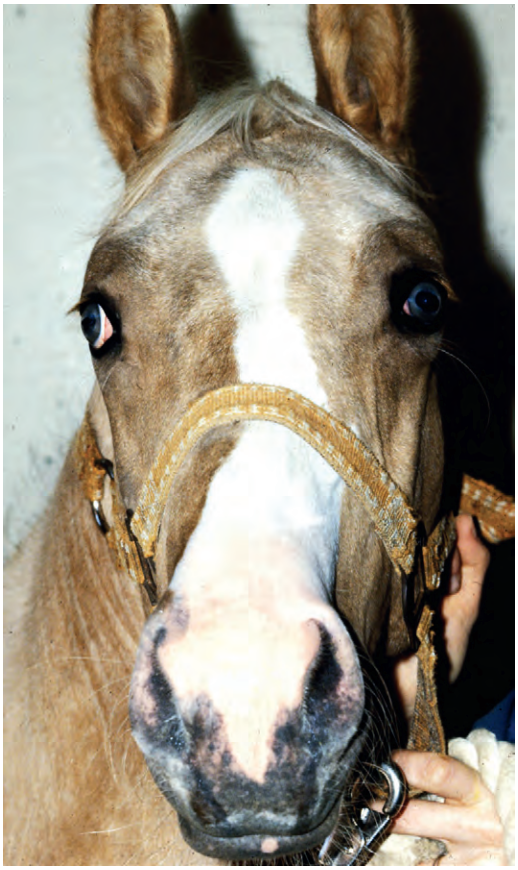


Figure 10-35. Appaloosa affected with congenital stationary night blindness, demonstrating dorsomedial strabismus and an unusual gaze associated with head elevation, termed *star gazing*.

not associated with any significant ocular problems.[59] In a survey of 204 Thoroughbred racehorses in Australia, a persistent hyaloid remnant was described in one horse.[13]

CLINICAL APPEARANCE AND DIAGNOSIS

Persistence of the hyaloid vasculature is uncommon in the horse compared with other domestic animals. It can be seen as an isolated finding or in association with other congenital anomalies such as posterior lenticonus, cataract, retinal dysplasia, coloboma, microphthalmia, or retinal detachment. If a posterior axial cataract is noted, it should be monitored for progression.

TREATMENT

No treatment is indicated.

LONG-TERM PROGNOSIS AND HERITABILITY

Most instances of an isolated persistent hyaloid artery will spontaneously regress by 6 to 9 months of age.[15] There is no known genetic component to this disease.

ACQUIRED DISEASES

OCULAR TRAUMA

The equine eye is often subject to severe traumatic injury, perhaps as a result of its prominent position in the head. Traumatic injuries are divided according to the tissues involved and the severity of the injury: contusions (overlying tissue is intact), penetrating injuries (tissue is abraded or partially cut), and perforating injuries (tissue is cut completely). Blunt trauma—whether contusive, penetrating, or perforating—generally results in more severe ocular damage than injury caused by a sharp object. Unfortunately, most ocular trauma in the horse is blunt in nature. In contrast to sharp perforating injuries, blunt trauma results in a rapid increase in intraocular pressure, an explosive rupture from the inside outward, and the expulsion of the intraocular contents (Fig. 10-36). The resulting rent in the fibrous tunic is often large and irregular, and portions of the cornea or sclera may be lost. The typical wound is one that originates at the limbus and extends forward into the cornea and posterior into the sclera. However, the posterior portion of the eye may rupture, and the horse may be presented with hyphema and decreased intraocular pressure. Ocular ultrasound examination is required for an accurate diagnosis and determination of prognosis (Fig. 10-37).

Figure 10-36. Traumatic rupture of the cornea, with expulsion of the intraocular contents as a result of blunt force trauma.

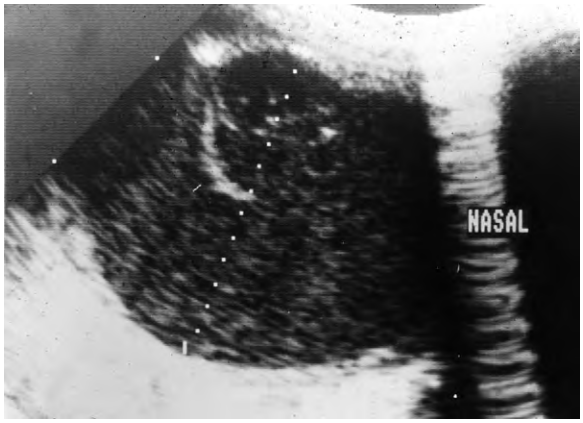


Figure 10-37. Ultrasound examination of a globe after acute traumatic hyphema. Vitreous hemorrhage and rupture of the posterior lens capsule are noted.

CLINICAL APPEARANCE AND DIAGNOSIS

Vitreous hemorrhage, lens luxation, retinal tears, retinal hemorrhage, retinal and choroidal detachment, and optic nerve

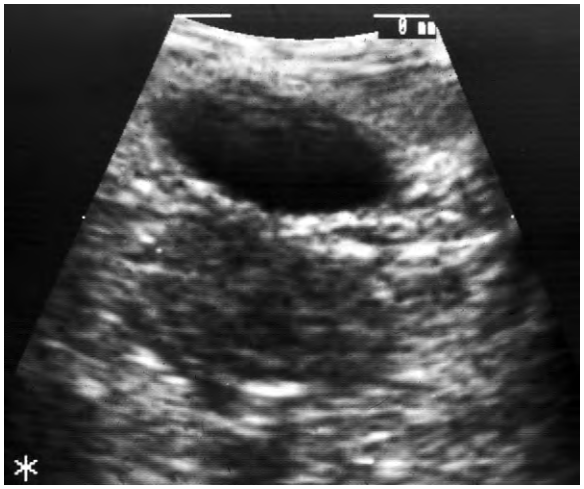


Figure 10-38. Ultrasound examination of a globe with acute blunt trauma. Lens appears anechoic, vitreous contains echoic blood, and posterior eye wall has been ruptured.

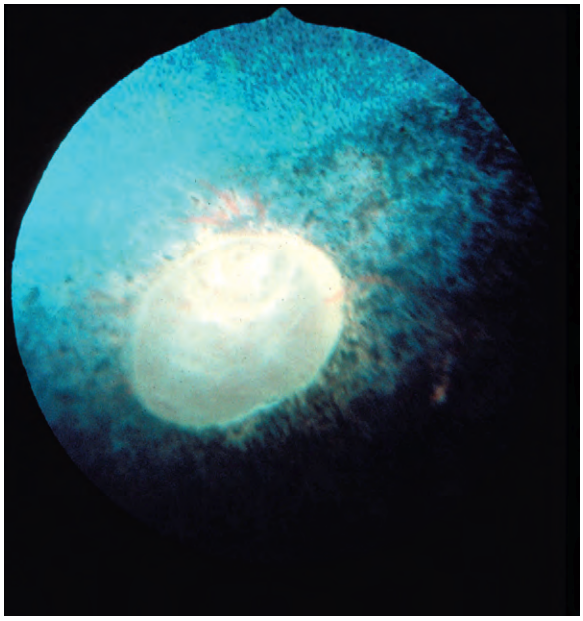


Figure 10-39. Posttraumatic optic nerve atrophy with retinal vascular attenuation and peripapillary depigmentation.

damage are all associated with blunt trauma to the eye and orbit.[22,60]

If the hyphema is complete and precludes the evaluation of intraocular structures, ocular ultrasound examination is indicated to assess the lens position, vitreous, retina, and posterior eye wall. The greatest resolution of the ocular tissues of interest is achieved with a 7.5-MHz or, preferably, a 10-MHz probe. If the cornea is intact, the probe can be placed directly on it; if the cornea is compromised, imaging can be performed through the eyelid or an offset device. Evaluation for lens rupture or luxation, vitreous hemorrhage, retinal and choroidal detachment, and posterior eye wall rupture should be performed (Fig. 10-38).

TREATMENT

Repair of these explosive ruptures is difficult, and the treatment of choice is often enucleation. If cosmetic repair is important, an intraocular silicone prosthesis can be used in some patients, provided there is sufficient tissue left to close the fibrous tunic. This procedure should be performed as soon as possible after injury. If the injury is chronic and atrophy of the globe has occurred, placement of an intraocular prosthesis is not possible. The only cosmetic alternative in these horses is an orbital implant with a cosmetic corneoscleral prosthesis.[61] This requires multiple procedures and referral to an ophthalmologist and ocularist to achieve an acceptable cosmetic outcome.

LONG-TERM PROGNOSIS

In general, damage to the posterior segment, especially in association with hemorrhage, carries a grave prognosis.

HEAD TRAUMA

Trauma to the head of the horse has been associated with acute unilateral or bilateral blindness without associated compromise of the globe. The pupil in the affected eye will be dilated, but the remainder of the findings on ophthalmic examination may be normal initially. Occasionally, retinal hemorrhage and papilledema are present. Fundic examination several weeks later may reveal optic nerve pallor, indicating optic nerve atrophy (Fig. 10-39). The cause of this lesion is hypothesized to be stretching of the optic nerve or trauma from bony fractures adjacent to the optic nerve. A small number of horses with head trauma may benefit from systemic antiinflammatory therapy in the acute phase. However, the prognosis is guarded, and treatment is usually unrewarding. For more information, see the discussion of traumatic optic neuropathy.

CHORIORETINITIS

Chorioretinitis, inflammation of the choroid and retina, may be the result of ERU or may be a manifestation of systemic disease. Chorioretinitis is the most common abnormality identified on examination of the equine fundus. ERU is a CD4+ T-cell mediated immune disease with both anterior and posterior segment manifestations. The retina has been demonstrated to be a specific target in ERU, and retinal Müller cells may play a role in this autoimmune inflammatory process.[62,63] It has been demonstrated that autoantigens S-antigen, interphotoreceptor retinoid-binding protein and cellular retinaldehyde-binding protein may also have a role in ERU.[63-66] The reader should refer to Chapters 6, 8, and 13 for complete discussions of uveitis, ERU, and ocular manifestations of systemic disease.

CLINICAL APPEARANCE AND DIAGNOSIS

The appearance of chorioretinitis on fundic examination depends on whether the lesions are active or old and on whether the etiology results in focal or diffuse changes. Active lesions are characterized by edema, cellular infiltrate, and hemorrhage or retinal detachment; they often appear gray, white, or hazy. The retina may be elevated by subretinal fluid and inflammatory cells (Figs. 10-40 to 10-42). Inactive lesions, or chorioretinal scars, appear as hyperreflective or hyperpigmented in the tapetal fundus and may appear to be depigmented or to have pigment clumping in the nontapetal fundus (Fig. 10-43). If the

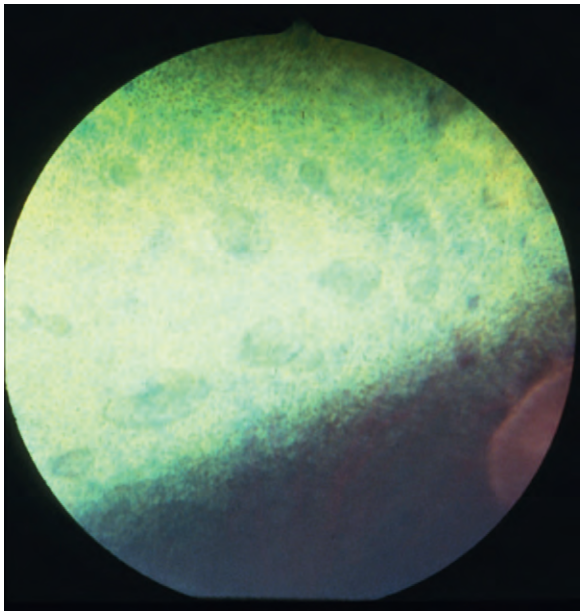


Figure 10-40. Multifocal chorioretinitis characterized by subretinal edema and tapetal hyporeflectivity. (Photograph courtesy Dr. Brian Gilger.)

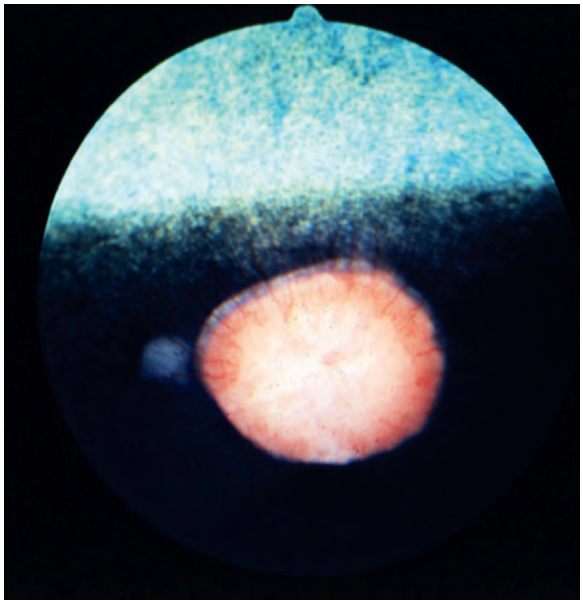


Figure 10-41. Focal area of retinitis, with cellular infiltrate seen as a gray-white lesion adjacent to the optic nerve. (Photograph courtesy Dr. Brian Gilger.)

retina was elevated during the active phase of the disease, it may reattach in a wrinkled or folded fashion, appearing as gray linear folds (Fig. 10-44). These folds are most commonly seen radiating from the optic nerve (Fig. 10-45). Chorioretinitis lesions can be focal or diffuse and unilateral or bilateral and are most commonly seen in the peripapillary region. The "classic" inactive chorioretinal scar is seen circumpapillary and is termed a *butterfly lesion* (Fig. 10-46). This is an area of depigmentation and pigment clumping that radiates nasally and temporally from the optic nerve. Lesions can be confined to one side of the optic nerve. During the active phase of the disease, the peripapillary retina may be elevated; soft or hard

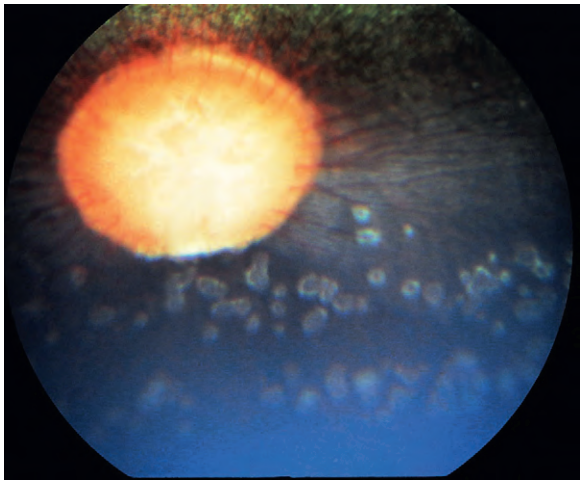


Figure 10-42. Multifocal chorioretinitis lesions. (Photograph courtesy Drs. Ingo Walde and Barbara Nell, University of Vienna.)

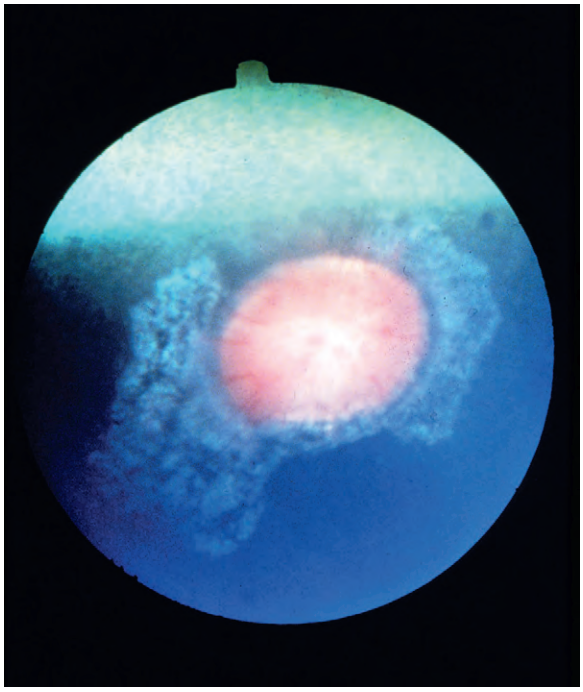


Figure 10-43. Peripapillary chorioretinal scar, also called a *butterfly lesion*.

exudates may be present; and retinal vasculitis, seen as indistinct margins and vascular cuffing, may be observed.[22] This lesion can be associated with ERU, but the anterior segment often appears normal (Fig. 10-47). The prevalence of peripapillary chorioretinal lesions in otherwise normal eyes has been reported to be 5% to 8%.[4,67] In a survey of 204 Thoroughbred racehorses in Australia, peripapillary butterfly lesions were described in 5 horses (2.5%), with an additional 16 horses (7.9%) described with linear peripapillary hyperpigmentation bands.[13] Posterior segment changes in the absence of anterior segment disease can and do occur with ERU; however, any optic neuritis or peripapillary chorioretinitis could result in similar changes. See Chapter 8 for more information on ERU and the equine retina.

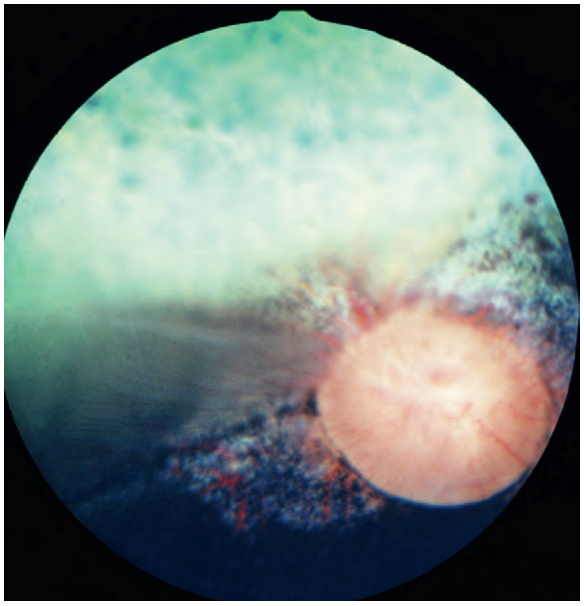


Figure 10-44. Peripapillary depigmentation and associated retinal detachment. (Photograph courtesy Drs. Ingo Walde and Barbara Nell, University of Vienna.)

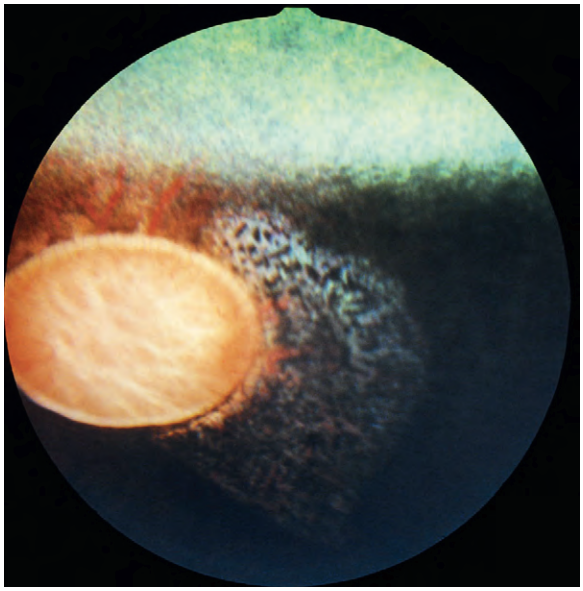


Figure 10-46. Peripapillary depigmentation and associated retinal vascular attenuation. (Photograph courtesy Drs. Ingo Walde and Barbara Nell, University of Vienna.)

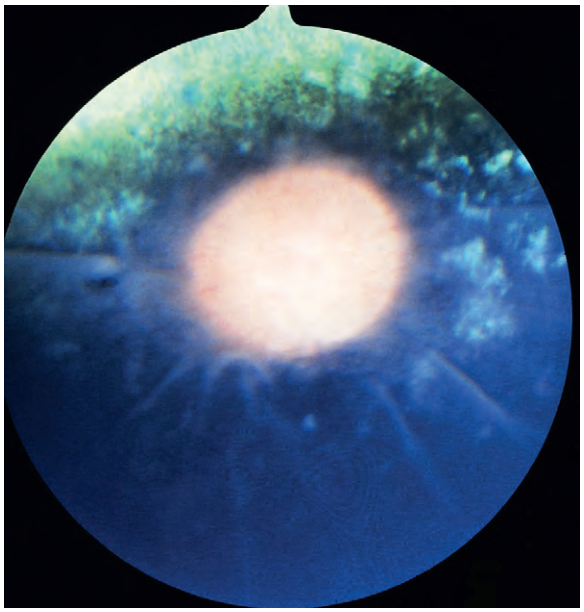


Figure 10-45. Peripapillary edema, retinal elevation, and retinal folds secondary to retinal detachment. (Photograph courtesy Drs. Ingo Walde and Barbara Nell, University of Vienna.)

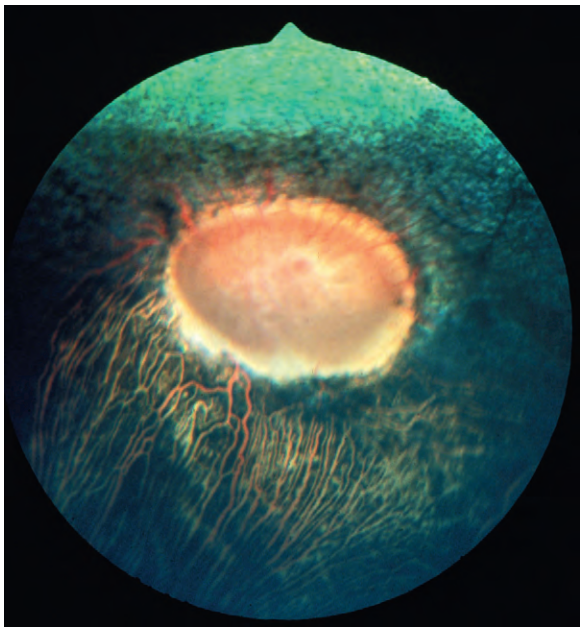


Figure 10-47. Choroidal depigmentation and degeneration of the ventral optic nerve after inflammation.

Immunohistochemical examination of the retinas from horses with naturally occurring ERU and from ponies with experimental *Leptospira*-induced uveitis demonstrated a range of findings.[68] Minimal to severe retinal changes were observed and were characterized by major histocompatibility complex class II antigen-expressing cells and T lymphocytes, suggesting an immunologic cause of retinal damage.[68] Ponies with *Leptospira*-induced uveitis demonstrated B lymphocytes that were seroreactive for *Leptospira interrogans* serovar Pomona.[68]

Additional studies have confirmed chorioretinal changes in horses with ERU that are characterized by T-lymphocyte infiltration and destruction of photoreceptor outer segments and inner retina.[69] T-cell-rich lymphoid follicle formation was noted in the iris and choroid.[69] Analysis of vitrectomy samples from horses with ERU demonstrates immunoglobulin G antibodies and autoreactive T lymphocytes specific for retinal antigens, which provides support for the possibility of a local autoimmune-mediated disease involving the posterior segment.[70] For a complete discussion, see Chapter 8.

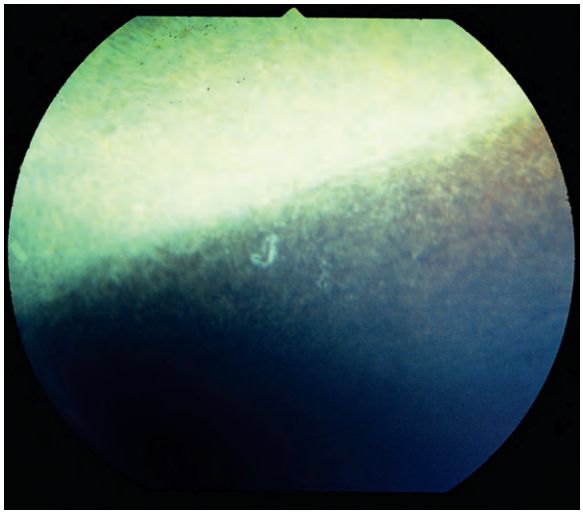


Figure 10-48. Focal "bullet-hole" lesion at the tapetal/nontapetal junction.

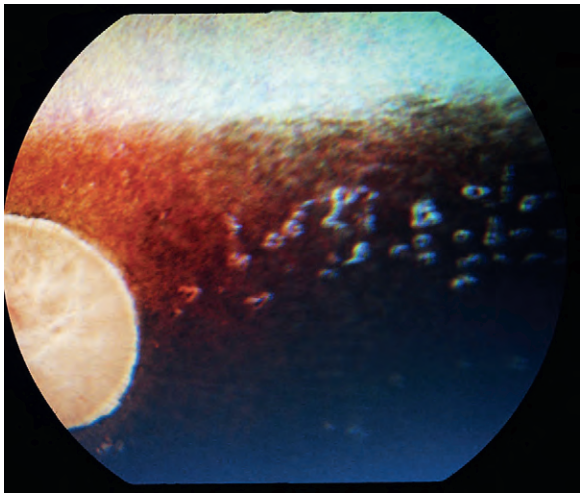


Figure 10-49. Bullet-hole lesions at the tapetal/nontapetal junction adjacent to the optic nerve. (Photograph courtesy Drs. Ingo Walde and Barbara Nell, University of Vienna.)

In experimental infection with EHV-1, chorioretinal lesions have been produced 6 to 8 weeks after intranasal infection.[24,71] On the basis of findings from fluorescein angiography, it is hypothesized that EHV-1 infection can result in infarction of the choroidal vasculature and subsequent focal loss of RPE. Clinically this appears as multifocal white lesions in the peripapillary nontapetal fundus.[24]

Focal chorioretinopathy, termed *bullet-hole chorioretinitis*, has been described.[5,21,22] Lesions are generally multifocal, appear ventral to the optic disc, and are white with a pigmented center (Figs. 10-48 to 10-50). They are small and do not appear raised or depressed. On histologic examination, a loss of normal retinal architecture, with RPE hyperplasia and migration of RPE cells into the retina can be observed.[15] It has been suggested that these lesions may be the result of previous chorioretinitis and may have a viral cause.[21] An association with respiratory disease in foals has been suggested.[22] Lesions are similar in appearance to those described in experimental EHV-1 infection.[24] These lesions have been seen as incidental findings in many horses of all age groups (D. Wilkie, unpublished data). One report suggests that 10% to 20% of horses are affected with bullet-hole scars.[22] In a survey of 204 Thoroughbred racehorses in Australia, peripapillary inactive bullet-hole chorioretinal lesions were described in 108 (52.9%) individuals. In the majority of these horses, the lesions numbered fewer than 20, while in five horses (2.5%) the lesions numbered more than 20 and were considered potentially vision threatening.[13] They are nonprogressive, and although they may be postinflammatory lesions, are best considered incidental findings.

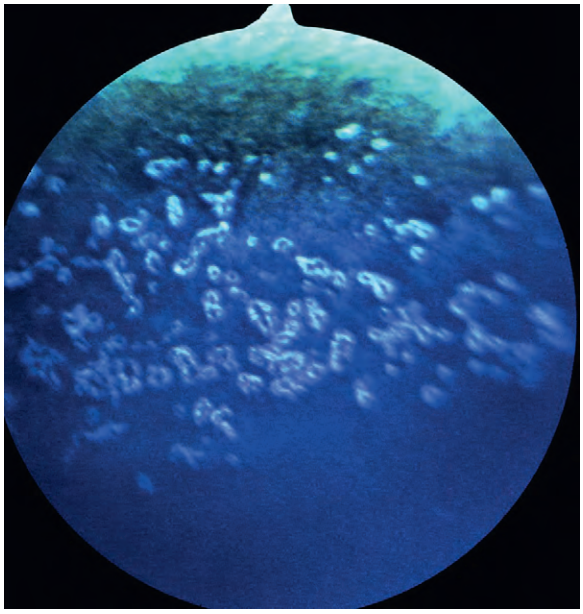


Figure 10-50. Numerous bullet-hole lesions at the tapetal/nontapetal junction adjacent to the optic nerve. (Photograph courtesy Drs. Ingo Walde and Barbara Nell, University of Vienna.)

A more diffuse chorioretinitis has been described in which lesions are vermiform, circular, or band shaped and are hyperreflective in the tapetum and depigmented in the nontapetal region (Fig. 10-51).[22] Similar lesions have occurred in association with severe blood loss. Optic nerve degeneration may be present in some instances. Vision is generally decreased, especially if the optic nerve is affected. Trauma and vascular infarction are also possible causes.[22]

Chorioretinitis or panuveitis may also be a manifestation of systemic disease and has been documented with equine infectious anemia,[72] adenovirus,[73,74] West Nile virus,[75,76] neonatal septicemia,[77] *Rhodococcus equi*,[76,78] *Streptococcus equi* var. *equi*,[79,80] Lyme disease,[74,78] brucellosis,[81] *Leptospira interrogans* Pomona, equine granulocytic ehrlichiosis,[82] toxoplasmosis,[83] *Halicephalobus gingivalis (H. deletrix)*,[84,85] and onchocerciasis.[86] In general, any infectious or parasitic agent that is hematogenously disseminated, is capable of causing vasculitis, or exhibits aberrant migration could result in anterior or posterior uveitis. Neonatal foals with septicemia or bacteremia are often presented with anterior uveitis that may occasionally extend to the posterior segment as a panuveitis. For a complete discussion of the effects of systemic disease on the equine eye, see Chapter 13.

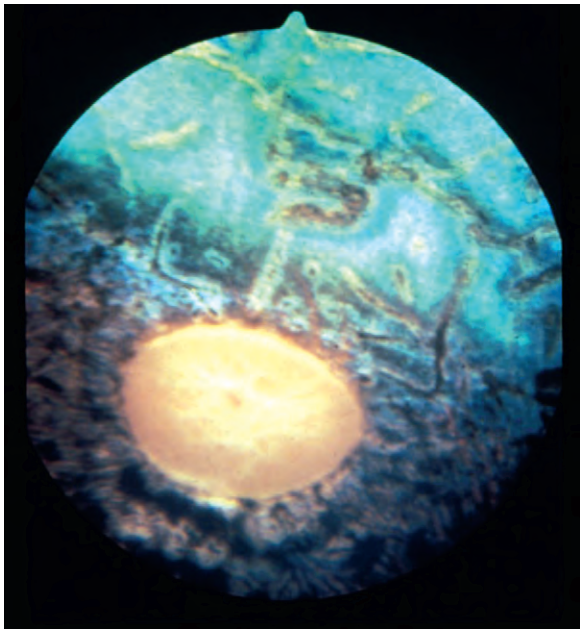


Figure 10-51. Retinal and optic nerve degeneration caused by severe blood loss.

TREATMENT

Treatment is directed at the underlying cause, but there is no specific medical or surgical therapy for focal or diffuse chorioretinitis. Systemic nonsteroidal therapy may help minimize inflammation and subsequent damage, and systemic corticosteroids may be used at an antiinflammatory dose, provided there is no contraindication.

LONG-TERM PROGNOSIS

Focal lesions are usually of no significance. Although it is hypothesized that numerous or diffuse lesions could result in visual changes, clinically these lesions appear to have no detectable effect on vision. However, vision should be assessed in affected animals, and attention should be paid to the purpose of each animal and the effect vision loss may have on function. In one report, when these lesions numbered more than 20, the authors considered this to be potentially vision threatening.[13] Lesions in the peripapillary region may have a greater impact on vision because they will affect a larger proportion of axons. In cases of peripapillary depigmentation, the veterinarian should perform a careful examination of the anterior segment, looking for subtle atrophy of the corpora nigra, pigment on the anterior lens capsule, and yellowing of the lens or vitreous—all of which suggest previous inflammation and support a diagnosis of ERU.

RETINAL DETACHMENT

A retinal detachment is the separation of the NSR from the outer RPE. The retina is normally supported in place by the vitreous and the RPE, which has metabolic pumps that maintain an osmotic gradient that keep the NSR in apposition with the RPE. The retina can detach as a result of fluid accumulation between the NSR and RPE, a retinal tear and migration of fluid from the vitreous into the intraretinal space, blunt force trauma, or traction toward the vitreous secondary to resolution of vitreal hemorrhage or after hyalitis. Accumulation of fluid between the NSR and RPE is most commonly the result of inflammation, with ERU being the most common cause. This is termed a *bullous detachment*, and reattachment can occur if the inflammation is resolved and the RPE is able to pump the fluid out of the intraretinal space. The retina may reattach with folds or wrinkles, most commonly radiating outward from the optic nerve. Such folds indicate previous bullous detachment.

Retinal detachments associated with a retinal tear are termed *rhegmatogenous detachments*. In such cases, fluid migrates from the vitreous side of the retina through the tear, forcing the NSR from the RPE. Dorsal tears are more likely to progress as gravity works to pull the retina down. Trauma, rupture of peripheral retinal cysts, anomalies of the RMH, and complications from intraocular surgery such as phacoemulsification or vitrectomy are all associated with rhegmatogenous detachments.

In a retrospective study of 40 horses (46 eyes) with retinal detachment, the detachment was unilateral in 34 horses and bilateral in six horses. The detachment was partial in 14 horses and complete in 32 horses. The diagnosis of retinal detachment was made clinically in 20 eyes and on ultrasound in 26 eyes. While there was no sex or breed predilection for retinal detachment, the mean age of affected horses (8.5 years) was significantly younger than the general hospital population. The etiology was diagnosed to be ERU in 27 horses (33 eyes, or 67.5%) and trauma in 10 horses (10 eyes, or 25%).[47] The prognosis for vision in horses with retinal detachment is grave, with many eyes going on to enucleation or evisceration.[47]

CLINICAL APPEARANCE AND DIAGNOSIS

Clinically, a retinal detachment can be partial or complete (Fig. 10-52). Partial detachments are not associated with detectable vision loss by the owner in most instances. They are most often discovered on a prepurchase examination or during examination of an eye for anterior segment disease. A focal bullous detachment appears as an elevated hazy area of retina with subretinal fluid. Bullous detachments may occur as a result of systemic disease (see the discussion of chorioretinitis).

With a complete detachment, the retina appears as a gray, floating veil of tissue extending into the vitreous toward the lens (see Fig. 10-44). If it is displaced far enough anteriorly, the retina may be visible by penlight examination. The retina is normally attached at the optic nerve and ora ciliaris retinae. As a consequence of a retinal detachment, the retina may tear at the ora and fall ventrally, obscuring the optic nerve (Fig. 10-53). This is called a *giant tear*. Once a retinal detachment has progressed to this stage in a horse eye, little treatment can be offered.

Traction detachments occur after intravitreal hemorrhage or inflammation, termed *hyalitis*. Trauma, ERU, and extension of chorioretinitis can result in vitreous hemorrhage and hyalitis. Traction bands may form, appearing as tan to gray strands in the vitreous. These may attach to the inner retina and undergo contracture, elevating the retina and leading to a retinal detachment. Treatment of traction retinal detachments consists of a vitrectomy and severing of the traction bands, but concurrent intraocular disease generally prevents this as a viable option.

Retinal detachment may also be noted in horses presented for examination because of a congenital or juvenile cataract or

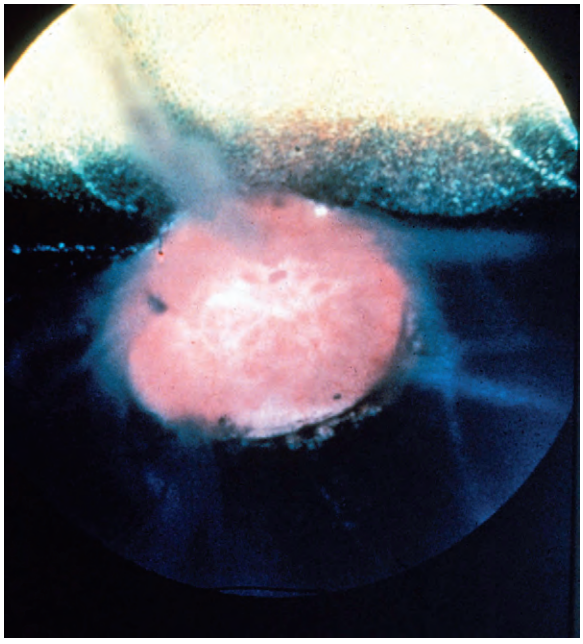


Figure 10-52. The peripapillary retina is detached, appearing as a gray veil of tissue over and around the optic nerve.

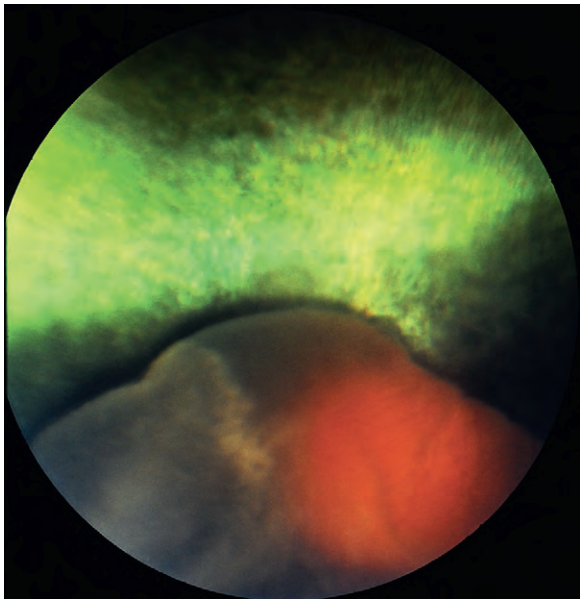


Figure 10-53. Complete retinal detachment with a giant tear and disinsertion as seen on fundic examination. The retina has fallen ventrally and is lying over and obscuring the optic nerve head. (Photograph courtesy Drs. Ingo Walde and Barbara Nell, University of Vienna.)

a cataract caused by chronic uveitis. An ocular ultrasound examination is indicated to evaluate the posterior segment in horses with a mature or hypermature cataract (Figs. 10-54 and 10-55).

TREATMENT

The underlying cause of inflammation needs to be managed, and if management is successful, a bullous detachment may

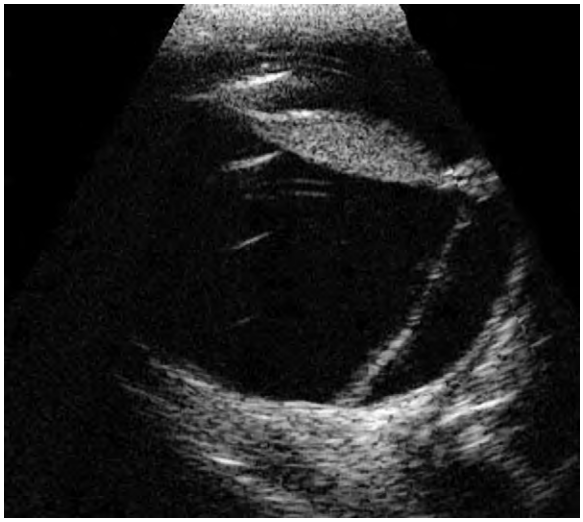


Figure 10-54. Ultrasound examination of a horse presented for cataract evaluation. The retina is partially detached, with a hyperechoic line present in the vitreous extending from the optic nerve posteriorly to the ora anteriorly. The lens is cataractous based on its echogenicity and is reduced in anterior-posterior axial dimension, indicating a hypermature cataract with resorption.

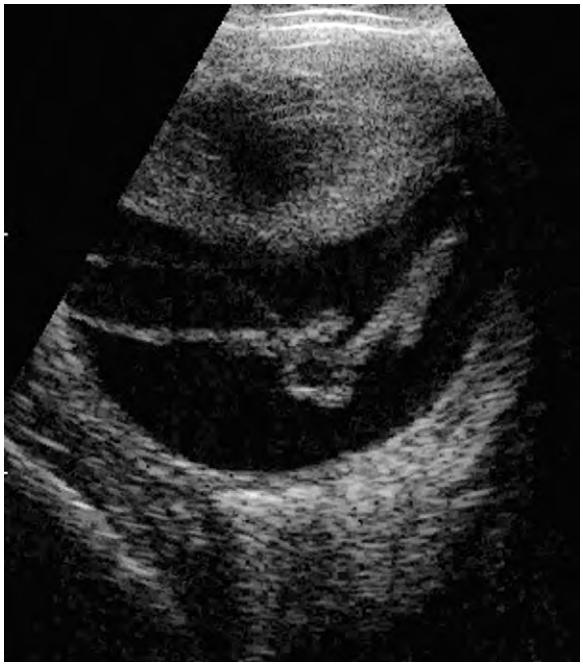


Figure 10-55. Complete retinal detachment with a mature cataract.

reattach if the inflammation is resolved and the RPE is able to pump the fluid out of the intraretinal space.

If detected early, retinal tears (rhegmatogenous detachments) can be isolated and prevented from progressing by laser retinopexy. The technique consists of delivering laser energy across the pupil through an indirect ophthalmoscope and a condensing lens. The diode laser is the instrument of choice, delivering a wavelength of 810 nm, which is preferentially absorbed by melanin. The energy is transformed into heat, resulting in thermal coagulation and a focal scar. Multiple scars are created to surround and isolate the tear, preventing progression of the detachment. In the future, retinal reattachment and

endolaser surgery, techniques used in human and canine eyes, may become applicable for the equine retina.

Treatment of traction retinal detachments consists of a vitrectomy and severing of the traction bands, but concurrent intraocular disease generally prevents this as a viable option.

LONG-TERM PROGNOSIS

The prognosis for a retinal detachment depends on the severity, underlying cause, and chronicity of the lesions.

RETINAL DEGENERATION

Retinal degeneration is far less common as a primary disease in horses than in dogs and cats. Primary retinal degeneration or progressive retinal atrophy will be bilateral and progressive, and Thoroughbreds may be predisposed.[20,22] Affected horses show progressive vision loss with areas of nontapetal depigmentation and hyperpigmentation, and in the later stages, optic nerve atrophy.[22] Similar changes can occur in association with aging and are referred to as *senile retinal degeneration*.[20,87] Retinal degeneration has also recently been found to occur in horses infected with the Borna disease virus.[88] It is thought that the BDV spreads via the CSF and intra-axonal transport from the CNS along the optic nerve and to the retina.[88] In one study of 83 geriatric horses, 35 animals and 64 eyes were noted to have senile retinopathy or retinal degeneration.[89] The prevalence of senile retinal degeneration increases with age.[89]

CLINICAL APPEARANCE AND DIAGNOSIS

Retinal degeneration appears as hyperreflective changes in the tapetal retina and as multifocal depigmentation and hyperpigmentation in the nontapetal retina (Fig. 10-56).[20] The optic nerve becomes pale, and the peripapillary retinal vessels are attenuated. Vision loss may begin with nyctalopia (night blindness) and progress to day vision loss. In one study, most cases of senile retinal atrophy observed were bilateral and most common in the peripapillary region.[89] Some of these cases were confirmed histologically by a variable loss of inner and outer retinal layers and retinal gliosis.[89] In other cases, a focal peripheral retinal degeneration associated with age has been described.[19] Peripheral cystoid retinal degeneration has also been noted in some geriatric eyes.[19,44,89] Peripheral cystoid retinal degeneration occurs at the ora and is observed in many species. Although generally an incidental finding, it can predispose to rhegmatogenous retinal detachment if a cyst ruptures. Unilateral retinal degeneration can be associated with glaucoma, trauma, or vascular ischemia.

A lysosomal storage disease, neuronal ceroid lipofuscinosis, has also been described in three horses that demonstrated neurologic symptoms and vision loss in one instance.[90] Clinical symptoms were noted by 1 year of age, and euthanasia was performed by 1.5 years of age. Eosinophilic, autofluorescent material was found in the perikarya of neurons in the brain, spinal cord, retina, and mesenteric ganglia.[90] Immunohistochemistry confirmed the diagnosis as ceroid lipofuscinosis.

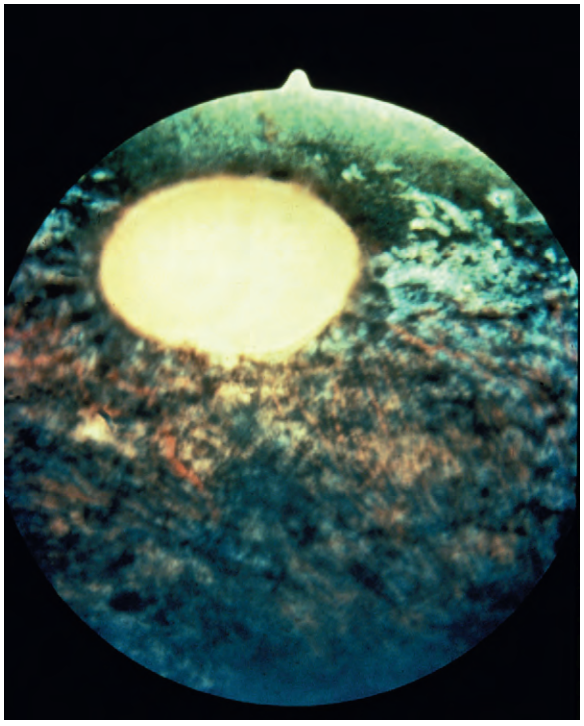


Figure 10-56. Retinal and optic nerve degeneration. Optic nerve pallor, pigment clumping, and depigmentation are all present.

TREATMENT

There is no treatment for retinal degeneration, and affected animals should not be used for breeding unless a definitive noninherited etiology can be documented.

LONG-TERM PROGNOSIS

The long-term prognosis for retinal degeneration in general is good, because the lesion is usually mild and slowly progressive; however, the prognosis depends on severity and the underlying cause. Neuronal ceroid lipofuscinosis is an inherited neurodegenerative disorder, and affected horses and their parents and siblings should not be used for breeding.

EQUINE MOTOR NEURON DISEASE

Equine motor neuron disease (EMND) is a neurodegenerative disease that occurs as a result of a chronic dietary deficiency of the antioxidant, vitamin E.[91,92] Ceroid-lipofuscin subsequently accumulates in the RPE in the tapetal and nontapetal fundus (Fig. 10-57).[91]

CLINICAL APPEARANCE AND DIAGNOSIS

On examination with an ophthalmoscope, equine motor neuron disease appears as an irregular, reticulated, or honeycomb pattern of accumulations of yellow-brown to black pigment in the tapetal and nontapetal retina (Figs. 10-58 and 10-59). In one study of 42 EMND-affected horses, 40 had ophthalmoscopic lesions.[91] Although vision impairment is inconsistent, a 50% reduction in the electroretinogram b-wave amplitude has been documented.[91] The ophthalmoscopic findings are used in conjunction with the musculoskeletal signs to make a diagnosis of EMND. The plasma vitamin E levels in unsupplemented EMND-affected horses has been found to be less than 1 µg/mL.[91] Clinically, horses affected with EMND may exhibit weight loss, weakness, muscle atrophy, trembling, low head carriage, and an abnormal stance. In North America, the risk factors for a horse having EMND were absence of grazing for more than a year and provision of poor quality hay; however,

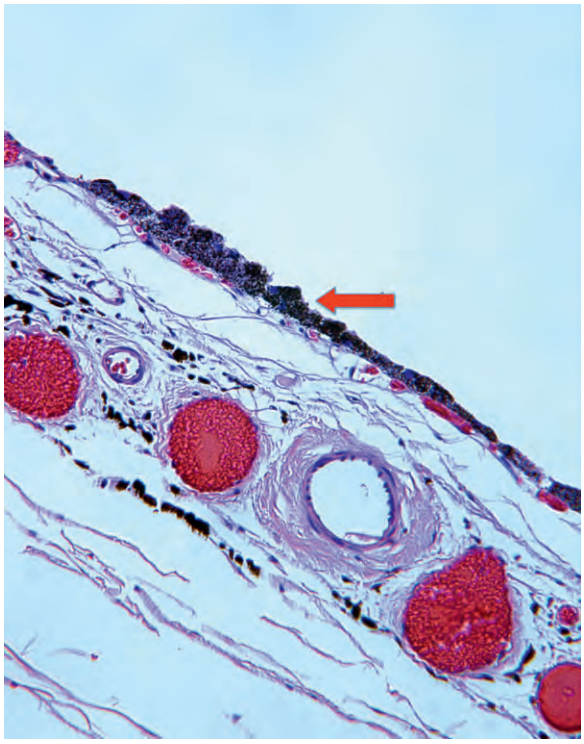


Figure 10-57. Histopathologic examination of the choroid and retinal pigment epithelium (RPE) of a horse with equine motor neuron disease. Note the accumulation of ceroid-lipofuscin in the RPE *(arrow)*.

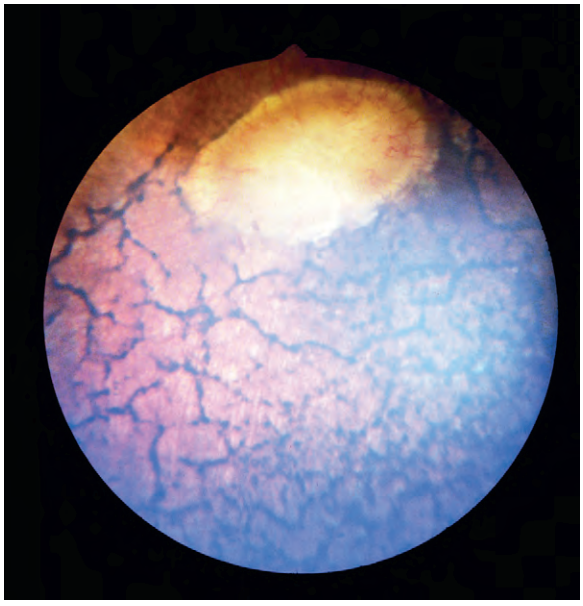


Figure 10-58. Optic nerve and nontapetal fundus of a horse with equine motor neuron disease. Note the honeycomb pattern of pigment deposits in the retinal pigment epithelium.

EMND has been described in Europe in horses with access to adequate pasture.[93,94]

TREATMENT

Supplementation with vitamin E and provision of fresh forage may stabilize the neurologic signs but do not appear to reverse the RPE changes. See Chapter 13 for further information.

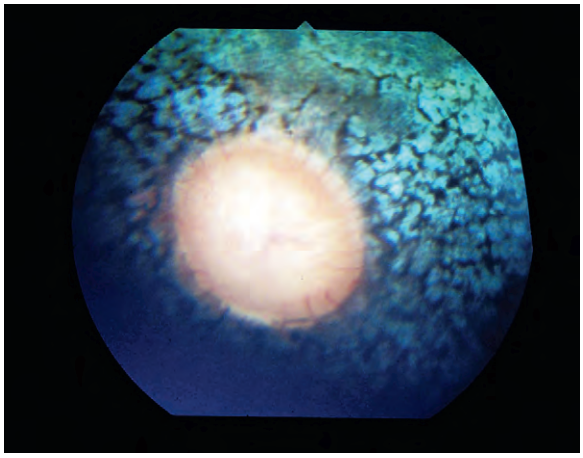


Figure 10-59. Tapetal photograph of a horse with equine motor neuron disease.

LONG-TERM PROGNOSIS

The prognosis depends on severity of disease and response to therapy.

PHOTIC HEAD SHAKING

A condition of head shaking or head tossing induced by exposure to light and eliminated by blindfolding, darkened environment, and contact lenses has been reported in the horse.[95,96] The problem is usually seen in the spring and summer, is exacerbated by exercise, and may be accompanied by sneezing, snorting, and nasal rubbing.[95]

CLINICAL APPEARANCE AND DIAGNOSIS

Differential diagnoses for photic head shaking include middle ear disorders, ear mites, guttural pouch mycosis, other ocular disorders such as vitreous floaters or uveal/corpora nigra cysts, and nasal and dental disease.[95] Findings on ophthalmic examination in animals with photic head shaking are normal. It is hypothesized that an optic-trigeminal response is occurring, with optic stimulation resulting in referred stimulation in areas innervated by the trigeminal nerve.[95]

TREATMENT

Oral administration of cyproheptadine (0.3 mg/kg) (Sidmark Laboratories Inc., East Hanover, NJ) every 12 hours has been effective in several horses.[95,96] Cyproheptadine is an antihistamine (H1 blocker) and a serotonin antagonist and is hypothesized to alleviate photic head shaking by moderating the trigeminal nerve sensation, having a central effect on melatonin, or inducing anticholinergic activity.[95] Bilateral infraorbital neurectomy has also been used for medically refractive cases. Before surgery, an infraorbital nerve block is performed to determine whether this procedure alleviates clinical signs and is warranted.[95,96]

LONG-TERM PROGNOSIS

Prognosis depends on severity of the condition and the response to treatment.

OPTIC NERVE DEGENERATION OR ATROPHY

Atrophy of the optic nerve occurs as a result of ocular and cranial trauma, inflammation, glaucoma, ischemia, pituitary neoplasia, sinusitis, and compression. Recently a report of sinusitis involving the sphenopalatine sinuses has been reported to result in optic nerve degeneration and blindness in three horses.[97] Distension of the sphenopalatine sinuses secondary to infection resulted in pressure on the optic nerves, with subsequent atrophy. Acute blood loss has also been implicated in optic nerve degeneration, with or without retinal degeneration (see Fig. 10-51).[44,98]

CLINICAL APPEARANCE AND DIAGNOSIS

Immediately following traumatic optic nerve degeneration, the pupil will be fixed and dilated, and the optic nerve will appear normal on ophthalmoscopic examination. If the lesion is unilateral, there will be an absent consensual PLR from the affected eye and an absent dazzle reflex in the affected eye. In many instances, on examination several days after the onset of sudden blindness, peripapillary edema/exudates are observed, and the optic nerve may appear hyperemic. Regardless of the cause, optic nerve pallor, visualization of the lamina cribrosa, and peripapillary vascular attenuation are common endpoints. If inflammation has been present, peripapillary depigmentation and pigment clumping may be present. Orbital mass lesions can result in compression of the optic nerve and are often also associated with exophthalmos (Fig. 10-60). Orbital masses can be inflammatory or neoplastic. Lymphosarcoma and extraadrenal paraganglioma are the most common equine orbital neoplasms.[99] Magnetic resonance imaging or CT scan may be of value in cases where trauma or sinusitis is suspected as the cause of the optic nerve degeneration.[97] Glaucoma in the horse is typically caused by intraocular inflammation and ERU. Chronic glaucoma will result in buphthalmia, corneal edema, lens luxation, and retinal and optic nerve degeneration (Fig. 10-61).[35] In one study of 83 geriatric horses, optic nerve atrophy was observed in seven eyes of four horses.[89]

TREATMENT

There is no treatment for optic nerve atrophy. Systemic antiinflammatory therapy implemented immediately following cranial trauma does not appear to affect long-term outcome. Treatment of sphenopalatine sinusitis has been associated with a transient improvement in vision, but vision loss progressed following cessation of treatment.[97] Glaucoma management and control of IOP may help prevent further optic nerve degeneration.

LONG-TERM PROGNOSIS

The prognosis for vision is poor.

TRAUMATIC OPTIC NEUROPATHY

Blunt trauma to the head can result in sudden unilateral or bilateral blindness.[60,100-102] Trauma may include rearing or falling backward, striking the poll, or blunt injury to the side of the face caused by a kick, twitch handle, or other blunt device. The trauma may result in fracture of the basisphenoid bone and compression or hemorrhage in the intracanalicular area of the optic nerve. Additionally, motion of the brain away from the fixed intracanalicular portion of the optic nerve may result in neuropraxia of the retinal ganglion cell axons. Cranial trauma may result in unilateral or bilateral optic nerve degeneration.

CLINICAL APPEARANCE AND DIAGNOSIS

The pupil is fixed and dilated, with absent menace response in the affected eye and an absent consensual PLR to the contralateral eye in the case of a unilateral lesion. Initially, the optic nerve appears normal on fundic examination. Papilledema, focal hemorrhages, hyperemia and accumulations of axoplasmic materials may occur in the first 24 to 48 hours but are not seen in all cases (Fig. 10-62). Within 2 to 4 weeks, the optic nerve becomes pale, and the fibers of the lamina cribrosa become apparent as the axons of the retinal ganglion cells disappear (see Fig. 10-39). Over time, atrophy of the NSR and hypertrophy of the RPE—which appears clinically as vascular attenuation, tapetal hyperreflectivity, and areas of hyperpigmentation—will be observed on histologic examination.[100]

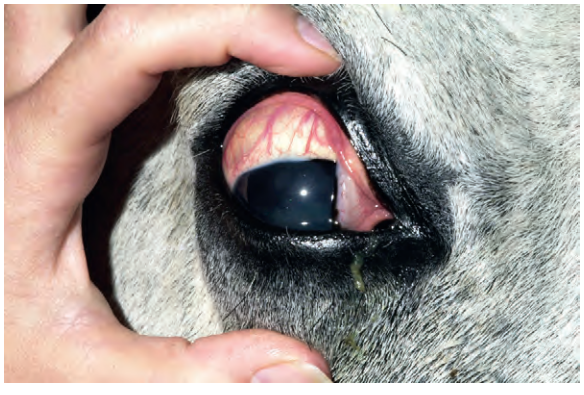


Figure 10-60. Exophthalmos and strabismus due to orbital lymphosarcoma.

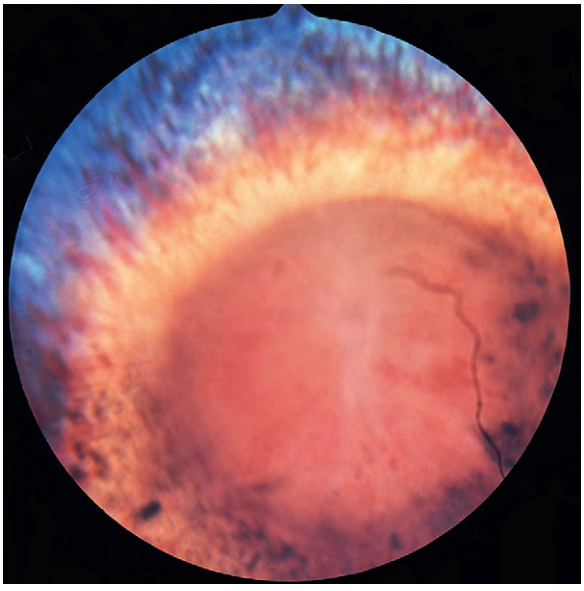


Figure 10-61. Optic nerve atrophy with retinal vascular attenuation, peripapillary depigmentation, and cupping secondary to chronic glaucoma. (Photograph courtesy Drs. Ingo Walde and Barbara Nell, University of Vienna.)

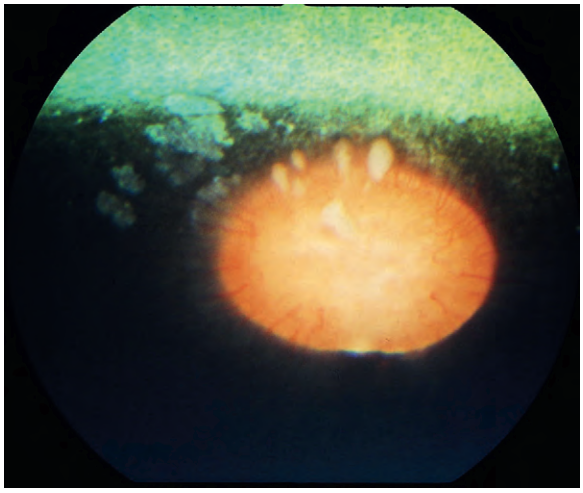


Figure 10-62. Peripapillary white exudates, likely axoplasmic material, are observed 10 hours following an observed head trauma and associated optic nerve blindness. This eye was blind with a dilated, nonresponsive pupil. (Photograph courtesy Drs. Ingo Walde and Barbara Nell, University of Vienna.)

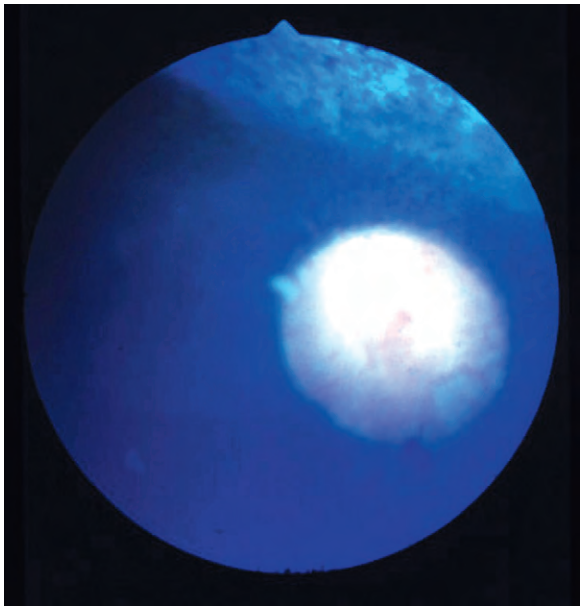


Figure 10-63. Twenty-four hours after occlusion of the vascular supply to the optic nerve, the nerve is edematous, and white axoplasmic material is seen at the margin of the optic nerve.

TREATMENT

Immediate treatment with antiinflammatory agents such as systemic corticosteroids, nonsteroidal antiinflammatory drugs (NSAIDs), and dimethyl sulfoxide is advised but appears to be of little benefit.

LONG-TERM PROGNOSIS

The prognosis for vision after traumatic optic nerve neuropathy is poor. If vision has not returned within 2 weeks, the prognosis is grave.

ISCHEMIC OPTIC NEUROPATHY

Ischemic optic neuropathy is caused by sudden hypoxemia of the optic nerve as a result of acute hypovolemia, thromboembolic disease, or surgical occlusion of the internal or external carotid artery.[20,104] Ligation or occlusion of the internal or external carotid artery is used as treatment for guttural pouch mycosis to prevent epistaxis associated with vascular invasion by fungal plaques.[104] With arterial occlusion, the affected eye will be on the side ipsilateral to the surgical site.

CLINICAL APPEARANCE AND DIAGNOSIS

Initially the affected optic nerve appears normal, but the affected eye is blind. The nerve becomes edematous and hyperemic within 24 hours. Focal peripapillary hemorrhages and accumulation of axoplasmic material may be observed in 24 to 48 hours (Fig. 10-63). This appears as white material extending vitread from the optic nerve (Fig. 10-64). Optic nerve degeneration, characterized by pallor and vascular attenuation, becomes apparent in 2 to 4 weeks.

TREATMENT

There is no treatment for ischemic optic neuropathy.

LONG-TERM PROGNOSIS

Prognosis for vision is grave.

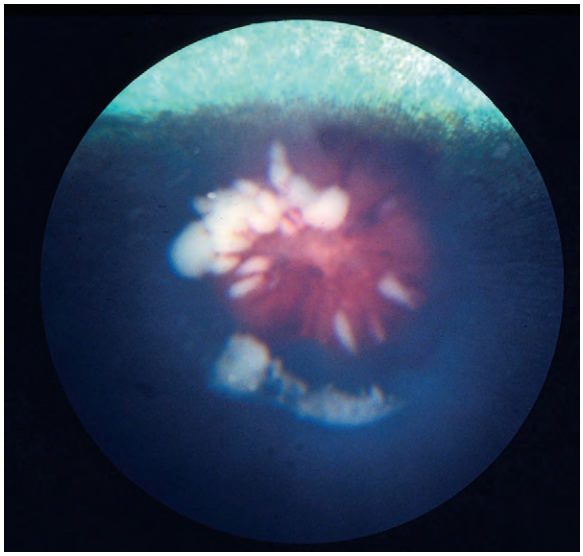


Figure 10-64. Several days after vascular occlusion, peripapillary hemorrhages, optic nerve hyperemia, and accumulation of axoplasmic materials are observed.

OPTIC NEURITIS

The optic nerve is an anterior extension of the CNS, and as such is subject to diseases that result from inflammation, edema, infection, parasitism, and neoplasia of the CNS. Diseases of the CNS must be considered when optic neuritis is diagnosed, but the converse is just as important. A complete ophthalmic examination with special attention to the optic nerve should be performed in all horses with diseases of the CNS. This would include cases of viral encephalitis (arbovirus, herpesvirus, Borna disease virus), CNS parasitism *(Trypanosoma evansi, Halicephalobus gingivalis)*, or mycotic (cryptococcosis) or bacterial meningitis *(Rhodococcus equi, Streptococcus equi*).

Parasites, such as *Halicephalobus gingivalis (H. deletrix)*, have been demonstrated to result in chorioretinitis and optic neuritis.[84,85] These are typically disseminated with lesions in multiple organ systems. Optic neuritis can also occur with ERU. Borna disease, a viral encephalomyelitis exotic to North America, has also been reported to cause optic neuritis and retinal degeneration.[22,44,88] See Chapter 13 for more information regarding systemic diseases and the equine eye.

CLINICAL APPEARANCE AND DIAGNOSIS

Clinically the optic nerve may appear hyperemic, hazy, and edematous, often with white exudates and hemorrhage (Fig. 10-65). The peripapillary retina may be elevated. Vision is generally decreased to absent, and the PLR will be slow to absent, with a mydriatic pupil. In cases of retrobulbar optic neuritis without intraocular involvement, the fundic examination may be normal. In these cases, there will be a visual deficit and mydriasis with a PLR deficit. An electroretinogram will confirm a functional retina and should be followed by a visual evoked potential, complete physical and neurologic examination, cerebrospinal fluid analysis, and CNS imaging by CT scan.

TREATMENT

Treatment for optic neuritis is directed at the underlying cause. A case of *Cryptococcus* meningitis and optic neuritis has been reported in a horse and was successfully treated with systemic fluconazole, with return of vision and PLRs.[103]

LONG-TERM PROGNOSIS

Prognosis for vision is dependent on the severity of disease and response to treatment.

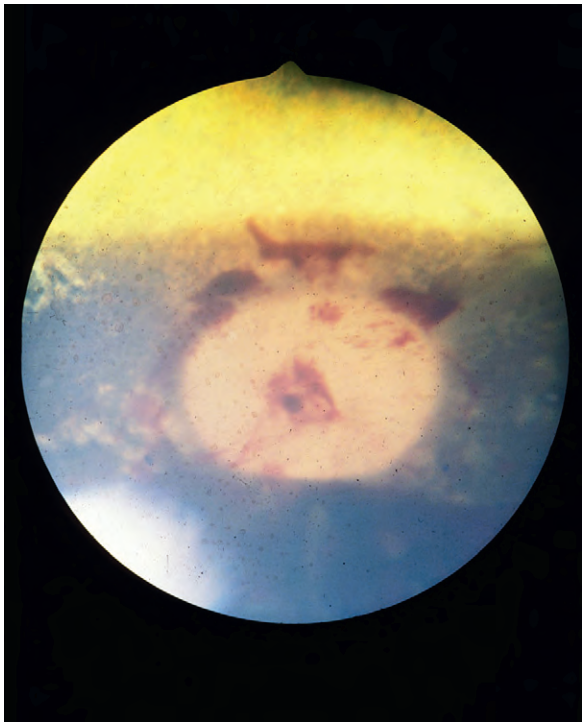


Figure 10-65. Optic neuritis is observed, along with hemorrhage, peripapillary edema, and cellular exudates.

PROLIFERATIVE AND EXUDATIVE OPTIC NEUROPATHY

Exudative optic neuritis has been described in older horses and may result in acute-onset bilateral blindness.[20,21,44] It must be distinguished from benign exudative/proliferative optic neuropathy, which occurs in aged horses (>15 years) and is generally an incidental finding.[22] Proliferative lesions may enlarge with time and can result in some vision or behavior changes if they become large enough to obscure portions of the retina.[22] In one study of 83 geriatric horses, proliferative optic neuropathy was noted in two animals and was unilateral in both.[89]

CLINICAL APPEARANCE AND DIAGNOSIS

Exudative optic neuropathy appears as a white to gray material obscuring the optic nerve, which if visible is edematous with or without hemorrhages (Figs. 10-66 and 10-67). The cause is not known, but it is hypothesized to be an ocular response to a variety of systemic diseases such as infection with *Streptococcus equi* or *Actinobacillus equuli*, septicemia, EHV-1, and possibly ERU.[20] This must be distinguished from benign exudative/proliferative optic neuropathy, a condition of white or gray material anterior to the optic nerve in a visual eye with otherwise normal findings on examination (Fig. 10-68).[20-22,44,105] On histologic examination, the lesion resembles a schwannoma.[106] Optic nerve neoplasia, traumatic optic neuropathy, and ischemic optic neuropathy are also differential diagnoses.

TREATMENT

There is no treatment for either condition.

LONG-TERM PROGNOSIS

The prognosis for vision with exudative optic neuropathy is generally poor; however, the prognosis for vision with benign

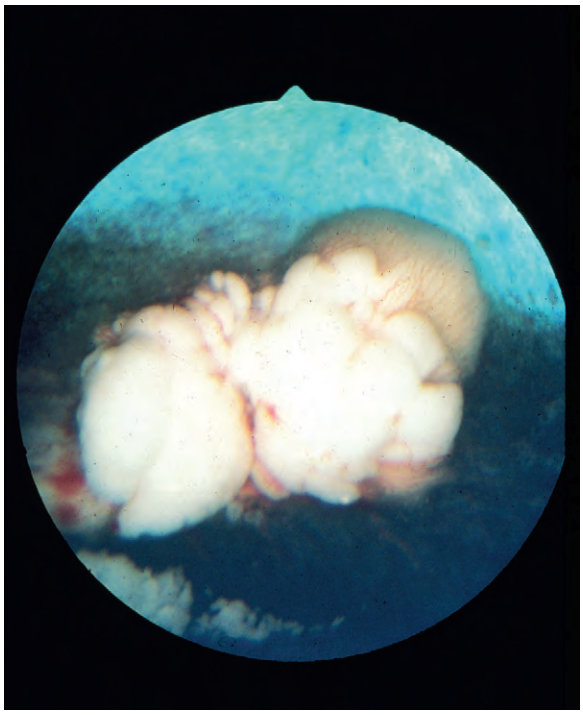


Figure 10-66. Exudative optic neuropathy.

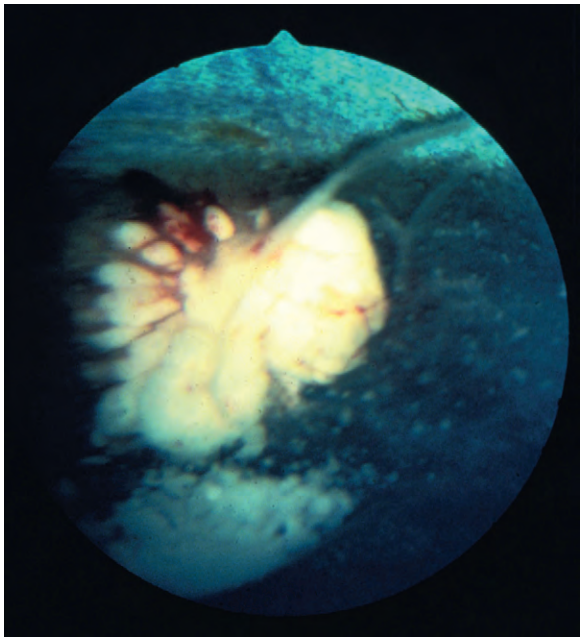


Figure 10-67. Exudative optic neuropathy with associated retinal detachment.

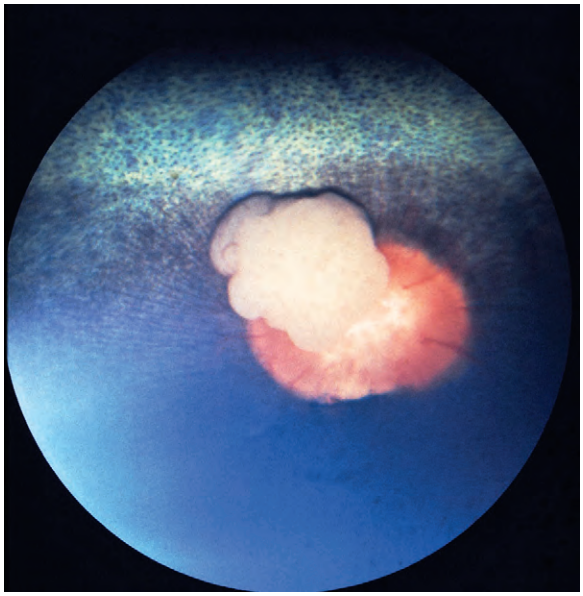


Figure 10-68. Proliferative optic neuropathy. (Photograph courtesy Drs. Ingo Walde and Barbara Nell, University of Vienna.)

proliferative optic neuropathy is excellent, because these lesions are usually incidental findings.

OTHER MISCELLANEOUS POSTERIOR SEGMENT DISEASE IN THE HORSE

NEOPLASIA

Primary neoplasia of the equine posterior segment is rare. Medulloepitheliomas (teratoid and non-teratoid) are seen most commonly in young horses and appear as white masses in the vitreous (leukocoria) (Figs. 10-69 to 10-71).[107-109] These can be rapidly growing, and enucleation is indicated and usually curative. Recently a primary primitive neuroectodermal tumor (retinoblastoma) has been described to affect a 14-year-old gelding, resulting in unilateral blindness.[110] Astrocytomas, gliomas, and schwannomas may occur and are typically benign (Fig. 10-72).[111] Choroidal melanoma is also a possible primary tumor of the posterior globe, and enucleation is advised. Metastatic tumors can also occur, with lymphosarcoma being most common. In general, metastatic tumors are associated with more significant inflammation and hemorrhage than are primary tumors. Retinal detachment, hyphema, glaucoma, blindness, and pain may be observed with metastatic neoplasia.

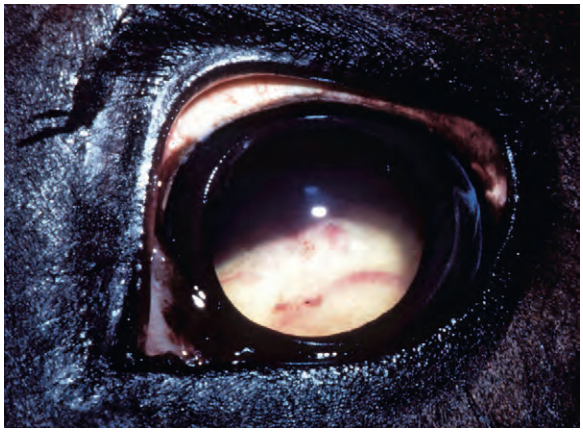


Figure 10-69. Gross photograph of a foal with leukocoria caused by a teratoid medulloepithelioma of the posterior globe.

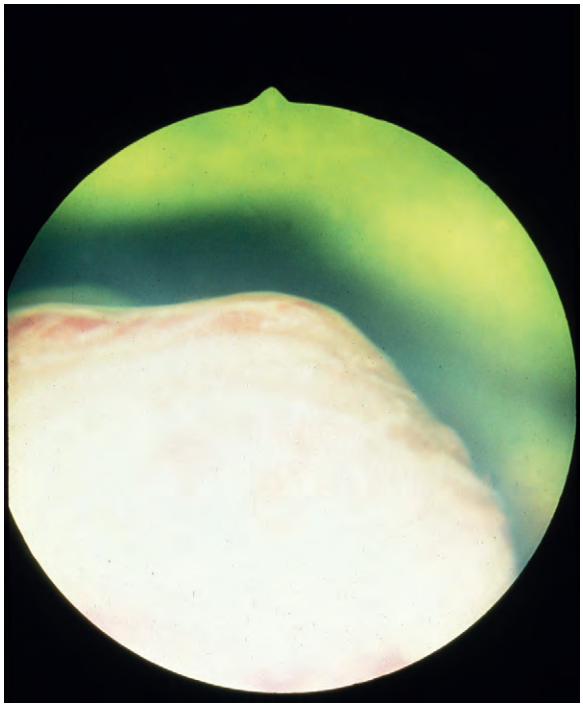


Figure 10-70. Fundic photograph of the teratoid medulloepithelioma seen in Fig. 10-69.

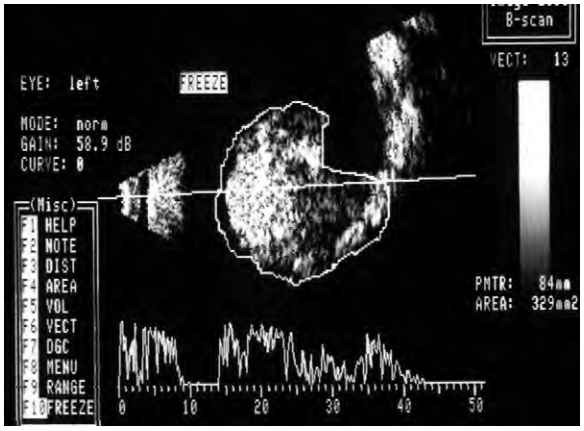


Figure 10-71. Ultrasound examination of the teratoid medulloepithelioma seen in Fig. 10-69. The mass measures 84 mm over the surface.

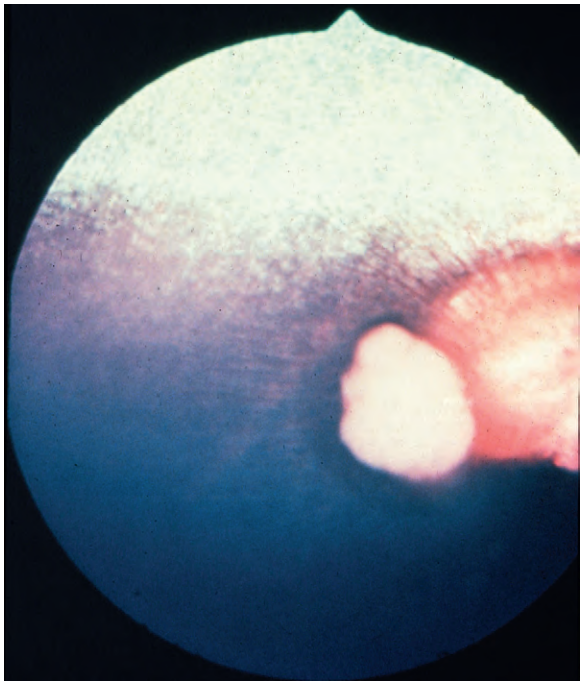


Figure 10-72. Astrocytoma of the optic nerve.

HYALITIS

Hyalitis or inflammation of the vitreous can be seen with ERU or as an extension of chorioretinitis. In Europe, hyalitis appears to be a common manifestation of equine uveitis. In evaluation of 130 vitreous samples from 117 European horses affected with ERU, which were collected during vitrectomy, leptospires were isolated in 35 samples (26.9%).[112] The most common serovar was Grippotyphosa.[112] In addition, 92 vitreous samples (70.7%) were positive for leptospiral antibodies.[112] Results of other similar studies have also confirmed the presence of leptospires in the vitreous of horses with ERU, with an additional finding of *Leptospira interrogans* in the vitreous of 52% of horses with ERU but not in any control eyes.[113-115] Further, it has been demonstrated that horses with ERU have an increase in vitreous IgA compared to serum IgA, suggesting a local immunologic reaction to antigens within the eye.[116]

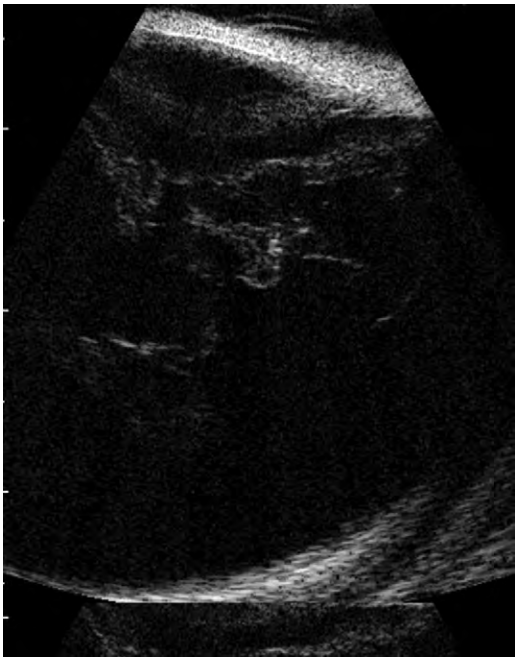


Figure 10-73. Ultrasound examination of an equine eye with a cataract and vitreous degeneration. Echogenic material is observed in the middle to anterior vitreous and is seen to move when evaluated in real time.

With hyalitis, the vitreous will take on a yellow-green appearance as a result of serum pigments. Vitreous debris, fibrin, and inflammatory cells in the vitreous and on the posterior lens capsule and vitreous collagen are often seen to float and swirl in the vitreous as the tissue/water components of the vitreous separate, leaving free water, which contains products of inflammation. Posterior cortical cataract and retinal detachment may occur as a result of hyalitis.

VITREOUS DEGENERATION OR SYNERESIS

Vitreous degeneration or syneresis is more common in aged horses and in such cases is a benign condition. Vitreous syneresis can also be a pathologic change associated with inflammation.[15] In one study of 83 geriatric horses, vitreous degeneration was the most common abnormality, being present in 38 animals and 72 eyes.[89] The prevalence of vitreous degeneration increased with age.[89] With syneresis may come vitreous floaters that can affect behavior, causing shying or head shaking (Fig. 10-73). Although examination for vitreous floaters in horses with the complaint of head shaking is an essential part of the ophthalmic examination, seldom are these the cause (D. Wilkie, unpublished data). Evaluation for photic head shaking, refractive errors, ear or nasal disease, or various behavior concerns is more likely to result in a diagnosis.

Asteroid hyalosis, deposits of calcium-phosphate crystals in the vitreous, also occurs in horses (Fig. 10-74). This is an incidental finding and is more common in aged horses.

VITRECTOMY AND VITREOUS SURGERY

Surgical management of ERU with vitrectomy has been described.[112,113,117] This appears more accepted among European veterinary ophthalmologists, and a large number of horses

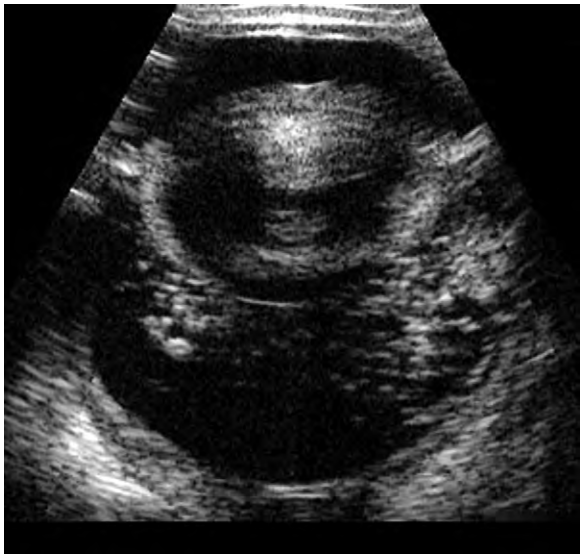


Figure 10-74. Ultrasound examination of an equine eye with a cataract and asteroid hyalosis.

have been treated with this technique. ERU in European horses may differ in its manifestation as a posterior segment disease with marked hyalitis, and therefore this technique has received more widespread recognition in Europe. Recently, this posterior manifestation of ERU does appear to be increasing in prevalence in North America. This is evidence that the vitreous may have a role as an effector in some instances of ERU, and pars plana vitrectomy has been advocated to control recurrent inflammation.[18] The anatomy for surgical entry into the vitreous through the pars plana has been described.[14] In addition to vitrectomy, insertion of a sustained-release cyclosporine implant into the vitreous or suprachoroidal space has been described for prolonged management of ERU.[118,119] For a more detailed discussion, see Chapter 8.

FUTURE RESEARCH

Future areas of investigation with respect to the equine posterior segment should expand our knowledge of infectious diseases and ocular immunology with respect to inflammation of the posterior segment. In addition, improvement in posterior segment surgical techniques, specifically vitreo-retinal surgery, with surgical equipment specifically designed for the equine eye are indicated. Examination of the equine posterior segment using advanced diagnostic procedures such as optical coherence tomography, electroretinography and multifocal electroretinography will help to better understand the equine eye in health and disease. While many lesions of the equine posterior segment have been described, we lack the clinical pathologic correlates for these lesions. These might be obtained through evaluation of eyes from abattoir or necropsy specimens. Finally, a better understanding of the genetics and heritability of certain disorders such as ERU, retinal degeneration and congenital abnormalities is required.

References

1. Murphy CJ, Howland HC: The optics of comparative ophthalmology, Vis Res 27:599–607, 1987.
2. Crispin SM, Matthews AG, Parker J: The equine fundus. I. Examination, embryology, structure and function, Equine Vet J Suppl 22:42–49, 1990.
3. Matthews AG, Crispin SM, Parker J: The equine fundus. II. Normal anatomical variants and colobomata, Equine Vet J Suppl 22:50–54, 1990.
4. Matthews AG, Crispin SM, Parker J: The equine fundus. III. Pathological variants, Equine Vet J Suppl 22:55–61, 1990.
5. Brooks DE: Equine ophthalmology. In Gelatt KN, editor: Veterinary ophthalmology, ed 3, Philadelphia, 1991, Lippincott Williams and Wilkins, pp 1053–1116.
6. Riis RC: Equine ophthalmology. In Gelatt KN, editor: Veterinary ophthalmology, Philadelphia, 1981, Lea and Febiger, pp 586–592.
7. Davidson MG: Equine ophthalmology. In Gelatt KN, editor: Veterinary ophthalmology, ed 2, Philadelphia, 1991, Lea and Febiger, pp 576–610.
8. Munroe GA, Barnett KC: Congenital ocular disease in the foal, Vet Clin North Am Large Anim Pract 6:519–537, 1984.
9. Gelatt KN: Ophthalmoscopic studies in the normal and diseased ocular fundi of horses, J Am Anim Hosp Assoc 7:158–163, 1971.
10. Scotty NC, et al: Diagnostic ultrasonography of equine lens and posterior segment, Vet Ophthalmol 7:127–139, 2004.
11. Molleda JM, Cervantes I, Galan A, et al: Fluorangiographic study of the ocular fundus in normal horses, Vet Ophthalmol Suppl 11:2–7, 2008.
12. Komáromy AM, Andrew SE, Sapp HL, et al: Flash electroretinography in standing horses using the DTLTM microfiber electrode, Vet Ophthalmol 6:27–33, 2003.
13. Hurn SD, Turner AG: Ophthalmic examination findings of Thoroughbred racehorses in Australia, Vet Ophthalmol 9:95–100, 2006.
14. Miller TL, et al: Description of ciliary body anatomy and identification of sites for transscleral cyclophotocoagulation in the equine eye, Vet Ophthalmol 4:183–190, 2001.
15. Barnett KC, et al: Equine ophthalmology: an atlas and text, London, 2004, Elsevier Limited, pp 201–246.
16. Gilger BC, Reeves KA, Salmon JH: Ocular parameters related to drug delivery in the canine and equine eye: aqueous and vitreous humor volume and scleral surface area and thickness, Vet Ophthalmol 8:265–269, 2005.
17. Turner RM, McDonnell SM, Feit EM, et al: Real-time ultrasound measure of the fetal eye (vitreous body) for prediction of parturition date in small ponies, Theriogenology 66:331–337, 2006.
18. Deeg CA, Altmann F, Hauck SM, et al: Down-regulation of pigment epithelium-derived factor in uveitis lesion associates with focal vascular endothelial factor expression and breakdown of the blood-retinal barrier, Proteomics 7:1540–1548, 2007.
19. Ehrenhofer MCA, et al: Normal structure and age-related changes of the equine retina, Vet Ophthalmol 5:39–47, 2002.
20. Cutler TJ, et al: Diseases of the equine posterior segment, Vet Ophthalmol 3:73–82, 2000.
21. Rebhun WC: Equine retinal lesions and retinal detachments, Equine Vet J Suppl 2:86–90, 1983.
22. Rebhun WC: Retinal and optic nerve diseases, Vet Clin North Am Equine Pract 8:587–608, 1992.
23. Altunay H: Fine structure of the retinal pigment epithelium, Bruch's membrane and choriocapillaris in the horse, Anat Histol Embryol 29:135–139, 2000.
24. Slater JD, et al: Fluorescein angiographic appearance of the normal fundus and of focal chorioretinal lesions in the horse, Invest Ophthalmol Vis Sci 36:S779, 1995.
25. Hebel R: Distribution of retinal ganglion cells in five mammalian species (pig, sheep, ox, horse, dog), Anat Embryol (Berl) 150:45–51, 1976.
26. Brooks DE, Komaromy AM, Kallberg ME: Comparative retinal ganglion cell and optic nerve morphology, Vet Ophthalmol 2:3–11, 1999.
27. Duke-Elder SS: System of ophthalmology, vol 1. The eye in evolution, London, 1958, Henry Kimpton, pp 446–504.

28. Guo X, Sugita S: Topography of ganglion cells in the retina of the horse, J Vet Med Sci 62:1145–1150, 2000.
29. Evans KE, McGreevy PD: The distribution of ganglion cells in the equine retina and its relationship to skull morphology, Anat Histol Embryol 36:151–156, 2007.
30. Guo X, Sugita S: Quantitative analysis of the organization of the inner nuclear layer of the horse retina, J Vet Med Sci 64:847–849, 2002.
31. Deeg CA, Amann B, Hauck SM, et al: Defining cytochemical markers for different cell types in the equine retina, Anat Histol Embryol 35:412–415, 2006.
32. Carroll J, et al: Cone photopigment spectral sensitivities in the horse, Vet Ophthalmol 2:257–262, 1999.
33. Carroll J, et al: Photopigment basis for dichromatic color vision in the horse, J Vis 1:80–87, 2001.
34. Hall CA, Cassaday HJ, Vincent CJ, et al: Cone excitation ratios correlate with color discrimination performance in the horse *(Equus caballus)*, J Comp Psychol 120:438–448, 2006.
35. Brooks DE, et al: Histomorphometry of the optic nerves of normal horses and horses with glaucoma, Vet Comp Ophthalmol 5:193–210, 1995.
36. Brooks DE, Komaromy AM, Garci-Fernandez MC, et al: Immunohistochemistry of the extracellular matrix of the normal equine lamina cribrosa, Vet Ophthalmol 3:127–132, 2000.
37. Roberts SM: Congenital ocular anomalies, Vet Clin North Am Equine Pract 8:459–478, 1992.
38. Munroe G: Survey of retinal hemorrhages in neonatal thoroughbred foals, Vet Rec 146:95–101, 2000.
39. Wheeler CA, Collier LL: Bilateral colobomas involving the optic discs in a quarterhorse, Equine Vet J Suppl 10:39–41, 1990.
40. Bildfell R, et al: Bilateral optic disc colobomas in a Quarter Horse filly, Equine Vet J 35:325–327, 2003.
41. Schuh CL: Bilateral colobomas in a horse, J Comp Pathol 100:331–335, 1989.
42. Martín-Suárez EM, Galán A, Gallardo JM, et al: Bilateral typical complete colobomas in a donkey: retinographic and fluorangiographic description, Vet Ophthalmol 12:338–342, 2009.
43. Williams DL, Barnett KC: Bilateral optic disc colobomas and microphthalmos in a thoroughbred horse, Vet Rec 132:101–103, 1993.
44. Rubin LF: Atlas of veterinary ophthalmoscopy, Philadelphia, 1974, Lea & Febiger.
45. Gelatt KN, Leipold HW, Coffman JR: Bilateral optic nerve hypoplasia in a colt, J Am Vet Med Assoc 155:627–631, 1969.
46. Ramsey DT, et al: Congenital ocular abnormalities of Rocky Mountain horses, Vet Ophthalmol 2:47–59, 1999.
47. Strobel BW, Wilkie DA, Gilger BC: Retinal detachment in horses: 40 cases, 1998–2005, Vet Ophthalmol 10:380–385, 2007.
48. Grahn BH, Pinard C, Archer S, et al: Congenital ocular anomalies in purebred and crossbred Rocky and Kentucky Mountain horse in Canada, Can Vet J 49:675–681, 2008.
49. Andersson LS, Juras Rytis, Ramsey DT, et al: Equine multiple congenital ocular anomalies maps to a 4.9 megabase interval on horse chromosome 6. BMC Genet 9:88, 2008.
50. Rebhun WC, et al: Clinical manifestations of night blindness in the Appaloosa horse, Compend Contin Educ Vet 6:S103–S106, 1984.
51. Witzel DA, et al: Night blindness in the Appaloosa: sibling occurrence, J Equine Med Surg 1:383–386, 1977.
52. Witzel DA, Joyce JR, Smith EL: Electroretinography of congenital night blindness in an Appaloosa filly, J Equine Med Surg 1:226–229, 1977.
53. Witzel DA, et al: Congenital stationary night blindness: an animal model, Invest Ophthalmol Vis Sci 17:788–795, 1978.
54. Sandmeyer LS, Grahn BH, Breaux CB: Diagnostic ophthalmology, Can Vet J 47:1131–1133, 2006.
55. Sandmeyer LS, Breaux CB, Archer S, et al: Clinical and electroretinographic characteristics of congenital stationary night blindness in the Appaloosa and the association with the leopard complex, Vet Ophthalmol 10:368–375, 2007.
56. Nunnery C, Pickett JP, Zimmerman KL: Congenital stationary night blindness in a Thoroughbred and a Paso Fino, Vet Ophthalmol 8:415–419, 2005.
57. Bellone R, Brooks SA, Sandmeyer LS, et al: Differential gene expression of TRPM1, the potential cause of congenital stationary night blindness and coat spotting patterns (LP) in the Appaloosa horse *(Equus caballus)*. Genetics 179:1861–1870, 2008.
58. Gelatt KN: Congenital and acquired ophthalmic diseases in the foal, Anim Eye Res 2:15–27, 1993.
59. Munroe G: Study of the hyaloid apparatus in the neonatal thoroughbred foal, Vet Rec 146:579–584, 2000.
60. Millichamp NJ: Ocular trauma, Vet Clin North Am Equine Pract 8:521–536, 1992.
61. Gilger BC, et al: Use of a hydroxyapatite orbital implant in a cosmetic corneoscleral prosthesis after enucleation in a horse, J Am Vet Med Assoc 222:343–345, 2003.
62. Hauck SM, Schoeffmann S, Amann B, et al: Retinal mueller glial cells trigger the hallmark inflammatory process I autoimmune uveitis, J Proteome Res 6:2121–2131, 2007.
63. Deeg CA: Ocular immunology in equine recurrent uveitis, Vet Ophthalmol 11(Suppl):61–65, 2008.
64. Deeg CA, Pompetzki D, Raith AJ, et al: Identification and functional validation of novel autoantigens in equine uveitis, Mol Cell Proteomics 5:1462–1470, 2006.
65. Deeg CA, Hauck SM, Amann B, et al: Equine recurrent uveitis: a spontaneous horse model of uveitis, Ophthal Res Epub 40:151–153, 2008.
66. Deeg CA, Hauck SM, Amann B, et al: Major retinal autoantigens remain stably expressed during all stages of spontaneous uveitis, Mol Immunol 44:3291–3296, 2007.
67. Roberts SR: Fundus lesions in equine periodic ophthalmia, J Am Vet Med Assoc 141:229–239, 1962.
68. Kalsow CM, Dwyer AE: Retinal immunopathology in horses with uveitis, Ocul Immunol Inflamm 6:239–251, 1998.
69. Deeg CA, et al: Immunopathology of recurrent uveitis in spontaneously diseased horses, Exp Eye Res 75:127–133, 2002.
70. Deeg CA, et al: Immune responses to retinal autoantigens and peptides in equine recurrent uveitis, Invest Ophthalmol Vis Sci 42:393–398, 2001.
71. Slater JD, et al: Chorioretinopathy associated with neuropathology following infection with equine herpesvirus 1, Vet Rec 131:237–239, 1992.
72. Hahn CN, Mayhew IG, MacKay RJ: Diseases of multiple or unknown sites. In Colahan PT, et al, editors: Equine medicine and surgery, vol 1, St Louis, 1999, Mosby, pp 884–903.
73. McChesney AE, England JJ, Rich LJ: Adenoviral infection in foals, J Am Vet Med Assoc 162:545–549, 1973.
74. Stiles J: Ocular manifestations of systemic disease. Part 3. The horse. In Gelatt KN, editor: Veterinary ophthalmology, ed 3, Philadelphia, 1999, Lippincott Williams and Wilkins, pp 1473–1492.
75. Anninger WV, et al: West Nile virus-associated optic neuritis and chorioretinitis, Am J Ophthalmol 136:1183–1185, 2003.
76. Kuchtey RW, et al: Uveitis associated with West Nile virus infection, Arch Ophthalmol 121:1648–1649, 2003.
77. Rebhun WC: Diseases of the uvea. In Mayhew IG, editor: Equine medicine and surgery, vol 2, St Louis, 1999, Mosby, pp 1253–1260.
78. Lavach JD: Ocular manifestations of systemic diseases, Vet Clin North Am Equine Practice 8:627–636, 1992.
79. Barratt-Boyes SM, et al: *Streptococcus equi* infection as a cause of panophthalmitis in a horse, Equine Vet Sci 11:229–231, 1991.
80. Roberts SR: Chorioretinitis in a band of horses, J Am Vet Med Assoc 158:2043–2046, 1971.
81. Jones TDC: The relation of brucellosis to periodic ophthalmia in Equidae, Am J Vet Res 1:54–57, 1940.
82. Pusterla N, et al: Digenetic trematodes, *Acanthatrium* sp. and *Lecithodendrium* sp., as vectors of *Neorickettsia risticii*, the agent of Potomac Horse Fever, J Helminthol 77:335–339, 2003.
83. McDonald DR, Cleary DJ: Toxoplasmosis in the equine, Southwest Vet 23:213–214, 1970.
84. Rames DS, et al: Ocular *Halicephalobus* (syn. *Micronema*) *deletrix* in a horse, Vet Pathol 32:540–542, 1995.
85. Kinde H, et al: *Halicephalobus gingivalis (H. deletrix)* infection in two horses in southern California, J Vet Diagn Invest 12:162–165, 2000.
86. Lavach JD: Parasitic diseases. In Lavach JD, editor: Large animal ophthalmology, St Louis, 1990, Mosby, pp 252–269.
87. Barnett KC: The ocular fundus of the horse, Equine Vet J 4:17–20, 1971.
88. Dietzel J, Kuht H, Stahl T, et al: Morphometric analysis of the retina from horses infected with the Borna disease virus, Vet Pathol 44:57–63, 2007.
89. Chandler KJ, Billson FM, Mellor DJ: Ophthalmic lesions in 83 geriatric horses and ponies, Vet Rec 153:319–322, 2003.
90. Url A, et al: Equine neuronal ceroid lipofuscinosis, Acta Neuropathol 101:410–414, 2001.
91. Riis RC, et al: Ocular manifestations of equine motor neuron disease, Equine Vet J 31:99–110, 1999.
92. Riis RC, Divers TJ: Effect of vitamin E deficiency on horse retinas, Vet Ophthalmol 3:254–259, 2000.

93. Divers TJ, Mohammed HO, Cummings JF, et al: Equine motor neuron disease: findings in 28 horses and proposal of a pathophysiological mechanism for the disease, Equine Vet J 26:409–415, 1994.
94. McGorum BC, Mayhew IG, Amory H, et al: Horses on pasture may be affected by equine motor neuron disease, Equine Vet J 38:47–51, 2006.
95. Madigan JE, et al: Photic headshaking in the horse: 7 cases, Equine Vet J 27:306, 1995.
96. Wilkins PA: Cyproheptadine: medical treatment for photic headshakers, Compend Contin Educ Vet 19:98–102, 1997.
97. Barnett KC, Blunden AS, Dyson SJ, et al: Blindness, optic atrophy and sinusitis in the horse, Vet Ophthalmology 11(Suppl):20–26, 2008.
98. Platt H, et al: Degenerative lesions of the optic nerve in Equidae, Equine Vet J Suppl 2:91–97, 1983.
99. Meisner T, Wilkie DA, Gemensky AG, et al: Extra-adrenal paraganglioma of the equine orbit: 5 cases, Vet Ophthalmology 12:263–268, 2009.
100. Matz K, et al: Bilateral blindness after injury in a riding horse, Tierarztl Prax 21:225–232, 1993.
101. Reppas GP, et al: Trauma-induced blindness in two horses, Aust Vet J 72:270–272, 1995.
102. Martin L, Kaswan R, Chapman W: Four cases of traumatic optic nerve blindness in the horse, Equine Vet J 18:133–137, 1986.
103. Hart KA, Flaminio MJBF, LeRoy BE, et al: Successful resolution of cryptococcal meningitis and optic neuritis in an adult horse with oral fluconazole, J Vet Intern Med 22:1436–1440, 2008.
104. Hardy J, Wilkie DA, Robertson J: Ischemic optic neuropathy and blindness after arterial occlusion for treatment of guttural pouch mycosis in two horses, J Am Vet Med Assoc 196:1631–1634, 1990.
105. Saunders LZ, Bistner SI, Rubin LF: Proliferative optic neuropathy in horses, Vet Pathol 9:368–378, 1972.
106. Riis RC, Rebhun WC: Proliferative optic neuropathy in a horse caused by a granular cell tumor, Equine Vet J Suppl 10:69–72, 1990.
107. Ueda Y, et al: Ocular medulloepithelioma in a Thoroughbred, Equine Vet J 25:558–561, 1993.
108. Eagle RC, Jr, Font RL, Swerczek TW: Malignant medulloepithelioma of the optic nerve in a horse, Vet Pathol 15:488–494, 1978.
109. Bistner S, Campbell RJ, Dhaw D, et al: Neuroepithelial tumor of the optic nerve in a horse, Cornell Vet 73:30–40, 1983.
110. Knottenbelt DC, Hetzel U, Roberts V: Primary intraocular primitive neuroectodermal tumor (retinoblastoma) causing unilateral blindness in a gelding, Vet Ophthalmol 10:348–356, 2007.
111. Dugan SJ: Ocular neoplasia, Vet Clin North Am Equine Pract 8:609–626, 1992.
112. Brem S, et al: 35 Leptospira isolated from the vitreous body of 32 horses with recurrent uveitis (ERU), Berl Munch Tierarztl Wochenschr 112:390–393, 1999.
113. Brem S, et al: Demonstration of intraocular *Leptospira* in 4 horses suffering from equine recurrent uveitis (ERU), Berl Munch Tierarztl Wochenschr 111:415–417, 1998.
114. Wollanke B, Rohrbach BW, Gerhards H: Serum and vitreous humor antibody titers in and isolation of *Leptospira interrogans* from horses with recurrent uveitis, J Am Vet Med Assoc 219:795–800, 2001.
115. Wollanke B, et al: Intraocular and serum antibody titers to *Leptospira* in 150 horses with equine recurrent uveitis (ERU) subjected to vitrectomy, Berl Munch Tierarztl Wochenschr 11:134–139, 1998.
116. Wagner B, et al: Demonstration of immunoglobulin isotypes in the vitreous body as a contribution to the etiology of recurrent equine uveitis, DTW Dtsch Tierarztl Wochenschr 104:467–470, 1997.
117. Fruhauf B, et al: Surgical management of equine recurrent uveitis with single port pars plana vitrectomy, Vet Ophthalmol 1:137–151, 1998.
118. Gilger BC, et al: Effect of an intravitreal cyclosporine implant on experimental uveitis in horses, Vet Immunol Immunopathol 76:239–255, 2000.
119. Gilger BC, et al: Long-term effect on the equine eye of an intravitreal device used for sustained release of cyclosporine A, Vet Ophthalmol 3:105–110, 2000.

Chapter 11

Equine Vision

Paul E. Miller
Christopher J. Murphy

An understanding of equine vision is important for a number of reasons. Equine practitioners are frequently asked to judge the suitability of a particular horse for specific uses, ranging from the visually demanding (e.g., identification and isolation of a calf) to those that can be performed by nearly blind animals, such as a broodmare walking in an enclosed pasture without injuring herself. Additionally, effective therapy of equine ocular disease requires the clinician possess not only a good working understanding of the normal visual capabilities and visually guided behaviors of the horse, but also how various ocular diseases alter the animal's vision and hence its utility. An understanding of equine vision also allows the clinician to provide a more accurate prognosis prior to initiating therapy and to more intelligently select from a range of potential therapeutic options for a particular disorder to maximize the probability of optimally preserving the eye's visual capabilities. After preservation of the globe and achieving a comfortable result for the patient, the clinician's therapeutic strategy must be one that best preserves vision.

Ophthalmic disorders add another layer of complexity to estimating a horse's visual capabilities. Some ocular diseases do not alter vision at all, whereas others have such a profound impact that even the ability to perceive light is lost. The externally apparent severity of the disease or size of an opacity does not always correlate with the impact the disorder has on the animal's vision. For example, eyes with copious ocular discharge or a large cataract in the lens periphery may retain essentially normal visual performance, but the presence of a small axial opacity in the posterior nucleus of the lens may significantly degrade visual acuity. In other instances, the clinician may be asked to examine a horse to determine whether an ocular disorder is the root cause of undesirable behaviors such as shying from objects or head shaking. The purpose of this chapter is to provide the clinician with a review of the normal visual abilities of the horse and describe how select ocular abnormalities may alter the animal's vision and behavior.

"SEEING"

Although a seemingly esoteric concept, it is critical to recognize that "seeing" is a perception and not a faithful rendition of the external world in all its factual detail. Indeed, the visual system of all species that have been studied to date takes great liberties with the data it receives from the external environment and uses a number of shortcuts to more rapidly process the image into information that can be used to guide behaviors. One such shortcut is to "see" things in context rather than as they truly are. Both horses and humans have been shown to be subject to the Ponzo illusion in which two horizontal lines of the same size are perceived by the brain to be two different sizes if they are presented in the context of a background set of lines similar to a converging pair of railroad tracks (Fig. 11-1).[1] Similarly, it is quite probable that horses also perceive light and dark in relative rather than absolute terms, potentially explaining certain behaviors such as resistance to crossing certain visual barriers or entering trailers or stalls, etc. (Fig. 11-2). In general, illusions such as these offer insight into how the brain processes images; objects in the environment may not be seen as they really are but in context with their surroundings.

The eye is often compared to a camera, possessing optical elements (cornea and lens) capable of changing focus (lens) and an adjustable diaphragm (iris) that assists in controlling the amount of light that passes to the photosensitive layer (retina) that captures the image. This represents only the initial process of vision, however, as there is active manipulation of the image

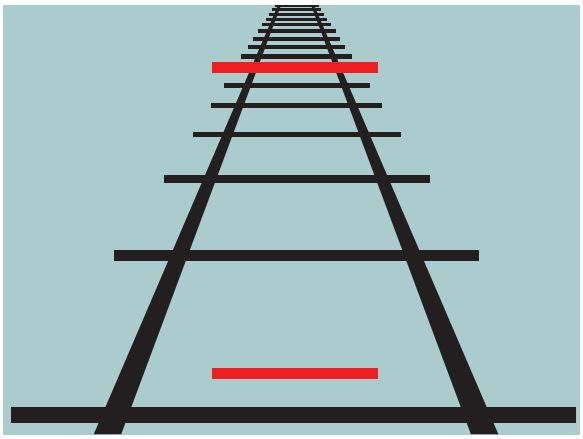


Figure 11-1. The Ponzo Illusion. Both horses and humans are subject to this illusion in which the brain estimates the size of an object *(red line)* based on its surroundings and not its true size. The two red lines are the same length, yet the upper line looks longer, since the brain interprets the converging black lines as receding into the distance. This perspective clue suggests to the brain that because the size of the image of the two red lines is the same on the retina, the upper red line must be larger—when in fact it is not.

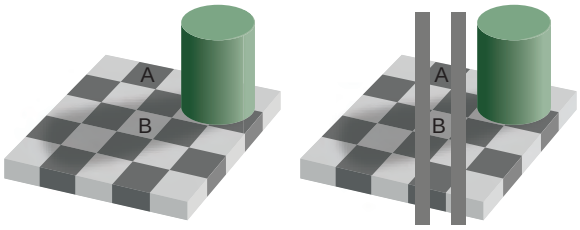


Figure 11-2. The Checkerboard Illusion. Although they appear different, blocks *A* and *B* are the same shade of gray. They appear different because the brain sees these blocks in the context of their surroundings and not as a light meter would. *B* appears lighter than it really is because it is surrounded by darker checks, it is in the shade. When bands of gray bridge the gap between *A* and *B*, the brain now recognizes that the two are actually the same shade of gray. This illustrates that the brain sees images in context and not as they really are. (Courtesy Edward H. Adelson.)

captured by the photoreceptors, both within the neural retina and subsequently by the central nervous system. Seeing is a complex process that depends on (1) light from the outside world entering the eye and being properly focused onto the retina, (2) the retina changing light energy into chemical energy and subsequently into electrical energy, (3) segregation of these responses into various categories (brightness, motion, location, etc.) and transmission of this information to the brain, (4) the brain processing this information to make it useful, and (5) selection of the relevant portions of the image for attention and further action (Fig. 11-3).[2]

The first two steps are comparable to a camera, but the act of seeing is not simply faithfully recording every feature of a scene as a camera would do, because that would quickly overwhelm the brain with huge amounts of information that would be irrelevant to the horse's lifestyle or survival. Instead the brain must decipher the relevant aspects of an image from the billions of photons that interact with more than 100 million photoreceptors in each eye every second. In reality, the optic nerves are flooding the brain with massive amounts of information, much like a large telephone cable serving a major metropolitan area simultaneously carries millions of phone conversations. The brain has coped with this information overload by evolving to not consciously "listen" to all these "conversations" at the same time, but instead to categorize them into specific "topics," which are channeled to specific areas of the brain for further processing.[3-6] Unlike a camera, the brain compares this input with previous images (emphasizing changing aspects of the image), images from the other eye, and input from other senses such as hearing, smell, and touch. Once this is completed, only the information relevant to the task at hand or the horse's survival rises to the level of conscious attention (Fig. 11-4). Interference with the process by which an object is determined to merit visual attention, even though it is clearly visible, is a common cause of accidents such as running into fences, the horse hitting its head on stall doors, throwing riders, etc. The act of seeing depends not only on the function and health of the eye but also on the cognitive processes in the brain that decide what information merits conscious attention and what is to remain subconscious or be discarded.

Extensive research into the visual pathways of numerous species, including the horse, has revealed that the information carried from the eye is packaged into many discrete topics such as an object's brightness and size, location of its edges, its "internal" features such as texture and contrast, direction of movement, velocity, overall orientation as represented on the retinal surface, shape, color, and many other parameters. The most critical aspect of vision, however, is the ability to identify an object (a wolf, for example) as separate from its surroundings (dense vegetation). Because this distinction is so important for survival, animals (including humans) with normal vision can "see" an object if it differs sufficiently from its surroundings in any one of six different aspects: luminance (brightness), motion, depth, texture (which is related to visual acuity), orientation, or color (Fig. 11-5).[6] On the basis of their luminance, motion, depth, and texture, objects are roughly differentiated equally well, but separations based on color are less easily made.[3-6] In this chapter, we describe these fundamental ways of seeing objects as different from their surroundings, but in reality, a complete description of how well a horse sees requires not only an understanding of each of these facets of vision but also an understanding of how the brain integrates the constituent parts into a unified perception of the world. Unfortunately, the horse's higher visual pathways remain poorly understood, so our understanding of equine visual perception has significant gaps.

LUMINANCE AND THE PERCEPTION OF LIGHT

The ability to perceive light is the most basic aspect of vision. Although some birds are able to see into the ultraviolet spectrum and some snakes use infrared wavelengths to hunt (using specific nonocular receptors located in pits), the eyes of most mammals, including horses and humans, are capable of detecting photons located in only a tiny portion of the electromagnetic spectrum—typically between 380 and 760 nm (Fig. 11-6).[7-10] Even in this visible spectrum, not all photons are detected equally well, and the specific photoreceptors which are optimally tuned to specific wavelengths are not uniformly distributed across the retina. For these reasons, light

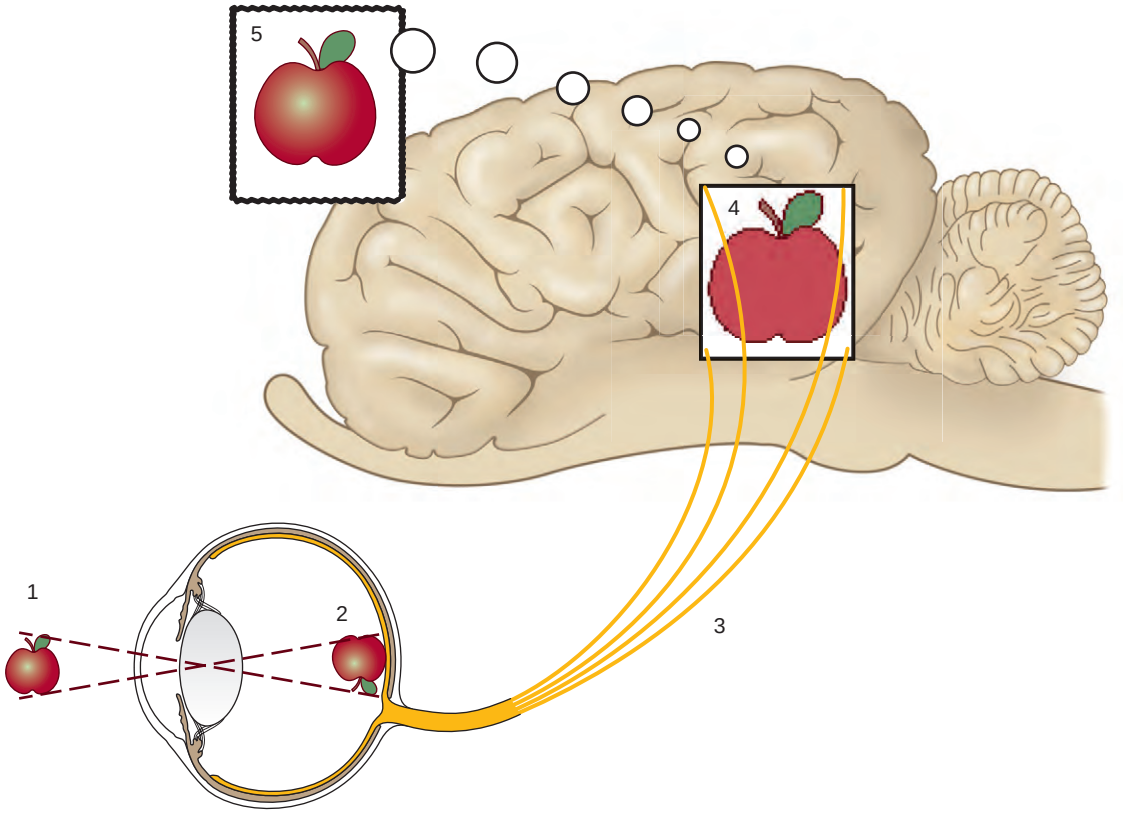


Figure 11-3. The steps in "seeing." *1,* Light enters the eye and is properly focused onto the retina. *2,* The retina interacts with these photons and biochemically triggers an electrical signal. *3,* These responses are segregated into various categories (brightness, motion, location, etc.) and transmitted to the brain. *4,* The brain further processes the information to make it useful. *5,* Relevant portions of the image are selected for attention and further action.

perception depends not only on the number of photons "raining" onto the retina but also on the spectral composition of the light entering the eye and the sensitivity of the eye's photoreceptors to particular wavelengths.[3,4] In other words, the ability to detect light in the visible spectrum depends on the type, density, and spatial distribution of photoreceptors that are present, and this will vary from species to species and even individual to individual.

The term *luminance* (sometimes called *value* by artists) is the perceived lightness of an object.[6,11] Luminance is not purely a physical phenomenon, because the perception of dim-appearing "blue" light and bright-appearing "yellow" light may result from exactly the same number of photons of these different wavelengths striking the retina. Luminance also depends on how sensitive the rod and cone retinal photoreceptors are to the wavelength of light striking the retina.[3,11] In bright light, where the cone photoreceptors are most active, the equine eye is generally more sensitive to wavelengths in the yellow end of the visible spectrum. Light in the green range of the visible spectrum is detected somewhat less effectively, followed by lesser sensitivity to red, and even less sensitivity to wavelengths in the blue portion of the visible spectrum. In dim light, where the rod photoreceptors are most active, light in the green-blue end of the spectrum is better perceived (peak sensitivity of rhodopsin is approximately 500 nm). Therefore, a yellow leaf may appear brighter than a green leaf under bright-light viewing conditions, which favor the use of cone photoreceptors that are most sensitive to yellow (peak sensitivity is approximately 545 nm). Under dim-lighting conditions, when the rod photoreceptors are most active, the green leaf may now appear brighter or more luminous than the yellow one. This phenomenon, called the *Purkinje shift,* also explains why blue objects appear lighter and red ones appear darker in twilight versus daylight (Fig. 11-7).[12] Another way of appreciating the difference between luminance and color is to remove all the color information with a computer program and look at a scene in shades of gray.[11] When this is done, it becomes obvious that many objects can be differentiated on the basis of their luminance alone; color is a less important clue (Fig. 11-8). Luminance is important because the perception of depth, three-dimensionality, movement (or lack thereof), and spatial organization are all carried by a part of the visual system that responds only to luminance differences and is insensitive to color.[4,5,11,13]

A major challenge confronting horses is to adapt to light intensities that vary from the dimmest star to bright sunlight on snow, a factor of as much as 1 to 40 billion.[14,15] As noted previously, humans, and undoubtedly horses, are largely unaware of this enormous variation in light intensity, principally because objects are perceived in the context of their surroundings and not in absolute terms. Several mechanisms are used to adjust to this wide range of illumination, one of which is the previously mentioned Purkinje shift wherein a duplex retina (possessing both rods and cones) uses rod photoreceptors for dim

light and cones for bright light.[3,14,16-18] Rod photoreceptors can reliably respond to a single photon of light and are the primary receptors used when the light levels range from virtually complete darkness on an overcast moonless night to those found at dawn and twilight.[14,19] By midmorning on a sunny day, the rods have become saturated by light, and in order for useful vision to be maintained, the eye must shift over to using primarily cones. This is analogous to a photographer switching from a fast-speed, "coarse-grain" black-and-white film designed for obtaining less detailed grayscale images in low light to a slow-speed, "fine-grain" film designed to produce highly detailed color images in bright light. However, as the eye shifts from rod to cone photoreceptors, what is lost in terms of sensitivity to light is replaced by improved color vision and visual acuity.

In addition to switching between rod and cone photoreceptors, there are several other mechanisms for adjusting to the wide range of lighting intensities that occur in the real world. Changing pupil size can rapidly alter the amount of light that reaches the retina, but this mechanism limits the range of light intensities only by about 10-fold in humans[14] and probably only by a few fold more in horses. The horse eye is superior to the human in this regard because its pupil diameter has a greater dynamic range.[20] Another relatively rapid but more robust mechanism involves changing neural processing by the retinal bipolar and ganglion cells. These cells can sum the light signals

Figure 11-4. Visual Attention: Find the cat. Although all the information is available all at once in this image, the brain must select which portions of the image to pay attention to in order for the information to be useful. It locates the cat amongst the plants by first identifying the main outlines or features of the object (eye, ear, white nose, back and overall "cat-like" shape). It then begins to find where the rest of the "cat-like object" is in the field of view and begins to look for further confirmation by trying to identify more specific confirmatory details such as legs, tail, etc. This process can take some time, and interference with the process of visual attention is a major cause of accidents even though the object was clearly visible.

Figure 11-5. The ability to see an object as separate from its surroundings is critical for a horse's visual performance. Objects can be seen as separate if they differ in luminance ("brightness"), motion (or relative movement), texture (how "grainy" an object is), depth (binocular disparity), or color. The inside rail and the outer perimeter fence of this race track can be differentiated from the dirt track by any one of these features.

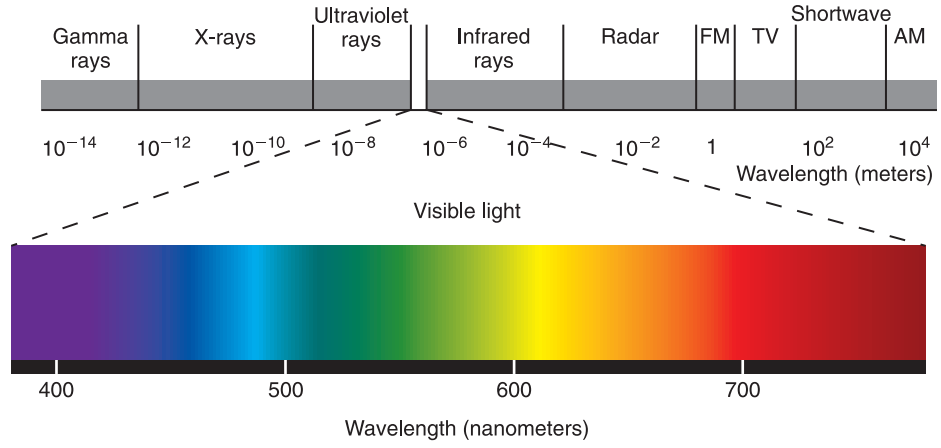


Figure 11-6. The electromagnetic spectrum and visible light. Although some birds can see into the ultraviolet (UV) range, and some snakes use infrared imaging to locate prey, most mammals including horses see only a tiny fraction of the electromagnetic spectrum.

Figure 11-7. Purkinje shift. **A,** A coffee plant under conditions favoring cone vision. The yellow colors in the leaves are brighter because this color more closely approximates the peak sensitivity of the cones. **B,** Same scene under conditions favoring rod vision. The green leaves are brighter than the yellow and red because these colors are closer to the peak sensitivity of the rods.

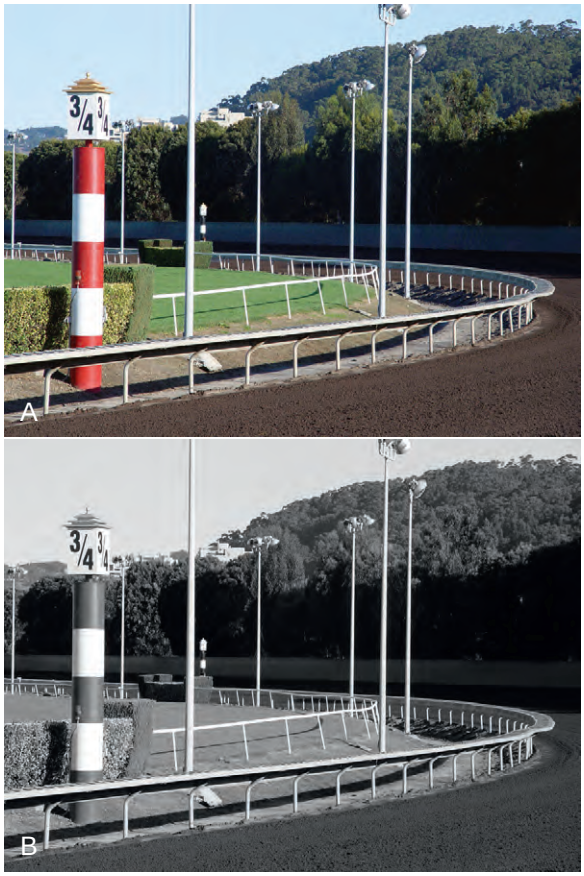


Figure 11-8. Luminance. **A,** A racetrack. **B,** Same scene with all color cues removed. It is still readily possible to distinguish objects based on their differences in luminance; for example, the poles and rails appear much brighter than the track and the outer wall and trees.

from a group of photoreceptors (spatial summation) or over time (temporal summation), and the retina can facilitate adaptation over a range of about 1000-fold.[14] The large size of the horse's eye serves to facilitate this process because it allows the light signal from neighboring photoreceptors to be summated, thereby brightening the retinal image. The summation process would potentially result in loss of the ability of the eye to resolve detail, but the large eye of the horse compensates for this by providing for a greater number of photoreceptors.[21] The major but slower mechanism for adjusting to varying light intensity is to chemically alter the sensitivity of the photoreceptors to light.[3,22] Light chemically dissociates the retinal photopigments into their constituent parts, and this depletion (photoreceptor bleaching) leads to a proportional increase in the amount of light required to trigger a response by the photoreceptor.[3,14,22] Conversely, when an animal is placed in darkness, the photopigment is reconstituted into its active form, and the eye becomes more sensitive to light. This light and dark adaptation occurs over a period of minutes (5 minutes for cones and 20 to 30 minutes for rods) and can easily be appreciated by simply walking into and out of a dark barn on a bright, sunny day.[3,14] In humans these photochemical changes can provide a range of adaptation to light intensity that varies on the order of 100 million–fold.[14] Hence, vision is maintained over an enormous range of light intensities by making relatively slow but massive changes in photoreceptor sensitivity and then fine tuning the intensity by faster alterations in pupil size and retinal processing.

OTHER OCULAR ADAPTATIONS

In addition to these mechanisms, horses have a number of other adaptations that improve vision in dim light that humans do not (Fig. 11-9). The horse has one of the largest eyes among the terrestrial vertebrates, and this allows more light to enter the eye through a large cornea and the pupil.[23,24] Admission of light to the eye is further enhanced by horizontal elongation of the cornea and pupil[25,26] and by the equine pupil's ability to dilate to an area six times larger than that of a human pupil (3 to 3.5 times greater than cat's or dog's).[20,27,28] An elongated slit-like pupil is common in species that are active at night and daytime, because in bright light this shape closes more completely than a round pupil, thereby better protecting a highly light-sensitive retina from very bright light.[29,30] Because the pupil is located in front of the nodal point of the optical system of the eye, the horizontally elongated, roughly rectangular shape of the horse's pupil in daylight also provides it with a wider view of the horizon than it would obtain with a circular pupil with identical surface area.[29] This allows the horse to scan the visual horizon while at the same time reducing the variations in luminosity the

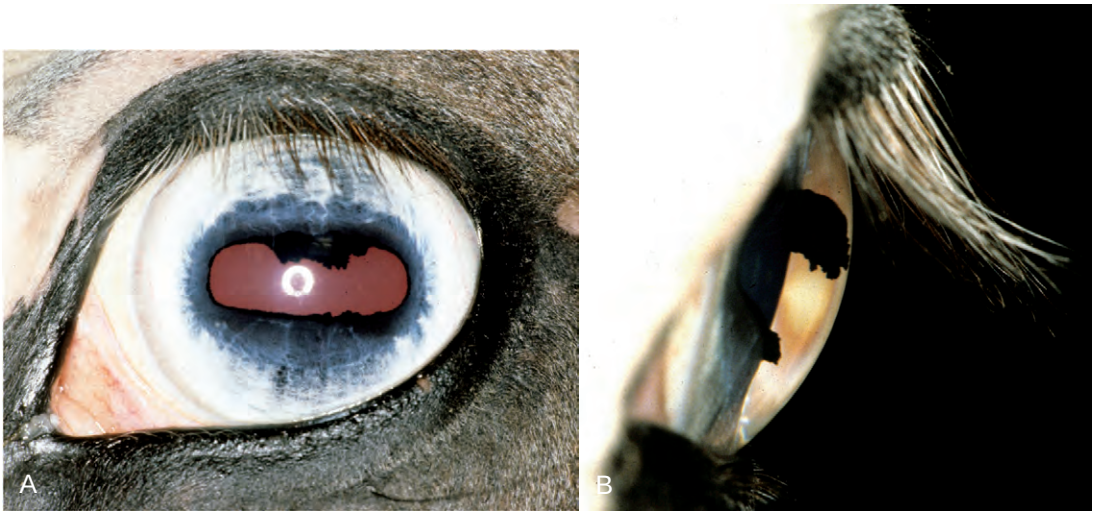


Figure 11-9. **A,** Normal equine eye, demonstrating several adaptations to vision in dim and bright light: a large elongated cornea, a horizontal rectangular pupil, and corpora nigra. **B,** Note how the superior corpora nigra functions as an "awning" and shields the retina from bright light originating from above. Similarly, the inferior corpora nigra may partially shield the retina from rays reflected off the ground.

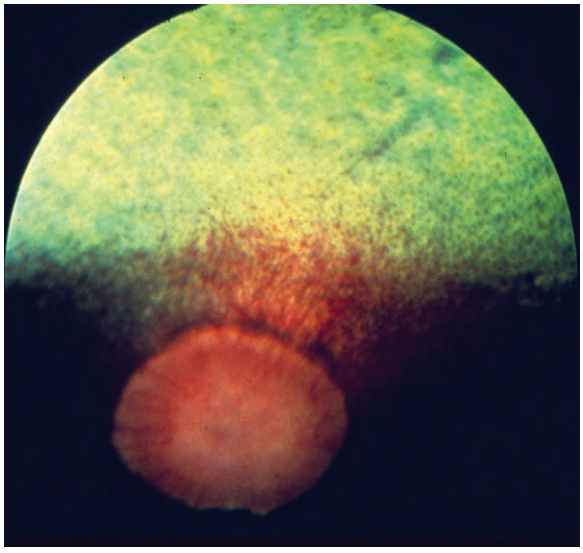


Figure 11-10. The fibrous tapetum of horses reflects light to enhance vision in dim light. However, this reflection may also scatter light and reduce visual acuity.

retina must cope with between the usually brighter sky and the usually darker ground. The equine version of the rod photopigment, rhodopsin, also differs somewhat from that of humans,[31] and like that of dogs and other species adapted for vision in dim light, it may continue to increase in sensitivity to light for a longer period when the animal is placed in the dark.[32-34] Indeed, it may take more than 30 minutes or more for a horse to fully adapt to dim light conditions.[18]

The horse's vision in dim light is also improved by a large, superiorly located, roughly triangular reflective tapetum lucidum that provides the photoreceptors a second chance to capture each photon (Fig. 11-10).[35-42] However, this improved ability to capture light comes at the price of reducing the potential visual acuity of the eye, because the retina is unable to determine whether the photon hit the photoreceptor on the first pass or was reflected there from a slightly different point in space. In horses, the tapetal reflection is accomplished by the regular spacing of uniform-diameter collagen fibrils in the choroid.[36,39,41] The color of the tapetum as seen with an ophthalmoscope is the result of the physical interaction of light with the fibrous tapetum, not the result of colored pigments in the tapetum.[36,39,41] Yellow or green tapetal reflections represent regions where these fibrils are more numerous, whereas deep blue to purple reflections represent thinner regions of the tapetum. In contrast to the fibrous tapetum characteristic of most mammalian herbivores, the tapetum of carnivores is typically composed of cellular elements.[35,41-43] Although the equine tapetum is not as efficient a reflector as the cellular tapetum of some nocturnal carnivores such as the cat (which can reflect up to 130 times more light than the human fundus),[42] it is undoubtedly superior to the human eye, which lacks a tapetum altogether. The modification of different constituents (collagen, cells, or even crystals in some species) to create a reflective layer in the fundus and thereby improve vision in dim light suggests that the tapetum has evolved separately on a number of occasions and represents an evolutionary "arms race" between various predator and prey combinations in which each is seeking a distinct survival advantage over the other.[24,26,35,37-41]

The presence of a tapetum suggests that the horse's lower limit for vision in dim light is much less than that for humans. It is not as low as that for cats, however, (5.5 to 7 times less than that for humans[44]) and perhaps that of certain other predators with a bright reflective tapetum. A recent behavioral study that required horses to discriminate between circles and triangles in a variety of dim-light circumstances in order to receive a food reward found that horses could readily make these kind of visual discriminations and navigate a room with obstacles at light levels that were so low a dark-adapted human could not see at all.[45] They were fully capable of discriminating between

shapes at light levels approximating those of moonlight, starlight on a moonless night, or under cloud cover at night. In fact, only when light levels approximated those of a dense forest with minimal visible sky at nighttime, or a dark enclosure devoid of almost all light, did they lose their ability to make visual discriminations. Even in this very dim lighting circumstance, however, the horses were still able walk around the testing area, locate a feed bowl, and walk through a small testing station set of stocks without bumping into objects.[45] These experimental observations are consistent with anecdotal observations that wild mustangs are able to run at full gallop over rough terrain while negotiating sagebrush, rocks, hills, and gullies with only starlight as the light source.[45]

Although the equine visual system appears to have evolved to function well in dim-lighting circumstances, it also has several features that improve vision in bright light, suggesting that the horse is adapted for an arrhythmic photic lifestyle. For example, the nuclear region of the equine lens contains yellow pigments (Fig. 11-11),[46] as do human lenses and those of other highly diurnal species such as squirrels.[47,48] These pigments filter out shorter (blue) wavelengths of light, much as yellow-tinted sunglasses do for humans, thereby reducing glare in bright light and improving the contrast of some objects against their background, since blue wavelengths of light are scattered 16 times more easily than red wavelengths.[47,48] This pigment also filters out higher-energy rays that are more likely to damage the retina, thereby protecting the delicate photoreceptors of the ventral retina in bright daylight.[47,48] The large corpora nigra on the central superior border of the iris also improves vision in bright light by augmenting pupillary constriction and acting as an internal visor that decreases the amount of light entering the eye from the superior visual field (where the sun is located), further reducing glare and improving vision in bright light. The much smaller corpora nigra on the inferior pupillary border may behave in a similar way to reduce the impact of light reflected off the ground. In fact, in very bright light, the horse's pupil may constrict to such a degree that the superior corpora nigra apposes the border of the inferior iris, effectively dividing the pupil into two segments. The impact of this on the animal's vision is unclear, but two pupils oriented in the same plane as the visual streak on the retina may improve the animal's vision in bright light[29] (see discussion of optical consequences of pupil shape). In a sense, the horse has evolved to be a visual generalist, with some degree of vision under all lighting circumstances, unlike humans who tend to function best in bright light and cats who function well in dim light.

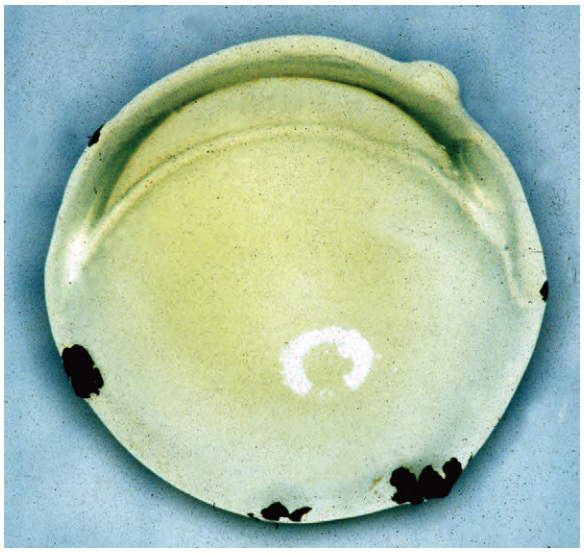


Figure 11-11. Yellow pigments present in the equine lens may filter out blue light, thereby reducing glare and improving contrast in bright light.

DETECTING MOTION

Detecting motion is another fundamental component of vision with great biological importance. Moving objects are more likely to demand some type of response on the part of the horse than stationary ones, and horses, like humans, detect moving objects more easily than stationary ones. This is especially true for objects in the horse's peripheral visual field, which has a visual acuity so low that it may permit only movement and brightness, rather than discrete objects, to be seen.[24] This poor peripheral visual acuity coupled with a prey mentality may explain why horses often shy from even innocuous objects that move in their peripheral visual field. Although the peripheral retina has often been described as being best at detecting motion, it is inaccurate to infer that animals with large peripheral visual fields are better at motion detection than those with better-developed central visual areas such as a fovea. The peripheral retina does have a greater number of the ganglion cell subtypes devoted to motion detection,[49,50] but the central retina has more densely packed photoreceptors. Because of this higher resolution, it actually has a much greater ability to detect motion than does the peripheral retina. In one study, the more densely packed human fovea had a 10- to 12-fold lower threshold for detecting motion than that of a cat.[51,52] Horses have significantly better visual acuity than cats, so it is likely they are better at detecting motion than cats but not quite as good at it as humans. It remains to be determined, however, whether there are differences between the peripheral retina and central retina of horses that would render their peripheral vision more sensitive to objects that are moving at specific speeds, in certain directions, or possess features that make them more "attention grabbing" for some reason.

In real life, detecting motion can be quite complex because movement may occur on part of the object, the horse, or both. Motion detection is most easily accomplished if the horse itself is stationary and the object is moving. In that circumstance, any change in the position of the object on the retina generally signals that it is moving. If both the horse and the object are moving, however, motion detection becomes quite complicated because the animal must now closely coordinate the movements of its eyes, head, neck, and entire body to prevent the retinal image from "bouncing" in such a jerky manner (like the image captured on a video camera when the operator is running) that the animal would be functionally blind.[14] When a horse is trotting, some compensatory mechanisms can be seen at work: the head and therefore the eyes bob only slightly because of a series of reflexive counterbalancing motions by the body and neck (Fig. 11-12).

Because maintaining vision while the horse or an object is moving is so critical to the animal's survival, several different systems have evolved to stabilize images on the retina. Virtu-

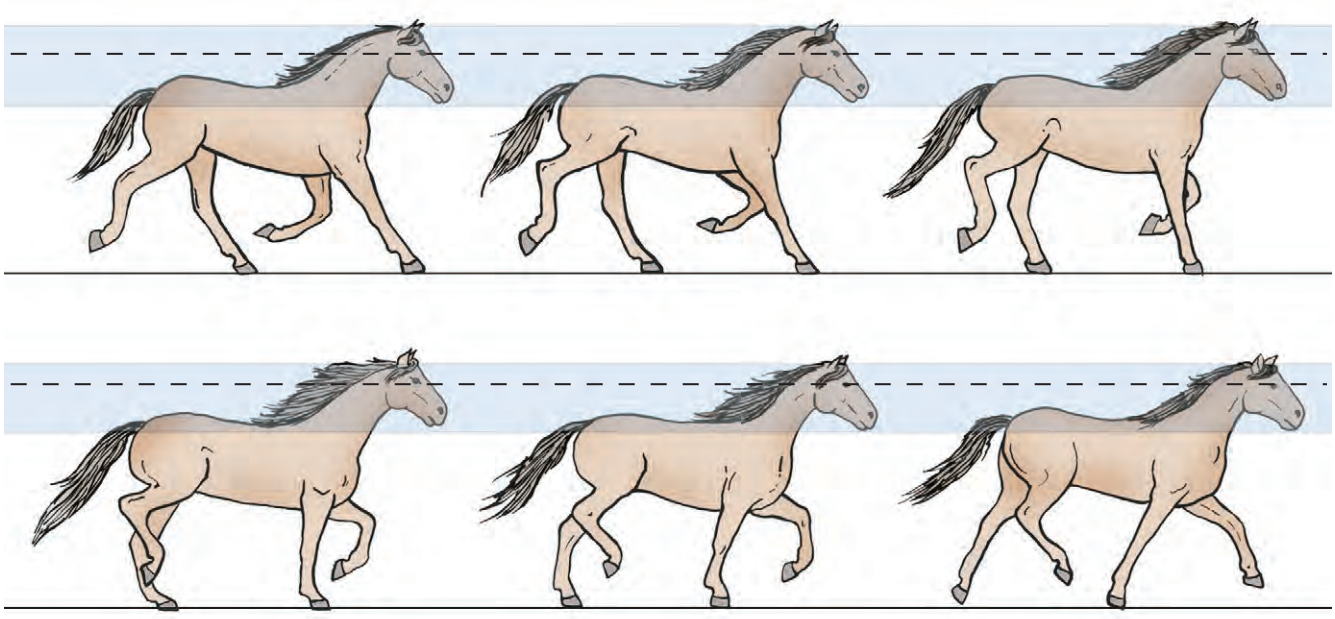


Figure 11-12. When trotting, the image on the retina remains relatively stationary during movement through a series of carefully coordinated movements of the head and neck.

ally all mammals, including horses, use a stabilization (fixation) system, a vestibulo-ocular reflex system, and an optokinetic system to stabilize images on the retina.[53-55] An additional set of more complicated eye movements—saccades, smooth pursuit movements, and vergence eye movements—are found in species that have forward-looking eyes, comparatively smaller fields of view, relatively well-developed extraocular muscles, a fovea (or at least a localized central region with heightened photoreceptor density such as the area centralis in cats), and improved binocular vision.[53-55] These movements allow the region of the retina with the greatest visual acuity to be aimed at and track an object, especially while both the animal and the object of interest in the environment are moving.

Most of a human's perception of vision (and presumably that of a horse) occurs when we fixate our gaze. The fixation system (1) attempts to keep objects of interest in a relatively stable position on the area of the retina with the greatest visual acuity and (2) helps prevent the image from being so stable on the retina that the retina undergoes sensory adaptation and the image no longer becomes visible. Although these two aims appear to be at odds with each other, it is important to remember that because the brain takes shortcuts and emphasizes changes in an object rather than its true physical nature, perfect stabilization of an object on the retina would soon result in it being no longer apparent (Fig. 11-13). Hence, the fixation system consists of both eye movements that keep the area of greatest visual acuity directed at an object and a set of very small, involuntary eye movements that prevent the image from being perfectly stable on the retina. The precision of these movements means that the fixation system works well only if the object is completely still or moving very slowly. It tends to quickly become inoperable if the object, the horse, or both are rapidly moving.

Two even faster reflexive eye movement systems also participate in retinal image stabilization. These pathways work to cancel out motion of an object across the retina when the horse itself is moving (the vestibulo-ocular reflex or "doll's eye" reflex) or when object is moving across the horse's visual field and the horse is stationary (optokinetic nystagmus). The differences between these two methods of stabilizing an image can be appreciated by holding up one finger at arm's length. The

Figure 11-13. Visual "shortcuts." Fixate on the red star while paying attention to the light blue annulus. After a few seconds, the blue annulus will disappear, and the red star will appear to be completely surrounded by a white field. Any movement of the eyes brings the blue annulus back into view. This exemplifies how the brain takes shortcuts in processing images by emphasizing changes; perfect stabilization of an image object on the retina would soon result in it being no longer apparent. This occurs because the receptive fields of the peripheral retina are much larger than those of the central retina, so the image appears stable in the peripheral visual field. Receptive fields of the central retina are much smaller than the red star, and micromovements of the eyes prevent that image from fading.

vestibulo-ocular reflex can be simulated by rotating your head side to side while at the same time having both eyes remain focused on your finger. You will notice that although your head is moving, the image of your finger remains relatively stable. This is because the semicircular canals of the vestibular system detect movement of the head, and this information can be used to rapidly direct the eyes to move to counteract the anticipated effects of that motion and keep the object in focus. In contrast, the optokinetic system can be simulated in this example by keeping your head stationary and moving your finger rapidly from side to side. In this situation, the image of your finger is much less stable and appears blurred. Here the stimulus for perceiving motion is not movement in the semicircular canals, but the retina detecting an image "slipping" very quickly across the visual field. Because the image must move before it can be detected, and only then can this information be used to redirect the eyes, the brain is always one step behind where the finger was in space, so the image appears blurred. Although the vestibulo-ocular reflex is better at stabilizing an image on the retina as the head is accelerating or decelerating, if the head begins to move at the same speed, the fluid in the vestibular canals soon begins moving at or near the same rate as the head and can no longer be used to direct the compensatory eye movements. The image, however, is still slipping across large regions of the retina, and now the phylogenetically old optokinetic nystagmus system takes over, and the brain switches over to using this visual stimulus to continue to direct the eye movements in an attempt to keep the image stationary on the retina.[53-55]

It is also possible to trick the brain into activating the optokinetic nystagmus system by keeping the animal stationary and making the surrounding environment appear to rotate around it. The latter trick, consisting of a rotating drum or projected series of bars (Fig. 11-14), has been used to estimate an animal's visual acuity because this type of nystagmus only occurs if the animal is actually able to distinguish the object in question (usually a series of light and dark bands) as separate from the background.[43] The limit of visual resolution in this case is determined by varying the width of the lines on the drum (or the speed in which the drum rotates) and establishing the maximum line width (or speed) at which the optokinetic response is no longer initiated. In effect, when the nystagmus disappears, the animal no longer sees individual light and dark bars, and the image appears uniformly grey. The spacing between the bars at which this occurs can be used to calculate the animal's visual acuity or ability to resolve fine details. This is a less than ideal method. The stimulus for the optokinetic reflex is the image "slipping" on large regions of the retina, rather than the fine details of the object as viewed by the visual streak or fovea.[53-55] Because estimates of visual acuity obtained in this manner are not limited to the regions of the retina responsible for the greatest visual acuity (visual streak) but include larger parts of the retina that have lesser acuity, this method may result in underestimating visual acuity. Nevertheless, the vestibulo-ocular reflex and the optokinetic system can be thought of as a single system that uses two different sensory signals, vestibular and visual, to help solve the same problem: maintaining retinal image stability during self-rotation and movement.

In addition to these three involuntary stabilizing reflexes, many species that have been investigated (and probably the horse) also have voluntary eye movements such as saccades and smooth pursuit movements that allow the animal to voluntarily shift its gaze to keep images on important regions of the retina.[53-55] *Saccades* are rapid (0.02 to 0.1 second) voluntary movements that quickly shift the eyes to keep a moving or new image on the area of the retina with the greatest visual acuity. These "jumping-ahead" movements may be quite large, covering up to 100 degrees in humans.[54] When the head is stationary, some species such as the rabbit and goldfish do not make saccades for all practical purposes.[54] These species have little need to do so because their laterally placed eyes already provide them with a large field of view, and their horizontally oriented visual streak allows them to scan the horizon without moving the globe. When a rabbit (and under certain conditions, a horse) makes a voluntary head movement, a saccade is initiated simultaneously with, or just before, the head movement in the direction the head is turning.[54] This causes the gaze to jump ahead, and while the head is moving, the eye holds its new position by means of the vestibulo-ocular reflex until the head catches up and the gaze is again properly aligned.[54] Humans and animals with a central area of particularly acute vision (area centralis), such as dogs and cats, can also make voluntary sac-

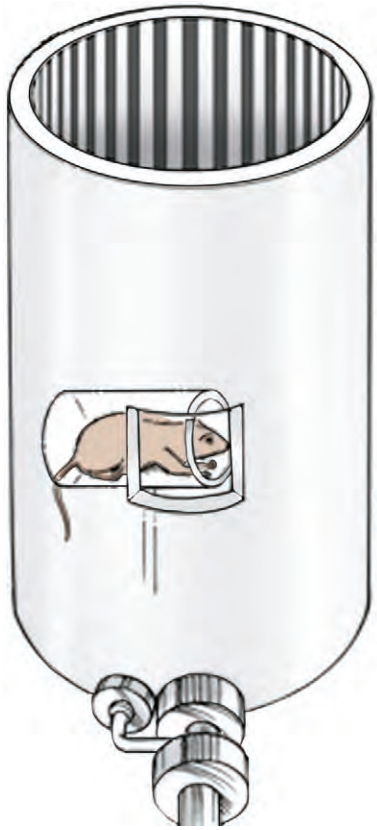


Figure 11-14. Optokinetic nystagmus testing for visual acuity. The animal is held stationary, and a grating pattern consisting of black and white bars is rotated around the animal's head. If the grating pattern is discernable, nystagmus will be detectable. If the pattern is not discernable, it will appear gray, and there will be no nystagmus. Alternatively the animal can be placed in front of a computer screen and its ocular movements noted as the grating pattern is varied in frequency and made to move across the screen. (Modified from Cahill H, Nathans J: The optokinetic reflex as a tool for quantitative analyses of nervous system function in mice: application to genetic and drug-induced variation, PLoS One 3:e2055, doi:10.1371/journal.pone.0002055, 2008.)

cadic eye movements without moving the head. Although the horse also has laterally placed eyes and a large field of view, it appears to be capable of making saccades without moving its head, especially when it is apprehensive, but does not seem to make these movements as often as animals with more frontally located eyes.

Because the eye rapidly "skips ahead" during a saccade, there is no time for the retina to process the intervening visual information or for the brain to correct or refine the movement during the shift. In effect, the eye is functionally blind during a saccade, and the target may be slightly undershot or overshot.[53-55] If the eye is shifting a large distance, the initial saccade moves the eye about 90% of the distance, and one or more smaller corrective saccades make up the remainder. The "smearing" of the image on the retina during a saccade is generally not consciously appreciated, and even though the eye has moved a large distance, the external world is perceived to be stable.[53-55] This is another way the eye differs from a camera; when a camera moves, the external world would also appear to move. Once the image stabilizes on the retina at the end of a saccade, the new information overpowers that which may have started during the saccade, and higher visual pathways "backward mask" the old information, thereby smoothing the image and rendering the animal unaware of the rapid, large shift that occurred.[54] It is tempting to speculate that because the horse has a large field of view, it needs to make fewer saccades, and this improves its vision (at least to a minor degree) by virtue of a reduction in the image smearing that occurs during these movements.

In many species, once the image has been captured on the visual streak by a saccade and any small catch-up saccades have been made, relatively voluntary, smooth-pursuit eye movements track a moving object so that its image remains on the retinal area with the greatest visual acuity (fovea or area centralis).[53-55] Like the saccadic system, smooth pursuit evolved with the development of retinal areas of greater resolution and is most well developed in species equipped with this type of retinal architecture. Under normal conditions, the stimulus for smooth pursuit is similar to that for the optokinetic system—for example, movement of the image across the retina (retinal slip).[54,55] Smooth pursuit differs in that the movement of the object is the point of interest. With the optokinetic system, the stimulus is much larger, and the goal is to follow the background, which is moving in the opposite direction, as the point of interest. Smooth-pursuit movements are driven by images that stimulate the fovea or area centralis and are usually small and relatively slow, whereas the slow phases of the optokinetic system are induced by large patterns that stimulate large areas of the retina.[53] To be effective, smooth-pursuit eye movements must override not only the fixation maintenance system, which tries to keep the eyes fixated on the same point in space, but also the optokinetic system, which tries to follow the massively slipping background images instead of the target.[54] If the horse's head is also moving, the vestibulo-ocular reflex needs to be cancelled out if smooth-pursuit movements are to allow the image to be examined more closely.[54] In all these circumstances, the central visual processing system of the horse must decide whether to consciously pay attention to the background or the more focal point of interest, and which system to override to achieve this goal.

Stationary objects are also viewed with smooth-pursuit eye movements, because there is always slight motion of the image on the retina as the muscles of the head, neck, and body attempt to maintain a steady posture.[14,53-55] Because smooth-pursuit eye movements track an image by using "retinal slip," the image on the retina is always moving to some degree. This is another way in which the visual system differs from a camera: in effect, it requires some degree of movement to function properly. Although the image of the object being observed may seem to be stationary, this is purely a perceptual phenomenon and is the result of central visual pathway processing of the image. Animals with visual streaks (such as horses) typically do not show smooth-pursuit movements when an object moves horizontally along the direction of the streak, but they appear to do so when an object moves vertically across the streak.[14]

Saccadic and smooth-pursuit movements result in the two eyes moving equally in a synchronous (conjugate) fashion, and the viewing angle between the two eyes remains the same. Typically, these movements are elicited when the object of interest is moving from side to side or up and down. If the object of interest is moving toward or away from the viewer, convergent or divergent "vergence" eye movements, respectively, are used to change the viewing angle between the two eyes to keep the object in proper focus. Convergence is also usually accompanied by accommodation (adjusting the focal power of the lens so that near objects are seen more clearly) and miosis that optically increases the animal's depth of field, thereby enhancing depth perception and visualization of near objects.[56] These three responses—convergence, accommodation, and miosis—are neurologically distinct, but because they generally occur simultaneously, they are referred to as the *near response*.[56] Vergence eye movements are typically fairly slow (taking up to 1 second in humans),[53] and as during a saccade, visual sensitivity is markedly reduced during the movement itself. The extent to which horses perform vergence eye movements has not been carefully investigated, but the relatively large area of binocular overlap and certain behaviors (see discussion of depth perception) suggest that they are readily capable of performing these types of movements. However, the comparably slower rate of pupillary constriction of horses versus that of humans suggests that horses may perform vergence movements more slowly than humans do.

THE PERCEPTION OF DEPTH

VISUAL PERSPECTIVE AND FIELD OF VIEW

The ability to differentiate objects on the basis of depth depends on a number of factors: the animal's visual perspective, field of view, the difference between the images acquired when both eyes view the same object (binocular disparity), and higher processing by the brain to fuse these images into a novel image that allows for depth to be perceived. The horse's visual perspective can vary greatly and depends to a large extent on whether the head is down and the animal is grazing, or the head is up and the animal is scanning the horizon. Furthermore, breed differences can result in the same environment being perceived quite differently. A field of tall grass may appear to be a dense, impenetrable brush to a Miniature horse but a wide-open savanna to a Clydesdale (Fig. 11-15).

The lateral position of the eyes in the skull affords the horse a wide panoramic view (Figs. 11-16 and 11-17),[16,24,30] and the nasal extension of the retina further enhances the horse's tem-

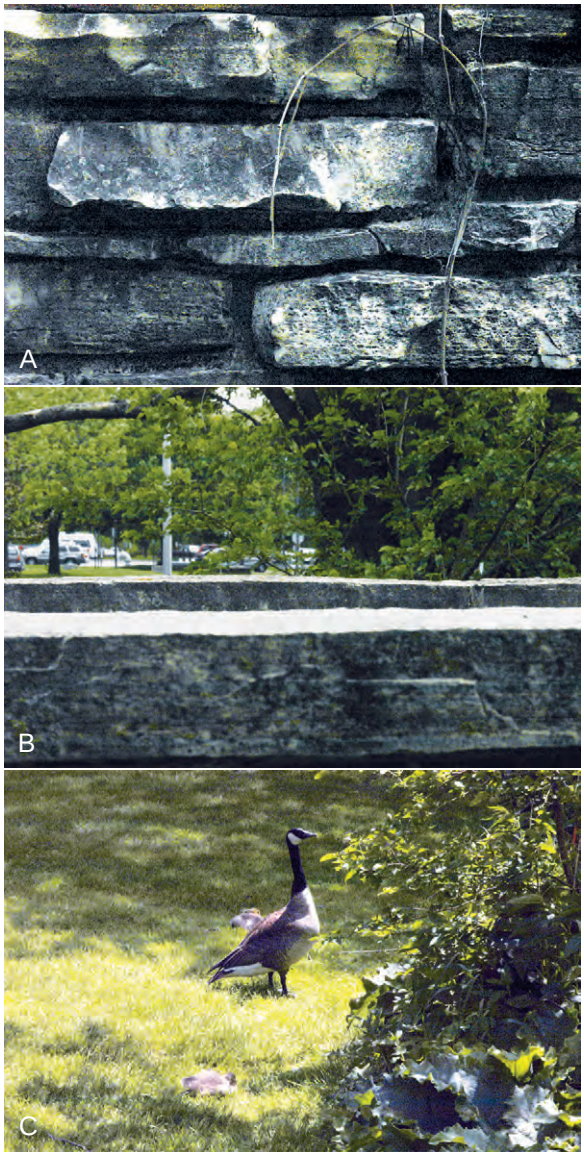


Figure 11-15. The visual perspective of horses varies greatly by breed, even when standing in the same location. **A,** Miniature horse only sees a stone wall. **B,** Arabian sees to the top of the wall. **C,** Belgian Draft horse sees what is on the other side of the wall.

poral peripheral visual field. On the basis of anatomic relationships, the horse is believed to have a total monocular visual field in the horizontal meridian (i.e., the portion of the horizon that can be seen by an eye when fixed on one point) of approximately 190 to 195 degrees, and up to 178 degrees in the vertical (superior to inferior) meridian. When the visual fields of the two eyes are combined, the total horizontal visual field is up to 350 degrees, and the horse has virtually a complete sphere of vision around its body, with only a few minor "blind spots."[16,24,30] These blind spots are small and located superior and perpendicular to the forehead, directly below the nose, in a small oval region in the superior visual field where light strikes the optic nerve itself, and the width of the animal's head directly behind it. Clearly, this extensive visual field makes it very difficult for a predator or human handler to sneak up on a horse.

The visual fields of the two eyes overlap anteriorly and below the nose for 55 to 65 degrees, although some authors suggest the overlap may be as great as 70 to 80 degrees.[16] This degree of binocular overlap rivals or exceeds that of domestic dogs, which ranges from 30 to 60 degrees, depending on breed.[24,57-59] This would seem to challenge the generally accepted view that predators have binocular vision superior to that of prey species. In reality, however, depth perception plays a significant role in breaking the camouflage of an object (e.g., a wolf) against its background, and this would be of distinct advantage to prey species.[60] As has been described for certain bird species, it is also possible the animal's lifestyle and the extent of the binocular field do not necessarily predict the quality of its stereoscopic vision.[61,62]

Stereopsis (binocular depth perception) results when the two eyes view the world from slightly different vantage points, and the images from the overlapping visual fields are fused into one.[60] If the relatively disparate images on the two retinas were not blended, viewing a scene with both eyes would simply result in double vision (diplopia), and depth perception would actually be impaired. The new information that stereopsis provides is as qualitatively important to the overall sense of vision as is the perception of motion, color, or contrast. The ability to perceive depth varies greatly between individual humans[63,64] and cats,[65] and although similar work has not been done with horses, some horses undoubtedly are better than others at detecting depth. How these differences may affect their usefulness for certain types of work is uncertain because a number of horses with one eye have been observed to still function well as jumpers or barrel racers, even though these tasks would seem to demand excellent depth perception. Also, several horses with only one functional eye have performed well in top-tier races such as the Kentucky Derby.[66]

Integration of binocular visual inputs is not the only means available to an animal to accomplish depth perception, however. As any artist can attest, animals and humans can appreciate depth with only one eye by using specific visual clues. These include relative brightness (brighter objects tend to be closer), size (larger objects are closer or objects progressively increasing in size are getting closer), contour and areas of light and shadows (the gradation in the intensity of a shadow on a curved object makes it appear to be projecting away from or toward the observer), object overlay (closer objects block distant ones), linear perspective (parallel lines like those of a railroad track converge onto a vanishing point at distance), aerial perspective (water vapor, dust, and smoke in the atmosphere make distant objects indistinct and relatively color-desaturated), density of optical texture (the fine details of the surface of an object become less apparent the farther away it is), relative velocity (near objects appear to move faster than distant ones), and motion parallax (objects at different distances appear to move at different speeds or in different directions, depending on the observer's point of fixation (Fig. 11-18).[60] There is good evidence that horses are able to use at least some of these static monocular clues to recognize depth in two-dimensional photographs, and it appears they are even susceptible to some of the pictorial visual illusions to which humans are susceptible.[1,67] Because of their huge monocular visual fields, it is clearly advantageous for horses to be able to use monocular clues to estimate depth.

Nevertheless, two eyes are better than one, because the binocular threshold for depth perception in horses is five times

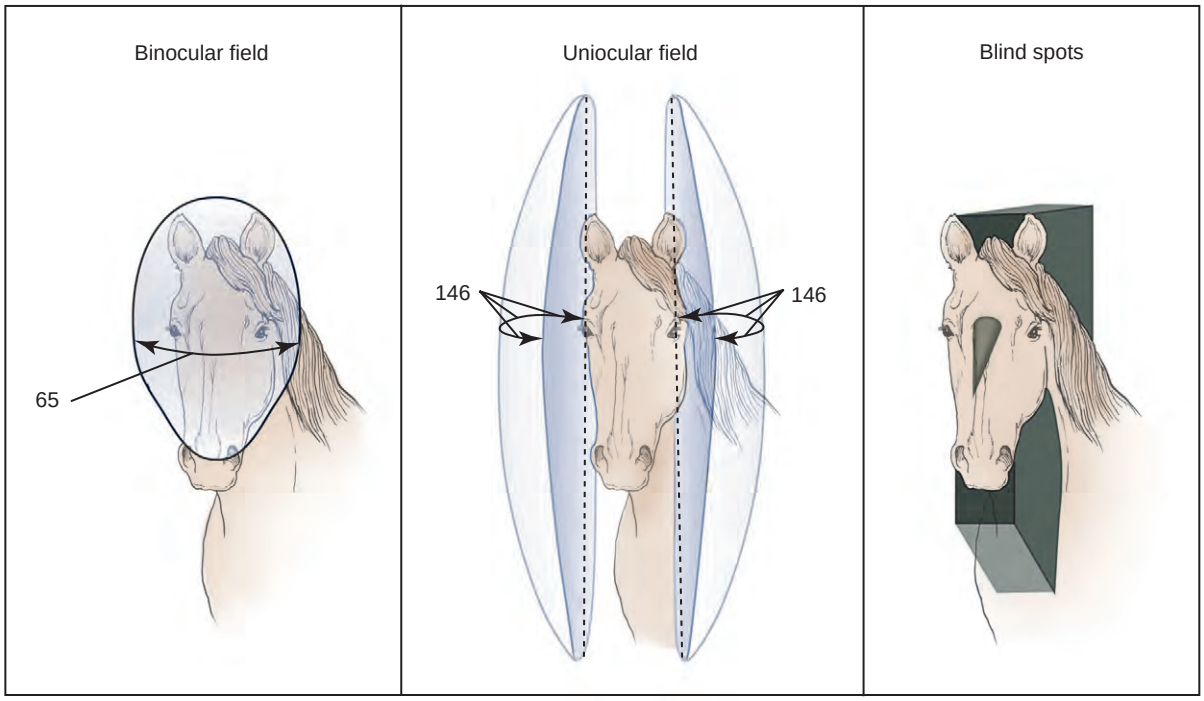


Figure 11-16. Visual field of view of the horse.

Figure 11-17. Simulation of the view seen by the left eye of a human and a horse looking over the city of Perth, Australia. **A,** Simulated view seen by a human with a small, high-acuity central region surrounded by a peripheral region of lower visual acuity. **B,** Simulated view of a horse. Note the much wider field of view with a linear area of higher acuity and a horizontal strip of lower acuity above and below. (From Harman AM, et al: Horse vision and an explanation for the visual behaviour originally explained by the "ramp retina," Equine Vet J 31:384, 1999.)

Figure 11-18. Depth perception with one eye. Several cues allow depth to be perceived with one eye or in a two-dimensional photograph. These cues include apparent size (the left tower appears closer because it is larger than the right), looming (cars moving toward the viewer appear to become progressively larger), interposition (near objects, such as the bridge, overlie the more distant hills), aerial perspective (water vapor and dust in the air make the more distant hills less distinct and relatively color desaturated), shading (shadows on the tower suggest depth), perspective (the parallel roadways appear to converge toward the horizon), relative velocity (the nearer cars appear to move faster than the more distant ones), and motion parallax (if the eye is fixed on the center of the bridge, the images of near objects appear to move opposite the direction in which the observer moves his or her head, whereas distant objects move in the same direction as the head).

better than the monocular threshold.[68] Although the two eyes of horses are farther apart than those of humans (resulting in a greater relative disparity between the two retinal images and theoretically better depth perception), humans still have better depth perception than horses. From 2 meters away, humans can detect a few millimeters' difference in depth, whereas from the same distance, horses can detect only a 9-cm difference (a 10- to 20-fold poorer performance).[68] The latter value approximates that of cats[69,70] and may have some biological relevance because it is also approximately the same difference in depth between grass in a pasture and the ground under it. The familiar behavior of a horse rotating its nose upward to better observe distant objects has been suggested to be a response to exploit improved depth perception, since binocular overlap is said to be oriented down the nose in horses (rather than straight ahead as it is in humans).[16,24,71] Evaluation of the eye position and forward visual field of the horse, however, would suggest that they are still capable of binocular overlap when viewing objects with their noses down and their eyes directed forwards, as when riding "on the bit."[72]

When stereopsis is combined with the perception of motion, horses and humans are able to make accurate judgments regarding the trajectories and distances of moving objects so as to allow them to be intercepted or avoided. A similar phenomenon occurs if the object is stationary and the horse is moving. If a fixed point of reference is present, it is easier to detect motion-in-depth than if the object is effectively by itself.[73] For example, it is easier to detect the motion-in-depth of a baseball bouncing along the ground than it is to detect its motion-in-depth against a clear blue sky. Predators use stereopsis and stereomovement (the ability to detect motion-in-depth) to improve the accuracy of their attacks, but as discussed previously, these visual components are equally important to prey species such as the horse because they enhance their ability to detect the predator's camouflage and avoid objects during their escape.[60]

The ability of humans with normal vision to detect motion-in-depth is 5 to 28 times poorer than their ability to detect a difference in depth if the object remains static (stereoacuity).[73,74] At first, this is somewhat surprising because (1) objects that are moving from side to side (e.g., in the frontoparallel plane) are much easier to detect than stationary objects, and (2) each eye working alone is readily able to detect objects that are moving across the visual field from nasal to temporal and also moving away from or toward the eye.[75] This phenomenon appears to be due at least in part to the fact that stereomotion detectors average the motion individually detected by the left and right eyes.[75] Additionally, objects moving across the visual field stimulate a series of photoreceptors over more widely separated regions of the retina, whereas objects moving in depth stimulate regions of the retina that are much closer to each other. Finally, this difference is not so much because detection of motion-in-depth is so poor, but more so because stereoacuity is so good. Brain processing of the images from both eyes allows details of an object that are not visible to either eye alone to be detected (see discussion of hyperacuity).

The ability to perceive depth develops after birth and depends on images being presented to both eyes for comparison purposes. This ability goes through a critical developmental period, and kittens that have had the eyelids of just one eye sutured closed for a brief period (5 days) will experience substantial permanent deficits in binocular depth perception. This is especially true if the deprivation occurs between 35 and 45 days after birth.[76] This developmental age may correlate with that of a newborn foal and suggests that if the vision in one eye is impaired by a corneal ulcer or the placement of a third eyelid flap during critical periods of maturation of the visual system, depth perception may fail to develop normally in that animal, despite subsequent resolution of the problem.

VISUAL TEXTURE

All surfaces of an object have a tactile texture—how they feel when touched. They also have a visual correlate of this called *visual texture*, which for our purposes refers to the appearance of the surface's texture. In other words, does the surface appear rough or smooth, homogenous or fragmented, full of fine details or uniform, composed of randomly arranged elements or elements that occur in a regular pattern, and so on. Visual texture can be a powerful mechanism for seeing an object as separate from other objects in the visual field (Fig. 11-19). Visual acuity and form perception are other critical elements in the horse's ability to see objects as separate from their surroundings.

VISUAL ACUITY

In general, *visual acuity* refers to the ability to see the details of an object separately and without blurring. It depends on (1) the optical properties of the eye, (2) the retina's ability to detect and process images, and (3) the ability of higher visual pathways to process and interpret these images. Visual acuity can be evaluated in many ways, and at times, the methods and terminology can be quite confusing. Measurements of visual acuity may be based on the size of a letter on an eye chart, the angle the object's image subtends on the retina (in seconds, minutes, or degrees of arc), or how close together an alternating pattern of black and white lines can be before they appear to

Figure 11-19. Visual texture. Objects may be differentiated from their background on the basis of differences in texture of their constituent elements. In this image, the deer can be identified in part because its coat has a more homogenous texture than either the forest floor or the oak trees.

Table 11-1 | **Comparison of Terms Used to Describe Visual Acuity**

SNELLEN VALUE	NUMERICAL VALUE	MINUTES OF ARC	MINUTES/ SECONDS OF ARC	CYCLES PER DEGREE
20/20	1.0	1	1′ 0″	30
20/25	0.80	1.25	1′ 15″	24
20/30	0.667	1.5	1′ 30″	20
20/35	0.571	1.75	1′ 45″	17.2
20/40	0.50	2.0	2′ 0″	15
20/45	0.444	2.25	2′ 15″	13.4
20/50	0.40	2.5	2′ 30″	12
20/55	0.364	2.75	2′ 45″	10.9
20/60	0.333	3.0	3′ 0″	10
20/65	0.308	3.25	3′ 15″	9.2
20/70	0.286	3.5	3′ 30″	8.6
20/75	0.267	3.75	3′ 45″	8
20/80	0.25	4.0	4′ 0″	7.5
20/85	0.235	4.25	4′ 15″	7.1
20/90	0.222	4.5	4′ 30″	6.7
20/95	0.21	4.75	4′ 45″	6.3
20/100	0.20	5	5′ 0″	6
20/150	0.133	7.5	7′ 30″	4
20/200	0.10	10	10′ 0″	3

Data from Borish IM: Clinical refraction, ed 3, Chicago, 1975, Professional Press.

be uniformly gray (the so-called grating acuity, which is measured in cycles per degree). All of these measurements are interrelated, and tables that allow one set of units to be compared with another have been created (Table 11-1).[77]

In humans, one of the most familiar methods of measuring visual acuity is to ask an observer to read a Snellen eye chart, which consists of rows of progressively smaller black letters on a white background (Fig. 11-20).[78] The size of the letters between rows varies in a geometric fashion (0.1 log unit), and the smallest line that can be reliably discerned in this high-contrast setting is called the *minimum resolvable* or *resolution acuity*.[78] There are a number of variations on the classical

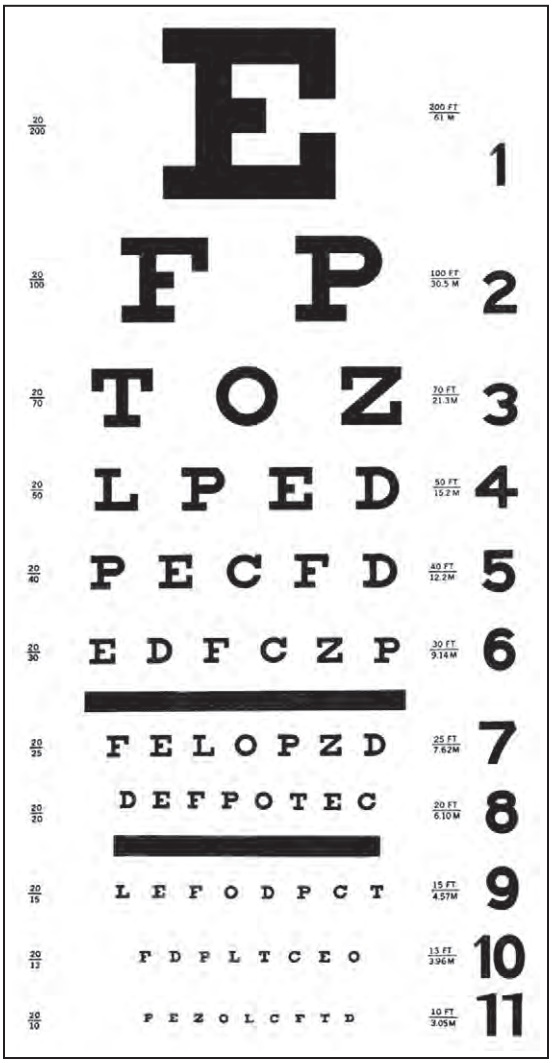


Figure 11-20. A Snellen-type visual acuity chart.

Snellen eye chart, and because not all letters are equally easy to read, other commonly used charts use only one letter (typically a "tumbling E" or "Landolt's C") and ask the observer to indicate the direction in which the letter is pointing (up, down, right, or left). The size of each letter in a row is based on the assumption that under these optimal but artificial conditions, normal human visual acuity is 1 minute of arc, so the width of the strokes forming the E or the gap in the C will subtend 1 minute of arc on the retina at a specified distance (e.g., 20 feet, 60 feet, 200 feet).[78] The results of these tests are then typically recorded as 20/20, 20/40, 20/60, and so on—the numerator representing the distance the subject is from the target (chart), and the denominator representing the maximal distance from which a person with statistically normal vision could identify a letter this size. In other words, *20/200 vision* means that the test subject can only make out the details of a letter from 20 feet away that a person with normal visual acuity could make out from 200 feet away.

In using Snellen acuity values to express visual acuity for animals, it must be recognized that the denominator is still using a statistically normal person for comparison. With this

type of notation, equine visual acuity varies from about 20/30 on behavioral testing,[79] 20/35 to 20/40 according to ganglion cell density calculations,[16] and approximately 20/60 when estimated electrophysiologically with the horse under general anesthesia.[80] By comparison, normal canine visual acuity is approximately 20/75, and normal feline visual acuity is 20/100 to 20/200.[81-83] In a recent study, it was shown that the horse could better visually discriminate between objects if they were located on the ground versus being placed 70 cm above the ground.[84] This suggests that the visual appearance of the ground surface should be considered in the management and training of horses.

The largest row of letters on most eye charts usually corresponds to 20/400 visual acuity. Vision poorer than this is commonly described as "counting fingers" (at a certain distance), "hand motion" (at a certain distance), "light perception," and "no light perception."[85] The latter two descriptions do not actually measure visual acuity but simply indicate whether any stimulus can be detected at all. If a person's best corrected (e.g., with glasses or contact lenses) visual acuity is 20/200, he or she is considered to be legally blind. In comparison, counting fingers vision at 2 feet corresponds to a visual acuity of approximately 20/2000, and hand motion vision at 2 feet corresponds to a visual acuity 10 times worse than this, or 20/20,000.[85] Because the stimulus for a menace response is essentially identical to that of hand motion vision, the veterinarian should be cautious about interpreting a horse's positive menace response to mean that it has useful vision. In reality, a positive menace response from 2 feet away only indicates that the animal's vision is at least 20/20,000, but such a response could also be present in a person with a visual acuity 100 times worse than someone who is legally blind. Unfortunately, in veterinary medicine there is no simple method such as an eye chart that allows the clinician to more precisely determine a horse's visual acuity, and the clinician is often forced to extrapolate the impact of a given disorder from humans to horses.

Lay people often regard Snellen visual acuity to be synonymous with how well an animal or person sees, but in fact, this is not the case. In the real world, the ability to see all the features present in a complex visual environment cannot be reduced to one number such as 20/20, and a horse or human may have "normal" Snellen visual acuity and still have marked visual impairment. This is because in part, Snellen acuity is so highly tied to the performance of a very small region of the retina with the greatest photoreceptor density.[3] For example, if the entire retina except for the fovea is lost, a person's visual acuity would still be 20/20, but the field of view would be only a few degrees in diameter and for all practical purposes, not very useful. Such a situation occurs in people with advanced retinitis pigmentosa in which the photoreceptors of the peripheral retina degenerate, and only foveal vision is preserved. Similarly, if only the fovea is lost, visual acuity drops to that of the peripheral retina (20/200 or worse in humans) even though most of the retina is still performing normally.[3] Although the horse lacks a fovea, and the reliance on such a very small region of the retina is lessened, lesions that affect the horse's visual streak, especially the temporal arm, will undoubtedly have an appreciable impact on an animal's ability to resolve fine details in its environment.[10,16]

For this and other reasons, a variety of other stimuli have been employed in assessing vision, including presenting targets with varying shades of gray, alternating bars or checkerboards, objects arranged in depth, various sets of colors, and a series of dots or short lines arranged in a row. Each type of target tends to activate different portions of the visual system, and the results are expressed in relatively unique ways. When the stimulus and viewing conditions are varied, it becomes apparent that a number of factors influence visual acuity:

Contrast (Reduced contrast reduces resolution.)
Luminance (Visual acuity decreases in dim light.)
Refractive error (Errors reduce visual acuity.)
Pupil size (Small pupils lead to greater depth of field and to a certain degree, improve visual acuity for targets located outside the plane of focus of the eye.)
Retinal eccentricity (The farther from the fovea or visual streak, the greater the reduction in visual acuity.)
Exposure duration (Visual acuity is decreased for target exposures in the 100- to 500-millisecond range compared with longer exposures.)
Target and eye movements (Saccades and rapid target movements reduce acuity but moderate movements do not.)[78]

The degree of contrast between the brightest and dimmest components of an object can greatly affect the object's visibility (Fig. 11-21).[6] Although it is important to use a highly contrasting standard such as black letters on a white background

Figure 11-21. Reduced contrast sensitivity, glare, and reduced visual acuity. The entire image is "washed" with light, and the contrast between objects is diminished in addition to a reduction in the visibility of fine detail (reduced visual acuity). Extreme glare is also present, which can occur naturally as in this case or as a frequent sequela of corneal scarring, cataracts, and other ocular opacities that scatter light towards the retina (versus bouncing it back out of the eye). All three can be quite debilitating and are frequent causes of accidents.

(e.g., the standard Snellen target), if the maximal visual acuity a visual system is capable of is to be determined, this situation is seldom encountered in the real world. It may be far more important for the horse to be able to differentiate between varying shades of gray, because its rod-rich retina has evolved primarily to perform well in dim light where contrast is not as great.

In a laboratory setting, contrast sensitivity is tested by using repetitive stimuli such as alternating lighter and darker bars (grating patterns), checkerboards, or varying shades of gray letters on a white background.[6] When this type of stimulus is used, visual acuity varies not only with the spatial grain of an image (how thin the black bars are and how far apart the alternating bars are from each other) but also with the contrast between various elements of the image. Very coarse patterns (very wide bars) can be seen at very low contrast (relatively little difference between the bars in terms of their shades of gray), but as the spatial grain is made finer (the bars become thinner), a higher degree of contrast is needed to see the pattern.[6] In general, objects with low degrees of contrast are more difficult to distinguish as separate from the background than highly contrasting objects, even if the objects are the same size and are viewed from the same distance. Therefore, although resolution acuity of black objects on a white background is important for establishing a minimum threshold for detection of an object, it is in reality only one small point on the contrast sensitivity continuum, and it does not fully describe an animal's visual capabilities.[6]

The degree of illumination of an object also affects visual acuity. In very dim light, visual acuity is reduced in humans and horses, with the human rod system being able to support a peak visual acuity of approximately 20/150.[78] As the light intensity increases to the point that cones can be used effectively, human visual acuity rises to 20/20 because the cones are more densely packed in the fovea than the rods. In very bright light (e.g., that exceeding a bright sky on a sunny day), human visual acuity tends to level off or be reduced from expected values.[78] Although these findings are likely to be applicable to horses in general terms, similar studies have not been performed in horses, and the presence of a large number of rod photoreceptors in the central retina of the horse may alter these values to some degree. For example, one study demonstrated that a 1-inch wide stimulus on an overcast day was more visible to a horse than a 2-inch stripe on a sunny day.[71] This suggests that the rod-dominated central area of the equine visual streak has impaired visual discrimination under bright light conditions compared with that of a human with a cone-rich fovea. In another experiment, it appeared that contrast stimuli underfoot were less visible to younger animals than older ones, but a subsequent examination of head/neck carriage showed that younger horses did not lower their heads to the same degree as older, more trained horses.[71] These types of findings indicate the difficulties associated with performing visual evaluations in horses and also highlight the role learning plays in a horse's visual performance.

OPTICAL FACTORS IN VISUAL ACUITY

In the ideal situation, the transparent optical elements of the eye (cornea, lens, aqueous and vitreous humors) would capture light emanating from every infinitesimal point in a scene and precisely focus these onto a correspondingly infinitesimal point on the retina.[86-88] However, in actuality, the optics of the eye invariably distort a precise point of light from a scene into a circular blur on the retina. When severe, this distortion can substantially limit the visual acuity of the eye, but humans and animals are relatively insensitive to small amounts of blurring, so objects located at a range of distances from the eye appear to be in sharp focus (depth of field).[3]

REFRACTIVE STATE

The refractive state of the eye has a direct impact on visual performance. For all the elegance of the retina and the higher visual pathways, their function is for naught unless an accurately focused image of the environment is formed on the retina. In ophthalmology, the term *resting refractive state* is generally used to refer to the plane in space where the eye is focused when at rest (not accommodating). When an object is placed approximately 20 feet away from the eye, all light rays emanating from the object that enter the pupil are essentially parallel (hence, this distance is regarded as essentially the same as optical infinity and is used for Snellen visual acuity testing). Proper focusing of parallel rays emanating from an object on the retina is called *emmetropia*, whereas focusing of the image in front of or behind the retina are called *myopia* (nearsightedness) and *hyperopia* (far-sightedness), respectively (Fig. 11-22). In astigmatism, the cornea, lens, or both have an uneven curvature (e.g., a football versus a sphere), causing the eye to have two (or more) focal points.

The extent of a refractive error is expressed in terms of the dioptric power of a lens that is needed to allow the eye to correctly focus on an object that is infinitely far away (e.g., ≥20 feet for practical purposes). The unit of optical power of a lens system is the diopter (D = 1/focal length in meters). This means that an eye that is in focus at rest 1/3 m away from the eye is 3 D myopic. In humans, simple myopic or hyperopic refractive errors can be corrected by placing appropriately powered spherical lenses in the form of glasses or contact lenses in front of the eyes. In the previous example, placement of a 3-D, concave (negative) lens in front of the eye would now allow images greater than or equal to 20 feet away to be properly focused on the retina. Astigmatism is more complicated, but it can be corrected by adding cylindrical-shaped lenses that refract (bend) light in one plane but not the other. Alternatively, refractive errors can be corrected by surgically recontouring the cornea with any one of several different procedures (e.g., LASIK). In theory, these procedures are also applicable to horses, but only rarely are contact lenses used to attempt to correct refractive errors in horses.

The resting refractive state of the living equine eye can be objectively determined by streak retinoscopy, and over the past 100 years, numerous studies involving more than 16,000 equine eyes have been performed in which this technique was predominately used.[16,24,89-100] As is often the case, in most recent reports, the large number of studies performed in the 1800s and early to mid-1900s have been ignored. Each of these reports varies as to the mean refractive state and the relative frequency and magnitude of reported myopia and hyperopia.[16,24,89-100] This may reflect regional and perhaps temporal variations in the equine populations screened, rather than inconsistencies in technique. It has been well documented in dogs that the refrac-

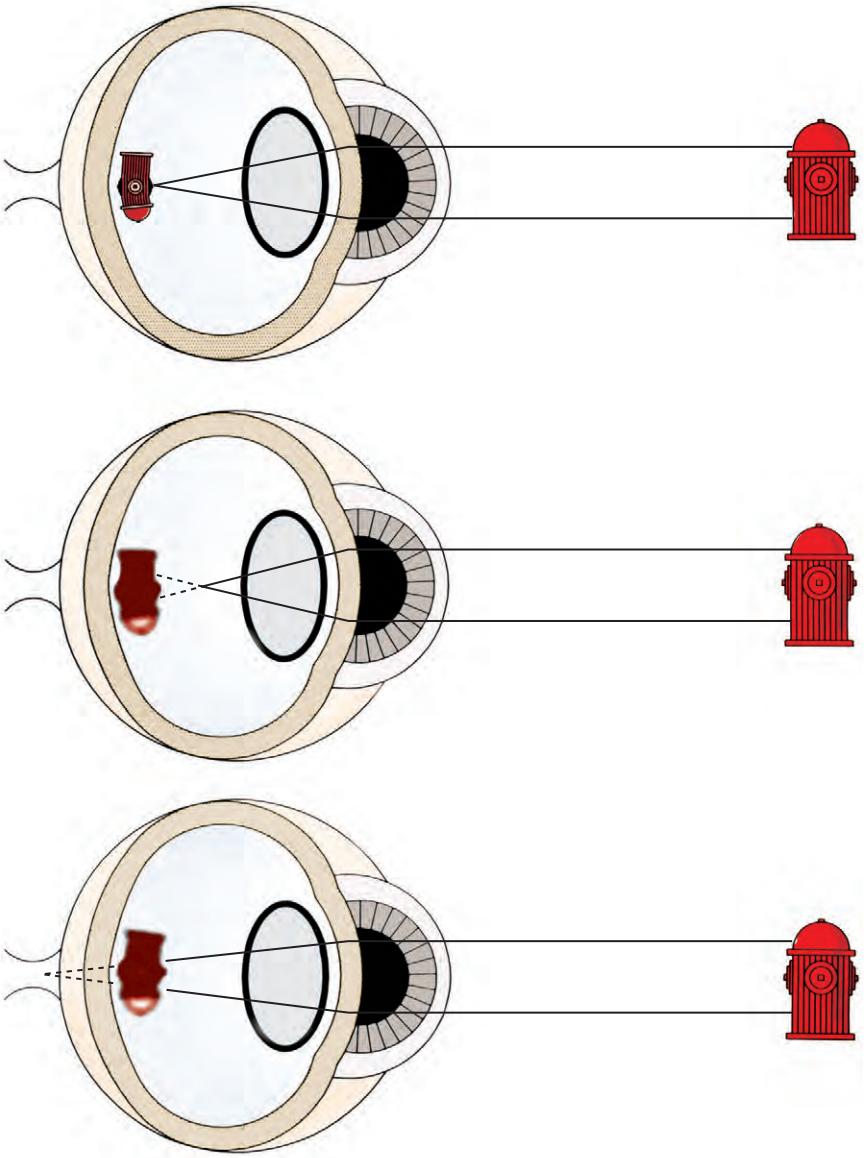


Figure 11-22. Ray diagrams showing emmetropia (proper focusing of images on the retina, *top*), myopia (near-sightedness, or focusing of images in front of the retina, *middle*), and hyperopia (far-sightedness, or focusing of images behind the retina, *bottom*). (From Miller PE, Murphy CJ: Vision in dogs, J Am Vet Med Assoc 207:1623–1634, 1995.)

tive state can vary with breed and with selective pressures imposed by performance requirements.[101-103]

In general, the average resting refraction of the horse in most modern studies is near emmetropia (normal), but some individuals are significantly (≥3 D) myopic or hyperopic. In one study of 215 equine eyes in Europe,[100] 3% were hyperopic, 15% were emmetropic, and 82% were myopic, although most of these were within a diopter of emmetropia. Significant astigmatism was not found in this study.[100] In a study of 15 horses of various ages and breeds in England,[92] the refractive state varied from −3 to +3 D, and 43.3% of these horses were hyperopic, 33.3% were emmetropic, and 23.3% were myopic. Finally, a survey of 83 horses of varying breeds, ages, and performance demands living in the midwestern United States[98] revealed a mean resting refractive state after cycloplegia of +0.25 D and low frequencies of astigmatism (≥0.5 D in six horses) and anisometropia (a difference in refractive status between the two eyes of 0.5 D in 10 horses). In this study, 55% of horses were within 0.5 D of emmetropia, whereas 24% were greater than or equal to 0.5 D hyperopic and 21% were greater than or equal to 0.5 D myopic.[98] Horses with moderate to severe vitreal degeneration tended toward myopia, although this was not statistically significant.[98] In a study by Wouters and De Moor[100] that demonstrated a high frequency of myopia, a high incidence of vitreal degeneration was recorded in the study population.

The resting refractive state of a species can also be estimated from analysis of ray tracings with schematic eyes. A schematic eye is an internally consistent mathematical model that is constructed for a particular species with three sets of data: (1) the

refractive index of the optical media, (2) the position along the optical axis of each optical interface (front and back of the cornea, the front and back surfaces of the lens, and the retina), and (3) the radius of curvature of each optical interface. Three schematic eyes for horses have been reported.[93,96,104] As pointed out by Farrall and Handscombe,[92] an unresolved issue in the schematic eyes presented by Sivak and Allen[96] and Knill et al.[93] is the prediction of marked hyperopia, a finding incongruous with the data obtained by refraction of the living horse eye. In contrast, the schematic equine eye constructed by Coile and O'Keefe[101] predicts a refractive state of +1 D, which is closer to that obtained by streak retinoscopy.

DIFFRACTION

Even in the absence of any optical abnormalities, an infinitesimal point of light cannot be brought into focus on the retina because light waves are bent (diffracted) as they pass through a hole in an obstruction, in this case the pupil.[3,87] This results in a precise point of light being converted to a fuzzy disc surrounded by dimmer rings (airy disc) by the time it reaches the retina. The smaller the pupil, the greater the impact diffraction has on vision.[3,87] Although diffraction is a fundamental physical phenomenon and may significantly affect human visual acuity, the role it plays in equine vision is unclear.[78] This is due in part to differences between humans and horses in the shape and size of the pupil and to the fact that in very bright light, the equine pupil may have two distinct pupillary apertures, as described in the following section.

OPTICAL ABERRATIONS

Optical aberrations occur when the light rays originating from a point light source are not brought to a point of focus on the retina, typically as a result of inaccuracies and irregularities in the shapes of the curved refracting surfaces of the cornea and lens.[3] Along with diffraction, optical aberrations are potentially more serious than simple refractive errors because they are not easily correctable with the usual spherical or cylindrical lenses.[3] Aberrations can be classified as monochromatic, which may be seen with only one wavelength of light, and chromatic, which involves the differential focusing of various wavelengths (e.g., colors) of light on the retina.[87] Monochromatic aberrations can be further classified as spherical or cylindrical refractive errors (already discussed) and spherical aberrations, comas (in which a point source of light is distorted into a comet-shaped blur), and "higher-order" aberrations that are an amalgam of deviations that can take on complex patterns.[87]

Spherical aberration is a major distortion in many optical systems, inducing up to 2 D of blur in humans (Fig. 11-23).[86] Positive spherical aberration occurs when light rays passing through the periphery of the cornea and to a lesser extent, the lens, are brought into focus in front of those passing through the central portion of the cornea and lens. Negative spherical aberration occurs when the more peripheral rays are brought into focus behind the paraxial rays. At the level of the retina, the result is a focal light source appearing as a relatively intense circle of light surrounded by a less intense halo, provided that the eye is emmetropic.[87] Because the iris controls the amount of peripheral light that reaches the retina, spherical aberration is greatest when the pupil is large. In bright light, it is essentially negligible in humans. The proportionally larger, horizontally elongated cornea[25,26] and the large rectangular pupil in horses suggest that either spherical aberration plays a more significant role in horses than in humans, or horses have other mechanisms for controlling this aberration. Spherical aberration can be reduced by flattening the peripheral cornea, thereby reducing its optical power, or by reducing the refractive index of the peripheral lens versus the axial lens. The equine cornea does appear to have a flatter peripheral corneal curvature, although precise measurements have not been made.[25,26] In the equine pupil that is fully constricted, thereby creating two pupillary apertures as a result of occlusion of the midportion of the pupil by the corpora nigra, spherical aberration would be minimized. This is because rays would pass through portions of the lens that are roughly equidistant from the center of the lens. Spherical aberration may also be less of a problem for horses because they also rely more heavily on rod photoreceptors with larger receptive fields and because identification of large shapes or movement is more important than discrimination of fine details.

Chromatic aberrations occur when light of different wavelengths is focused at different distances from the posterior nodal point of an optical system (e.g., at different planes relative to the retina) (Fig. 11-24). In humans, the total chromatic aberration is about 1.5 to 3 D under daytime conditions.[86,105] Green light (medium wavelength) tends to be focused on the retina, red light (long wavelength) is bent less and is focused behind the retina, and blue light (short wavelength) is bent more and focused in front of the retina.[86,105] All things being equal,

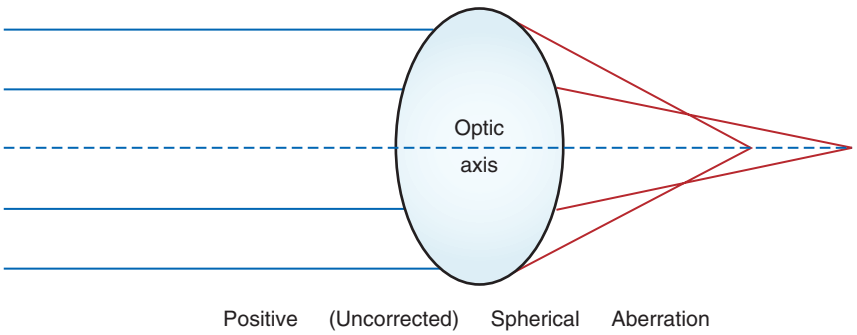


Figure 11-23. Spherical aberration. With positive spherical aberration, the more highly curved peripheral portion of the lens focuses light in front of light rays that pass centrally. (From Miller PE, Murphy CJ: Vision in dogs, J Am Vet Med Assoc 207:1623–1634, 1995.)

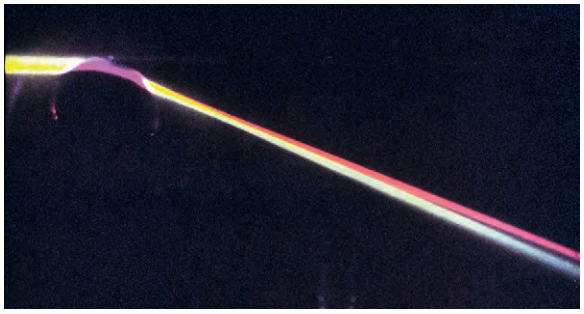


Figure 11-24. Chromatic aberration. Red and green lasers have been superimposed and subsequently passed through the isolated lens of a fish. The shorter-wavelength light *(green)* is focused in front of the longer-wavelength light *(red)*. (Courtesy Dr. Jake Sivak.)

this would produce colored fringes around a focused point of light, much like a rainbow is created by the chromatic aberration of water droplets in the atmosphere. Despite this physical phenomenon, humans do not see colored fringes around objects, in part because red and blue are less likely to be detected because of the cones' relative insensitivity to wavelengths at the ends of the visible spectrum.[86,105] Additionally, visual processing in the human retina and brain appears to be able to sharpen the edges of images and "erase" the colored blur.[86] The relatively minor effect of chromatic aberration is verified by studies that show that human visual acuity is not materially improved by wearing achromatic lenses that neutralize this phenomenon.[105] Chromatic aberration has been suggested to be an important factor in guiding accommodation, because the differential bending of various wavelengths of light can provide feedback to ensure that the image of interest is in as sharp focus as possible.[106] Chromatic aberration, however, may be relatively unimportant to horses because their cone photoreceptors are less numerous than those in humans, they accommodate little, they have yellow pigment in their lens (which reduces blue light reaching the retina), and they too are less sensitive to wavelengths at the ends of the visible spectrum.

THE POSTERIOR NODAL POINT

The optics of the eye are such that the majority of light rays emanating from objects in the environment pass through certain key points along the optic axis before continuing on to strike the retina (Fig. 11-25). One of these critical points is the posterior nodal point, which is located approximately at the level of the posterior lens capsule in humans. In the horse, it is estimated that this point is somewhat more anterior than in humans and located approximately 2.4 to 2.9 mm posterior to the center of the lens, or roughly in the posterior lens nucleus. Coile and O'Keefe's[101] schematic eye for the horse calculates the posterior nodal point to be located 2.94 mm posterior to the center of the lens. The value of 2.4 mm posterior to the lens center is obtained by using a calculation that estimates the anterior focal length of the eye to be approximately 0.665 times the axial length[107] and then using the following values from the literature: the average axial length of the eye is 43.68 mm,[108] the anterior focal length (equal to the posterior nodal distance in emmetropic animals) of the equine eye is 31.6 mm,[107] the equine lens is 12.7 mm thick axially,[108] and the posterior lens capsule is 19 mm posterior to the cornea.[108] Others have used

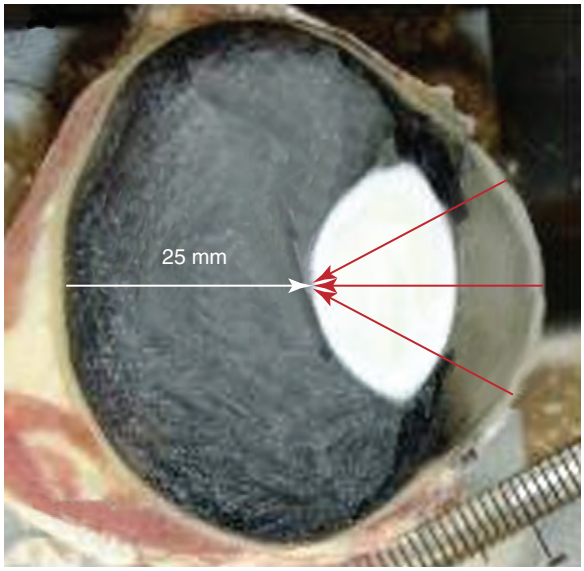


Figure 11-25. The location of the posterior nodal point of the equine eye *(tip of arrow)*. The majority of light rays *(red lines)* passing through the pupil are focused through this point. Opacities in this location will create substantially more visual impairment than anywhere else in the lens. (Modified from Roth LS, Balkenius A, Kelber A: The absolute threshold of colour vision in the horse, PLoS One 3:e3711, Epub 2008.)

frozen sections of the eye to calculate that the posterior nodal point of the equine eye is approximately 25 mm from the retina, which again puts it roughly at the level of the posterior lens nucleus.[21] Because of the critical importance of the posterior nodal point to the performance of any optical system, even small opacities in this region of the lens have a substantial impact on visual acuity. In humans, small cataracts present at this location can reduce visual acuity to the legally blind range. Because this phenomenon is a function of the physics of every lens system, animate or inanimate, there is no doubt that small opacities in this region can significantly impair a horse's vision as well. The fact that these visual deficits may not be discernable on routine examination is more of a testament to the crudeness of ones' ability to fully evaluate the visual performance of the horse than to the real impact of these opacities.

GLARE

Scattering of light within the eye (glare) reduces the contrast of an object against its background and renders low to moderately contrasting objects difficult to see in a high-glare environment (see Fig. 11-21).[6] Anyone who has driven a car in the direction of the sun, faced a car with "bright" headlights on at night, or gazed at the water from a beach on a sunny day has experienced the visually disabling affects of glare.[6] Given these situations, it is easy to understand why glare is a notorious cause of motor vehicle accidents. Undoubtedly, glare also plays a substantial role in some accidents in which a horse inadvertently runs through a low-contrast object such as a barbed wire fence.

Disease states may increase glare by further increasing forward light scattering in the eye. Some of the causes of pathologic glare include early cataract (especially posterior subcapsular cataracts), light entering through the iris (especially in

blue eyes or those with iris atrophy and polycoria), and corneal edema or scarring.[6] In humans, a 30% increase in corneal thickness caused by stromal edema may not alter Snellen visual acuity, but it can produce significant alterations in contrast sensitivity and susceptibility to glare.[109] It is likely that a similar phenomenon occurs in horses. Slit-lamp biomicroscopic examinations highlight cataracts by scattering light back toward the examiner, whereas the disabling effect of glare is caused by light that is scattered forward onto the retina.[6] Consequently, slit-lamp examinations do not necessarily indicate the degree of glare disability experienced by individual patients.[6] The equine eye's defense against glare includes yellow pigments in the lens that preferentially absorb the more highly scattered blue light, the dark brown pigment of the uveal tract and retinal pigment epithelium, an eyebrow, eyelid, and granula iridica (superior ones may block the sun, smaller inferior ones may block reflected light), and an orientation of the rods and cones such that they behave as light guides in which light must enter at a specific (nonscattered) angle to be sensed.

ACCOMMODATION

A method of adjusting the focus of the eye (accommodation) is needed if objects at different distances are to be seen with equal clarity. As an object is moved closer than 20 feet to the eye, more divergent rays emanating from the object can pass through the pupil. Because these rays are no longer roughly parallel to each other, the refractive status of the eye must be altered to maintain the image in sharp focus on the retina. In older texts, the horse is said to have a "ramp retina" that obviates the need for an active accommodative mechanism. In a true ramp retina, such as that possessed by the stingray, the retinal plane is "ramped" relative to the optic axis such that the superior retina is farther from the nodal point than the inferior retina.[110] In such a situation, near objects would be imaged on the superior retina, whereas distant objects would be imaged on the inferior retina. More recent research has indicated that although there are small variations in the distance from the nodal point to the retina, the horse does not possess a true ramp retina.[16,96]

Humans are generally believed to accommodate by contracting the sphincter-like ciliary muscle, thereby reducing the resting tension on the lens zonules.[106] This frees the elastic lens capsule to bring the remainder of the lens into a more spherical shape and increase its focal power, improving near vision.[106] This method of accommodation, however, is not used by all animals. A few of the many ways in which different species effect accommodation include moving the lens anteriorly or posteriorly, changing the curvature of the cornea, and squeezing the lens with the ciliary musculature or iris.[106,111] Mammals typically accommodate by either increasing the curvature of the lens[24,77,106] or forward translocation of the lens within the eye.[111] When streak retinoscopy and dynamic photorefraction (which allows real-time imaging of the refractive state of the eye[112,113]) are used, horses rarely evidence accommodative shifts greater than 1 to 2 D (P. Miller, C. Murphy, unpublished data). This is in accord with estimates of less than 2 D of accommodative range for the horse, on the basis of an evaluation of the optics of the equine eye.[96] In an emmetropic eye, an accommodative shift of 2 D would allow the horse to bring into sharp focus objects located from visual infinity to 0.5 m from the eye. This accommodative range is well suited for the lifestyle of the horse.

The exact mechanism by which the horse accommodates is not fully understood. Approximately 100 years ago, Tscherning suggested that accommodation in horses and cattle may be the result of flattening of the peripheral lens surface and increasing the curvature of the central lens surface.[114] He noted, in contrast to the previously described mechanism of accommodation in humans, that if he pulled on the lens zonules, the lens curvature actually increased in these species.[114] Similarly, in a more recent study of bovine lenses, Schachar et al.[115] found that when the sclera and ciliary body were stretched radially, the equatorial diameter of the lens increased, and the effective optical power of the lens also increased. The mechanism underlying this phenomenon is unclear, but it has been proposed that constriction of the ciliary muscle increases the tension on the lens zonules that insert on the equatorial lens capsule (thereby increasing lens diameter and flattening the peripheral region of the lens) and relaxes the tension on the zonules that insert on the anterior and posterior portions of the lens capsules (thereby allowing the central lens surface curvature to increase).[116] Definitive evidence to support this theory remains to be presented, and this mechanism of accommodation is controversial. If the functional structure of the equine eye is carefully considered—ciliary muscles are strictly longitudinal in orientation and relatively poorly developed—it is more likely that accommodation occurs in the horse by anterior translocation of the lens during accommodative excursions. This hypothesis could be tested by using ultrasonography in combination with pharmacologic agents.

Regardless of the mechanism by which it occurs, the stimulus for accommodation is blurring of the retinal image and/or divergence of the two eyes. As noted previously, the eye may detect that the image is defocused on the retina by using chromatic aberration to fine tune accommodation.[106,117-119] This then drives the parasympathetic nervous system to cause the ciliary musculature to constrict and also evokes pupil constriction and convergence of the two eyes (the near response).[106] The two eyes are linked so that if one eye is made to accommodate, the other will as well.[106] Although the impact on the optics of the eye is often overlooked by veterinarians, drugs such as pilocarpine also elicit accommodation, and atropine inhibits it. Whether topical atropine interferes with ciliary muscle motility and accommodation for the same prolonged period during which it can affect pupil size is unknown.[20] If the musculature of the equine ciliary body contracts at the same relatively slow rate as the iris sphincter muscle, it is likely that the horse is slower to accommodate than humans and domestic carnivores. For the same reasons, it is also likely that the "near response" in horses is quite slow to develop.

THE EFFECT OF PUPIL SIZE

The exact magnitude of the loss of image quality resulting from focus errors, aberrations, and diffraction depends on the size of the pupil. A small pupil not only reduces spherical aberration but also increases the depth of field. However, when the pupil diameter becomes exceedingly small, the impact of diffraction increases, and the image projected onto the retina is degraded. These competing factors balance out for humans when the pupil is about 3 mm in diameter, or about the size it tends to achieve under normal bright-light conditions.[3] When the pupil is this size, the quality of the retinal image is quite high and deviates only slightly from an ideal system limited by diffraction.[3]

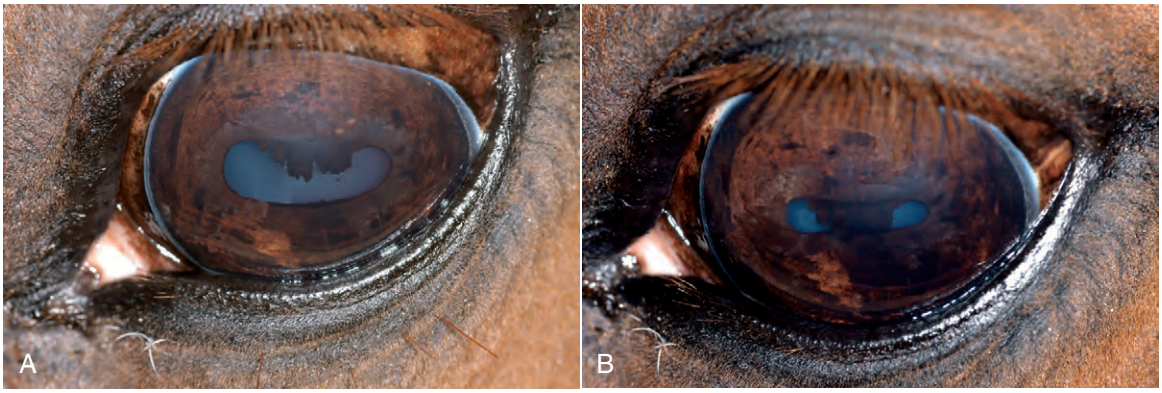


Figure 11-26. In bright light, the equine pupil can constrict to the point at which two pupils are effectively created. This phenomenon may reduce spherical aberration and also serve as a range-finding device.

OPTICAL CONSEQUENCES OF PUPIL SHAPE

At mid-dilation, the equine pupil is horizontally elliptical. Because the pupil is located in front of the nodal point of the optical system, the field of view will be greatest in the horizontal plane, a situation that is best suited for scanning the horizon.[120] The vertical field of view will be further limited by the presence of the granula iridica, located superiorly and inferiorly. In bright daylight, the superior granula can contact the inferior pupil edge, occluding the central region and creating two roughly spherical pupillary apertures at the lateral and medial extent (Fig. 11-26). Walls[24] reports that many felids will form two apertures at the superior and inferior limits of the pupil under bright-light conditions. The provision of two pupils located in front of the posterior nodal point of the eye has several optical consequences, including provision of a relatively larger visual field than would be achieved with a circular pupil of equivalent surface area.[24] By limiting the passage of rays to regions that are roughly equidistant from the axis of the lens, the presence of two pupillary apertures would also serve to diminish any spherical aberration that may be present in the optical system. Additionally, the possession of multiple pupillary apertures creates a Scheiner's disc phenomenon.[29,121] Scheiner's disc is an optometric device that has two pinpoint apertures separated by several millimeters; it is used to determine the near-point focus of the human eye. When both apertures are situated over the pupil of the human patient, only objects that reside in the plane of focus of the eye form a single image on the retina. Objects in front of or behind the plane of focus form two images on the retina (Fig. 11-27). In the horse, the presence of two pupils in very bright light may decrease the light flux to the retina while preserving a shallow plane of focus (a single, small pupillary aperture would greatly increase the depth of field). In the chameleon, which has a well-developed fovea that can be used as a focusing indicator, it has been shown that the degree of accommodative effort is able to be integrated by the brain to provide a type of automatic range finder.[122,123] Although the horse lacks a fovea and has limited accommodative ability, it is possible that the presence of two pupils in very bright light would allow the horse to better discriminate relative distances, a distinct advantage in determining how far away a predator may be.

Figure 11-27. Simulated view through the multiple pupillary apertures. Only objects that reside in the plane of focus of the eye form a single image on the retina. Objects located in front and behind the plane of focus form two images on the retina. Some species have been reported to be able to use this Scheiner's disc–like phenomenon as a focusing indicator.

RETINAL FACTORS AFFECTING VISUAL ACUITY

The size of each photoreceptor and the spacing between adjacent photoreceptors are two of the rate-limiting factors in determining how small of an object can be resolved. In a sense, this packing is analogous to the number of pixels on a computer screen or the number of brush strokes in a painting. Humans have the greatest density of photoreceptors in a roughly circular, densely packed fovea temporal to the optic disc. Horses have a relatively thin (1 mm wide) visual streak located about 3 mm dorsal to the disc in or near the tapetal zone and extending approximately 22 mm in the nasal and temporal directions.[16,17,50] In the temporal arm of this visual streak, ganglion cell density increases slightly (area centralis rotunda), but an indistinct field of relatively high density also continues along the nasal arm to near the ora serrata (Figs. 11-28 and 11-29). As in all species, there are many fewer ganglion cells in the periphery of the retina than in the center, greatly reducing the visual acuity of the peripheral visual field.[50,124,125] The temporal

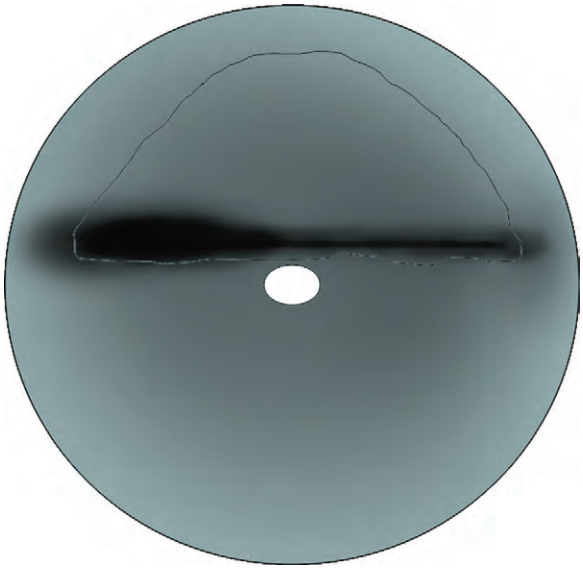


Figure 11-28. Schematic representation of the visual streak of the right eye of a horse. The greater the density of ganglion cells and photoreceptors, the darker the shading is in this image. The density of these cells is greatest immediately superior to the optic disc *(oval)*, which facilitates scanning the horizon. There also is a somewhat greater density of these cells temporal to the disc, which facilitates greater visual acuity, binocular vision, and some color vision, because there are three to four times more cones in this area. (Modified from Hebel R: Distribution of retinal ganglion cells in five mammalian species (pig, sheep, ox, horse, dog), Anat Embryol 150:45–51, 1976.)

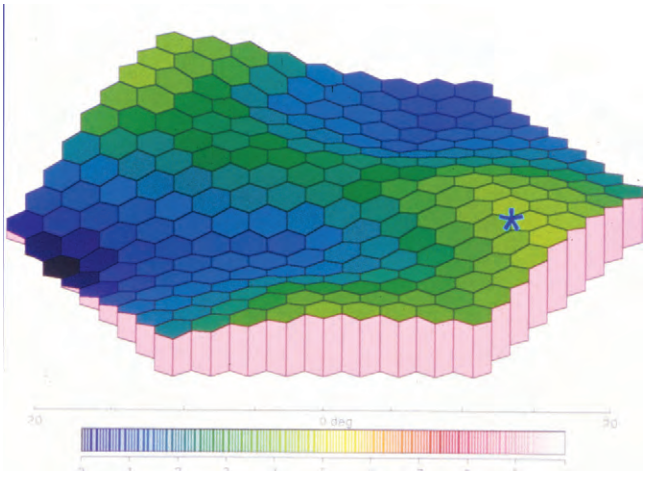


Figure 11-29. The visual streak of a horse as determined electrophysiologically with multifocal electroretinography. Green indicates relatively higher sensitivity, whereas blue indicates lower sensitivity. The optic disc is just to the left of the dark black region. A band of heightened retinal sensitivity corresponds to the location of the horizontally arranged visual streak.

portion of the streak provides the greatest visual acuity and perhaps some color vision, because this region appears to have a three- to fourfold increased density of cones.[126] Mammals that live on the open plains (or steppes in the case of horses) generally have a visual streak pattern that conforms to the projection of the horizon at the intersection of the earth and sky, and this provides a particularly acute image of this part of the environment. The tapetal location of the streak further enhances vision in dim light, but at the expense of light scattering and degraded visual acuity in bright light.

Unlike a computer screen or a painting, the images collected by the photoreceptors are then passed up to the brain via a series of neurons, and visual acuity becomes limited by the least densely packed element in this chain, which is typically the ganglion cells of the optic nerve. To make matters more complex, there are a number of ganglion cell types, each most responsive to a specific component of a visual stimulus, and each point on the retina is covered by at least one ganglion cell of each functional class.[127] This arrangement means that a single visual stimulus is reported in several ways to the higher visual centers.[127] The optic nerve of the horse is somewhat unique in that it also contains a substantial number of large-diameter axons that are involved in motion detection, depth perception, and sensitivity to dim light.[49,50] Although the horse has the lowest ganglion[16,17,50,125] and Müller[128] cell density of the domestic mammals (peak ganglion cell density ranging from 4000 to 6500/mm^2), its very large eye means that its total number of ganglion cells (hence, information-carrying capacity) is comparable to that found in humans. In this packing of ganglion cells, the tradeoff between high visual acuity and improved vision in dim light is made because optimizing visual acuity requires a 1:1 ratio between the numbers of photoreceptors and the numbers of ganglion cells, whereas optimizing light detection requires a greater number of photoreceptors to synaptically converge on a single ganglion cell. Although this convergence improves vision in dim light, it also reduces visual acuity, just as high-speed film produces a "grainy" image in daylight.

In the human fovea, the ratio of cones to ganglion cells is approximately 2:1, but because the ganglion cell output is divided into parallel on and off channels, the functional relationship is approximately 1:1.[127] This close association, even in just a small area, results in an eye with quite high visual acuity. The exact peak ratios for horses have not been determined, but because of what is known about their relatively high visual acuity, it seems likely that there is at least a small region of retina in which the ratio is only a little greater than 1 : 1. In the human peripheral retina, the ratio of cones to ganglion cells increases to roughly 10 cones per ganglion cell; allowing for the same on/off channels, the functional ratio is five cones per ganglion cell.[127] Because horses have a lower peak cone density and perhaps fewer cones than humans, it is likely this ratio is substantially greater for horses and that rod photoreceptors rather than cones may be the operative elements. In cats, it has been estimated that in the peripheral retina, approximately 75,000 rod photoreceptors drive 5000 rod bipolar cells, which in turn drive 250 amacrine cells, which then converge on one ganglion cell.[129] A similar phenomenon occurs in humans, and although the density of the rods in the midperipheral retina is nearly as high as the density of cones in the fovea, the visual acuity of the peripheral retina is poor because of the convergence of so many rods onto a single ganglion cell.[127] The tradeoff is that in dim light, the peripheral retina is much better at detecting light than the foveal region.

In certain circumstances, it appears that the eye is able to get around the limits to ordinary resolution acuity (also called the *minimum resolvable acuity*) imposed by the diameter of the smallest photoreceptor.[78] In humans, the shortest distance between the foveal cone photoreceptors is approximately 25 seconds of arc, and this forms the basis for the ordinary visual acuity limit of about 30 seconds of arc.[78] If the task is switched

from determining in which direction a letter (e.g., an E) is pointing to determining whether an object is present or absent (minimum visible) or identifying the relative relationship of two objects to each other (minimum discriminable), the eye can resolve differences as little as 1 second of arc and 3 seconds of arc, respectively.[78] A classic method of determining the minimum visible is to measure the width of a telephone wire that can be seen against a uniformly blue sky. This task is actually a difference-in-brightness discrimination and not a true spatial discrimination,[78] because under these conditions an individual photoreceptor is being struck by many photons, and all that is being determined is how many photons the wire needs to block before a detectable change in brightness occurs in an individual photoreceptor. Hence, the sensitivity of this discrimination is much less than the diameter of one photoreceptor.

Minimum discriminable acuity does require making a spatial discrimination. Because it is approximately 10 times better than ordinary acuity, it is sometimes called *hyperacuity*, and it appears to have a fundamentally different physiologic basis rooted in the neural processing of images at the level of the brain or retinal ganglion cells.[78,130-133] There are several types of hyperacuity, and they are usually evaluated by tasks that require determining the relative relationship of two or more objects to each other. For example, the most common task is the so-called alignment or vernier acuity in which the subject is asked to determine whether the two line segments in "–" are offset from each other. In other circumstances, the subject may be asked to determine the relationship of a line segment to the point of a chevron (>-) or whether a line is perfectly vertical. Stereoacuity is also a form of hyperacuity, as is the ability to make color discriminations, because in the latter the just-noticeable difference in wavelength (color) is far less than the range of wavelengths to which any of the three cone types responds.[78] Hyperacuity-like phenomena are not unique to the eye but appear to be used by many senses including echolocation in bats, the jamming avoidance response of electric fish, and differential pitch sensitivity experiments in humans to enhance detection of various forms of energy in the environment.[134] Although the magnitude of the minimum detectable difference in cats varies from that seen in humans, cats have vernier acuity that is approximately six times better than their ordinary grating visual acuity, so hyperacuity is not limited to humans.[135]

THE PERCEPTION OF FORM

Several studies evaluating equine form perception have been conducted.[45,136-140] In general, these are behavioral studies in which a food reinforcer is used to "chain" a series of behaviors together (e.g., walk into the testing area, look at a visual target, walk up to the target, touch the target, walk back to the stocks for the next trial) that teaches the horse to work independently of the evaluator (Fig. 11-30).[45,136-140] This minimizes the potential for inadvertant cueing by the examiner or other observers, as in the case of "Clever Hans" who was carefully reading the body language of human observers instead of actually doing arithmetic and other calculations.[141] Although time consuming to perform, these types of studies evaluate not only the eye but the shortcuts the brain takes to use this information in the real world, and they provide hints as to what features a horse considers important.

Behavioral studies have demonstrated that horses can understand the general concept of size and learn to select the largest object regardless of its shape.[138] It was also found that horses can visually learn to prefer one object over another even though they differ only in color (e.g., a blue toolbox over a red one) or shape (an orange ball over an orange tube). Furthermore, these learned visual discriminations can be remembered for many years even though they are not reinforced in the intervening time period.[140] Horses have also been demonstrated to be capable of visually transferring information between three-dimensional (3D) objects and two-dimensional (2D) photos.[139] For example, once the horse is trained to select a specific 3D toy over another 3D toy, this behavior can be readily transferred to 2D photographs of the toys. Horses have also been shown to categorize visual stimuli into specific classes, such as open center versus solid center, by being trained to select a triangle or square with an open center over a triangle, circle, square, or keyhole with a solid center.[137] Behavioral studies have also dispelled the common myth that what horses see with one eye is "novel" and possibly frightening if seen with the other eye.[136] In these studies, it was shown that horses can recognize with one eye an object that was previously learned about only with the other eye.[136]

ORIENTATION

The orientation of the "broad strokes" of an object provides considerable information very rapidly at even very low levels of visual acuity (Fig. 11-31).[142] In fact, much of the information we act on is at this low level of acuity. Work ultimately leading to a Nobel Prize by David Hubel and Torsten Wiesel in 1981 demonstrated that at a fundamental level, the brain is geared towards identifying the orientation of lines and edges of an object that define it.[143] The neurologic wiring associated with this phenomenon is complex, but at its basis are single neurons that only respond to lines with specific orientations and surrounding cells that respond in an on/off fashion so as to further highlight this orientation or the edges of an object.[143,144]

COLOR VISION

The perception of color is another fundamental component of vision that allows for objects to be seen as separate and distinct from their surroundings. The basis for this distinction comes not from the intensity of the light but instead from the differential retinal response to differing wavelengths of light striking the retina. The ability to detect color has gone through numerous permutations during evolution, and this informs our understanding of the differences between human and equine color perception. Approximately 350 to 400 million years ago, vertebrates developed five major families of visual pigments (one rod and four distinct cone classes), enabling color vision that was based on four cone pigments (tetrachromatic color vision).[145-147] One of these cones was also sensitive to ultraviolet light, which is retained by many modern-day birds and used for foraging, mate selection, and perceiving color in a region of the electromagnetic spectrum humans cannot discern.[8,145-147] Over time, as mammals evolved to exploit a more nocturnal niche, two of these four cones (including the UV cone) were lost, resulting in color vision that was based on only two cone types (dichromatic color vision).[145-147] Modern

Figure 11-30. Chaining behaviors for visual performance testing to avoid inadvertant cueing. **A** and **B,** The horse in the station awaiting a trial. **C,** If the horse selects the correct stimulus, it receives a food reinforcer. **D,** It then walks away from the apparatus, **E,** enters the station, and **F,** stands quietly while waiting for the next trial. Typically the correct stimulus must be chosen at least 80% of the time to be considered a visible stimulus. (From Hanggi EB, et al: Color vision in horses *[Equus caballus]:* deficiencies identified using a pseudochromatic plate test, J Comp Psychol 121:65–72, 2007.)

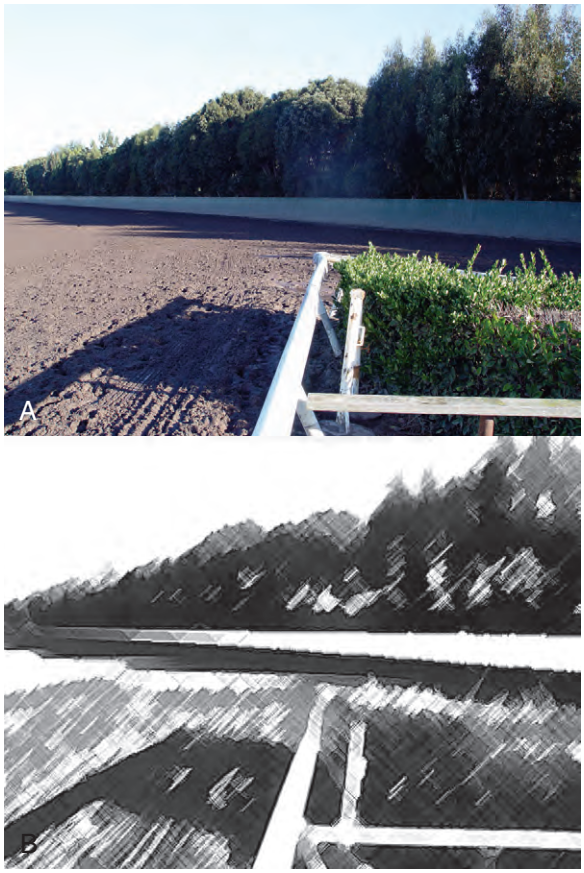


Figure 11-31. Discrimination on the basis of orientation. **A,** A racetrack. **B,** Simulation of the principal orientation of the visual elements in the image. Even though orientation provides only black-and-white clues with very low visual acuity, it is a very rapid method of identifying critical features in an image and using that information to direct gross behaviors.

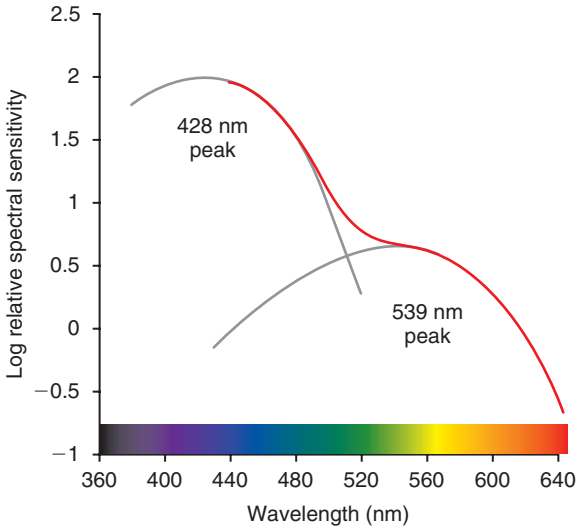


Figure 11-32. Sensitivity curves of the two principal cones of the horse. Each cone pigment has a uniquely varying sensitivity to different wavelengths of light. The relative stimulation of each of the cones is used by the brain to ascribe a certain color to an object. (Modified from Carroll J, et al: Photopigment basis for dichromatic color vision in the horse, J Vis, 1:80–87, 2001.)

horses and the substantial majority of other mammals alive today have only these two cone pigments. As primates evolved approximately 35 million years ago, the long wavelength–sensitive cone pigment underwent a favorable mutation that allowed the animal to distinguish yellow-orange fruits from green foliage, resulting in trichromatic color vision in a few primates and humans.[10,97,147-151] Even within a species, numerous mutations have continued to occur in the genes coding for these pigments such that there are subtle differences in the peak sensitivity of the two cone pigments from individual to individual. The relative ratios of the three cones types may vary by as much as 30-fold among humans with normal color vision.[148,152-155] This considerable diversity suggests that even within the same species, there may be substantial differences in color perception among individuals with normal vision.[148,152-155]

The basis for equine or human color vision is how different wavelengths of light interact with each of the distinct cone pigments.[3] Each cone pigment has a unique sensitivity to different wavelengths of light, with a peak sensitivity to one wavelength and diminished sensitivity to adjacent wavelengths (Fig. 11-32). Once receiving input from two or more types of cones, the brain compares the relative stimulation of the different cone types and uses this to ascribe a certain color to an object. Therefore, color vision does not occur at the level of the eye, but instead at the level of the brain. Although there is considerable overlap in sensitivity to different wavelengths of light, each cone has a peak sensitivity which is used to categorize the cone as to type. In humans, the three cones have peak sensitivities near 430 nm (called the *blue wavelength–sensitive*, *short*, or *S cone*), 530 nm (called the *green wavelength–sensitive*, *middle*, or *M cone*), and 560 nm (*red wavelength–sensitive*, *long*, or *L cone*).[145,156] In horses, the peak cone sensitivities are at approximately 428 to 429 nm (blue or short cone) and between 539 and 545 nm (a middle to long wavelength–sensitive cone) which is intermediate between the human red and green cones.[148,150,155]

The number and location of cones within the retina is also important. In both humans and horses, the overall ratio of rod to cone photoreceptors is approximately 20 to 118,[157] but the distribution of these cells is quite different between the two species. In humans, the blue wavelength–sensitive cones comprise about 7% of all cones and are roughly uniformly distributed over the retina,[145,147] whereas the green wavelength–sensitive and red wavelength–sensitive cones (at least in monkeys) are concentrated primarily in the fovea and the immediately adjacent central retina.[158] In humans, the cones are densely packed in the central retina (fovea) and rapidly fall off to low numbers just 1 to 2 mm away from the fovea.[157] The distribution of cones is believed to be more uniform across the retina in horses, with perhaps an increase in the temporal region of the visual streak (Fig. 11-33).[17,125] Horses have a significant population of patchily distributed blue cones, which comprise approximately 10% of all cones in the visual streak and 20% to 25% in the midperipheral and peripheral retina, and a larger population of a more regularly arranged second type of cone, with its peak concentration in the region of the visual streak and declining toward the peripheral retina.[126] Cone densities in the horse range from around 5000/mm^2 in the peripheral retina to 15,000 to 20,000/mm^2 in the visual streak, whereas in humans, peak cone density averages almost 200,000 cones/mm^2.[157] This density suggests that in order to differentiate an object on the

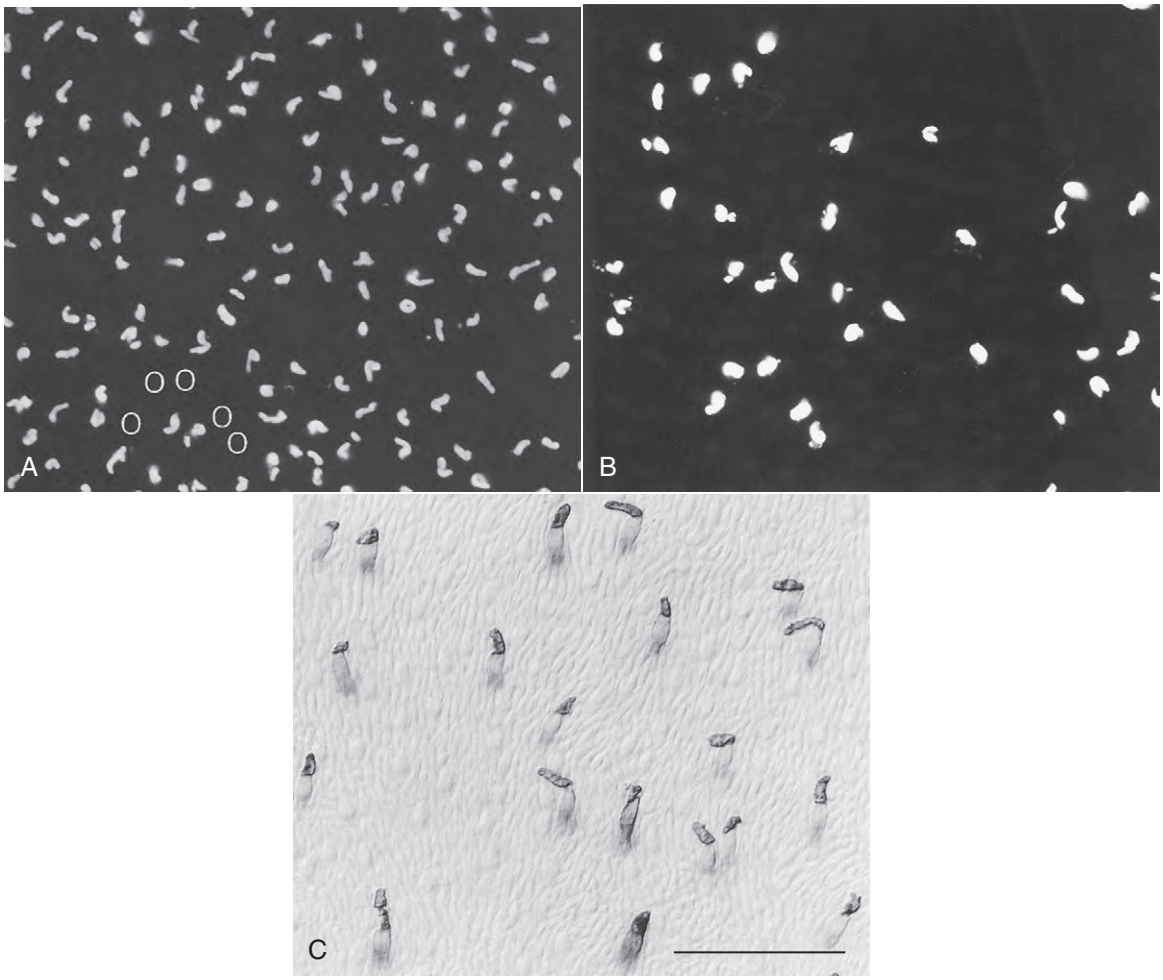


Figure 11-33. Cone photoreceptor subtypes in the peripheral retina of a horse. **A,** The M/L cone distribution is of rather high density with some irregular spacing. **B,** Same field as in panel **A** but labeled to show the S-cone mosaic. The S cones have a low density and are irregularly distributed between the M/L cones. Five open circles in panel **A** show the position of a group of five S cones in **B. C,** S-cone pattern in another retina (this method also labels the inner segments and cell body). In addition, unstained M/L cones (ovoid in appearance) and more numerous rods can be identified (bar = 50 mm). (From Sandmann D, et al: Blue-cone horizontal cells in the retinae of horses and other Equidae, J Neurosci 16:3381, 1996.)

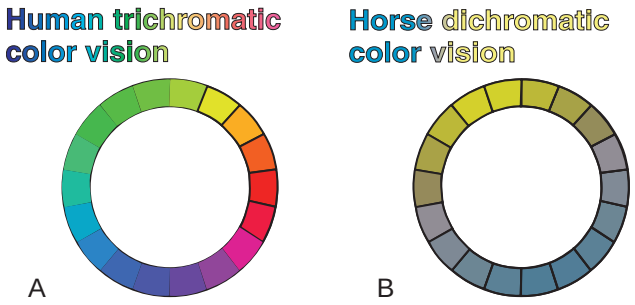


Figure 11-34. Difference between dichromatic color vision of the horse and normal human color vision. **A,** Color wheel representing the spectrum of colors perceived by the trichromatic human visual system. **B,** Reducing the number of types of cone from three to two results in dichromatic color vision and an enormous reduction in the number of different colors seen. (From Carrol J, et al: Photopigment basis for dichromatic color vision in the horse, J Vis 1:80–87, 2001.)

basis of color, the stimulus may need to be larger for horses than for humans, especially if it is in the animal's peripheral visual field.

Humans with normal vision see four basic unique hues—blue, green, yellow, and red—and about 100 intermediate colors, which can be thought of as varying blends of pairs of the four unique colors—for example, yellow green, reddish yellow (orange), reddish blue (violet), and so forth (Fig. 11-34; see Figs. 11-6, 11-32, and 11-33).[148,159] Similarly, if different combinations of wavelengths of light produce the same pattern of activity among the cone subtypes, the two different wavelengths will be perceived to be the same (so-called colorblindness) even though the composition of the light is quite different. However, colorblindness does not mean that an individual person or animal is blind and unable to detect photons with these wavelengths. Instead, it only means that the individual has difficulty using this information to differentiate between two colors solely on the basis of their hue. Various degrees of congenital colorblindness such as red-green color deficiency (daltonism) can affect up to 8% of white men.[3,145]

Figure 11-35. Real-life implications of dichromatic color vision for the horse. **A** and **B,** Two unaltered digital images. **C** and **D,** Digitally altered forms of same pictures simulate the dichromatic color vision of the horse. The images were also adjusted to take into account the reduced visual acuity of the horse to more closely approximate the horse's visual experience. (From Carrol J, et al: Photopigment basis for dichromatic color vision in the horse, J Vis 1:80–87, 2001.)

All studies of equine color vision to date suggest that it is very likely horses perceive colors differently than humans, because they have only two types of cones, their cone types have different peak sensitivities than those in humans, and they have many fewer cones in the central retina than do humans.* The most dramatic impact of having two cone types instead of three is that dichromatic horses (and humans with red-green color deficiencies) have only two unique hues, believed to be something similar to blue and yellow. When both cones are approximately equally stimulated (as white light would do for us) the result is a so-called neutral point at about 480 nm (blue green for humans with normal color vision). In theory, light of this wavelength should be perceived as colorless and a variation of white/grey/black depending on the intensity of the illumination.[148,162] As the illuminating wavelength is shifted to either side of the neutral point, the two cones again become differentially stimulated, and color may again form a basis for making distinctions between objects. It is quite possible that because horses have many fewer cones in the central retina than do humans, their perception of color may not be as vivid as a human's and colors may appear as washed-out pastels or sepia.[10,148] Additionally, because cones in horses, and even humans, are primarily located in the central retina, color vision is largely restricted to the central retina in horses (the fovea in humans), and the ability of the peripheral retina to detect color is substantially reduced.[3]

Behavioral tests of equine color vision have been conducted to verify that the cone pigments identified histologically and electrophysiologically are actually useful to the horse.[21,97,143,149-151,160-162] Such studies are confounded by the need to ensure that the brightness of the test objects is not also a clue, and the various filters used to create different colors (e.g., different shades of green) do not actually allow other color cues to pass through as well (e.g., yellow).[70,160,161] Although these behavioral studies have somewhat different conclusions, most of them show that horses can differentiate blue (470 to 482 nm) and yellow (579 to 583 nm) from gray (Fig. 11-35; see Fig. 11-34). Green (532 to 545 nm) and red (609 to 615 nm) are less accurately differentiated from grey in many but not all studies, suggesting that in the aggregate, horses behaviorally have a form of red-green colorblindness.[97,149-151,160-164] Electrophysiologic studies would suggest that for horses, orange and a light blue appear similar (e.g., neither may have much if any color and appear to be similar to gray). This process is similar to color vision in human dichromats who are red-green colorblind and cannot differentiate between red and green, but it is shifted for horses such that they are orange-blue colorblind (see Figs. 11-34 and 11-35). Despite these "deficiencies," the absolute threshold for discriminating between objects on the basis of color is comparable between horses and humans.[21] In this study, one horse and most humans were able to discriminate between

*References 10, 21, 97, 148-151, 160, and 161.

colors at a light intensity level that approximated that of moonlight (0.02 cd/m^2).[21]

The real question, however, is how horses perceive colors, especially those near the neutral point. This is important because much of the food a horse consumes is in the green spectrum, and yet this is also near the neutral point and would seem to be evolutionarily nonadaptive. Although we cannot know for sure, Fig. 11-35 offers a suggestion as to how specific colors may appear to a horse. Recent behavioral studies into how horses perceive the color spectrum suggest that horses "think" of colors in relation to each other (e.g., this one is more green or less blue than that one) and not on the basis of an absolute scale.[162] Work with human dichromats, who have a similar neutral point, recently found that they use the term *green* to describe all colors at the neutral point, rather than describing the neutral point as being shades of grey, as would be predicted solely on the basis of photopigment sensitivity profiles.[165] This is interesting because humans readily see grey/white as qualitatively different from colors such as red and green and presumably so would a horse.[165] Although requiring confirmation via other methods, behavioral tests also suggest that the neutral point does not divide the colors horses perceive into two separate categories (a short-wavelength blue and a longer-wavelength green yellow), but instead, like human dichromats, they perceive the neutral point as a "color" (e.g., a type of green) just like any other they can distinguish (Fig. 11-36).[162] It has been suggested that this phenomenon is the result of color information being carried to the brain in two channels, one that is the more traditionally understood and based on the relative ratios of stimulation of each cone a specific wavelength affords, and a second channel that codes color in a nonlinear way with high gain and rapid saturation.[162] This second channel may provide some color-based information at the neutral point that allows the brain to put the wavelengths near the neutral point into a general category such as "green."

Although the added information obtained by differentiating between photons on the basis of their wavelengths can be very useful in certain circumstances, black and white images alone can capture most of the visual content in the environment. Even in species with highly developed color vision, distinguishing form, shape, depth, and movement is far more important than distinguishing color.[3-5,11] Additionally, as vibrant and real as color vision may appear, it is not only the result of the physical interaction of photons with a set of cone photopigments but also a cognitive and psychological sensory experience in the central nervous system that does not even begin to accurately represent physical reality. For example, very different stimuli such as a combination of green (544 nm) and red (679 nm) lights can appear exactly the same as a pure yellow light (589 nm), even though the actual wavelengths of the photons composing these lights are completely different.[3,11] Similarly, changes in wavelength of only a few nanometers in the green portion of the spectrum result in humans perceiving quite different colors, but similar changes in the red region (680 nm onward) do not (see Fig. 11-6). Again, photons in the yellow portion of the spectrum are more easily detected than photons in the blue portion, making yellow lights appear brighter than blue ones, even though the same number of photons are striking the retina. Finally, the exact color a person experiences depends not only on the object itself but on the illuminating light, the spectral properties of the objects immediately surrounding it, and the fact that the brain attempts to maintain the perception of the constancy of colors even though dramatic changes may be occurring.[3,11] In aggregate, these studies suggest that in humans there is no simple correspondence between the spectral properties and physical stimulus of an object and the color humans perceive, and it is highly probable that a similar phenomenon also occurs in horses.

Figure 11-36. Two theories as to how the neutral point may be perceived by a horse. **A,** As a divided chromatic space, with the white/gray-appearing neutral point separating the two ends of the spectrum. **B,** As a continuous chromatic space. Electrophysiologic and biochemical studies of the human and equine cones suggest that the neutral point would suggest **A** is how the neutral point should be perceived. Behavioral studies of both horses and humans with comparable color vision abnormalities, however, suggest that the brain alters this input, and the neutral point is perceived as if it were a shade of green, as proposed in theory **B.** (Modified from Roth LS, et al: Colour perception in a dichromat, J Exp Biol 210:2795–2800, 2007.)

When color vision is considered, it is tempting, especially from an anthropocentric point of view, to conclude that compared to humans, most mammals have inferior visual abilities, and only humans and some primates have achieved the pinnacle of vision by possessing the ability to detect a greater range of colors. However, this does not take into account the fact that mammals with only dichromatic color vision have been extremely successful on an evolutionary basis or that up to 8% of Caucasian men have congenital red-green color vision abnormalities.[3,145] An alternative perspective is that humans have acquired the ability to see more colors at the expense of the light sensitivity of their retinae—a "choice" the vast majority of other mammals would not make.[166] Therefore, instead of developing color vision so as to better identify a ripe, yellow fruit hanging in a green tree, the equine visual system, like that of most mammals, has evolved to function under a greater range of lighting conditions and to afford a more panoramic view so as to avoid predators. Because the horse's food is essentially immobile and not particularly challenging to identify or capture, being able to perceive a broader palette of hues does not offer as much advantage to a horse, especially if it comes with the tradeoff of degrading its visual capabilities for detecting predators. Dichromatic color vision may also present an adaptive advantage for horses. Humans with dichromatic color vision can "break the camouflage" of certain colored objects that humans with normal color vision cannot,[167] and it is debatable whether humans with color vision abnormalities actually have a lower light perception threshold than those with normal color vision.[166,168] Therefore, because many predators have also evolved coat colors that closely match the background in terms of color and in some cases visual texture, color may be a relatively poor way of breaking the camouflage of a predator; and dichromatic color vision, instead of being detrimental, may actually confer a survival advantage to the horse.

EFFECT OF SELECT OCULAR ABNORMALITIES ON VISION

Ocular disorders can have a profound impact on a horse's visual performance. Impairment of vision in one eye can often

be masked by normal vision in the fellow eye, and in general the extent of visual impairment from bilateral ocular disease can be predicted by how well the less impaired eye performs. In some cases, the effect is obvious (e.g., no light perception), but in others, the disorder may affect multiple components of a horse's vision, and although each alone may be tolerable in the aggregate they can become unacceptable. For example, a small peripheral corneal ulcer may have little impact on vision, but if it creates reflex anterior uveitis, the resulting miosis, possible synechia, and a small cataract located in the posterior nucleus (at the posterior nodal point) may be associated with a marked decrease in vision. The inability to readily detect such substantial changes in vision is more of a testament to the imprecision with which one can easily determine an animal's visual capabilities than an indication that animals can tolerate abnormalities humans cannot.

EFFECT OF DRUGS ON VISION

Less obvious, but potentially as important as the ocular disorder itself, is the effect therapy may have on an animal's vision. For example, atropine ophthalmic ointment is frequently used to relieve ocular pain and decrease the probability of synechia formation in horses with equine recurrent uveitis.[25] However, if it is not used judiciously, the persistence of pupil dilation for weeks after the drug is discontinued may impair vision more than it helped. It is easy to understand how pharmacologic pupil dilation may increase sensitivity and photophobia in ordinary daylight, and in some horses, this is as debilitating as the disease itself. Less obviously, but probably of even greater significance to visual performance, ointments in general distort the normally smooth precorneal tear film, and this can induce marked blurring of vision. Increased mucoid ocular discharge or pooling of tears at the inferior eyelid margin can also distort vision considerably through a similar mechanism. For these reasons alone, humans do not typically tolerate ointments applied during the daytime. Even less obvious, but again potentially significant, atropine can reduce tear production, which may induce optical blur and haze as the corneal epithelium dries and becomes a less effective refractive surface. Mydriasis may unmask the more highly curved lens periphery and increase spherical optical aberrations, and ciliary body paralysis with the drug can eliminate even the mild degree of accommodation the equine eye is capable of. All pharmacologic therapy for ocular disorders demands a careful balance between the potentially beneficial and potentially deleterious effects of a drug.

VITREOUS FLOATERS

We have identified several horses with excessive "shying" behavior that have had a normal ophthalmic examination (including refraction) except for the presence of vitreous floaters (P. Miller, C. Murphy, unpublished data). It can be difficult, however, to accurately determine whether an abnormal behavior is associated with a vitreous floater because most middle-aged to elderly horses have vitreous floaters in one or both eyes but do not display abnormal behavior. The theoretical mechanism for this association is that movement of consolidated vitreous proteins (particularly those close to the retina, because the shadow they cast on the retina is more intense), especially if they are in the periphery of the animal's vision, cause it to move its head so as to "clear its vision" or "shake off an annoying fly" that is just beyond visual resolution. It appears that for a vitreous floater to result in abnormal visually directed behavior, the horse must be unusually "sensitive" and predisposed to overreacting to the perception of movement in its visual field.

Floaters can on occasion be the organic cause of visual dysfunction on the basis of our (the authors') observations. (1) Previously healthy horses with normal vision have developed behavioral abnormalities coincident with the onset of appreciable vitreous degeneration and the formation of floaters. (2) Horses with vitreous opacities firmly seated in the normal vitreous gel displayed normal behavior, but with subsequent syneresis of the vitreous and mobilization of the opacities (becoming floaters), exhibited excessive startle reactions. (3) Horses that startled only in response to visual input directed from one side were observed, and the floaters were present only on that side. (4) A horse that was presented because of shying was found to have an intraocular parasite in a syneretic vitreous. The shying behavior resolved in association with resorption of the parasite.

EFFECT OF REFRACTIVE ERRORS ON VISION

Although the impact of a refractive error on vision is easily understood by anyone who wears corrective glasses or contact lenses, these abnormalities often go undetected and unappreciated in veterinary medicine, in part because the methods of determining the presence or absence of these errors is not easily understood by those without specific training in physiologic optics. It is tempting to speculate that myopia (nearsightedness) could certainly impair a horse's ability to perform activities such as cutting a calf from a herd, jumping fences, or properly responding to its owner at distance on the other side of a pasture or prairie; it may even render the animal more fearful and easily "spooked." Indeed, we have recognized horses with aberrant visual behavior resulting from refractive error. Such horses typically exhibit somewhat clumsy or unpredictable behavior but have normal findings on ophthalmic examination unless they are refracted. In general, when the refractive error approaches 2 D, most humans will report a noticeable improvement in their vision with corrective lenses. Spontaneous astigmatism appears to be uncommon in horses, but severe astigmatism often follows corneal injury and ulceration (Fig. 11-37). This may be appreciated by observing the distortion that occurs in the shape of a light beam (or camera flash) reflecting off the cornea. Astigmatism may cause objects in certain regions of the visual field to assume a distorted or bizarre shape.

We have refracted many horses that were referred for shying, spooking on one side of the visual field, or for development of a reluctance to perform adequately at jumps. Although most of these animals have had normal findings on streak retinoscopy, we have identified horses in which the unwanted behaviors have been associated with a refractive error. Anisometropia (a difference in resting refraction between the two eyes) was present in several cases in which the horse displayed an inappropriate responsiveness to visual stimuli on only one side. In these animals, the affected side was always myopic (generally ≥1.5 D). We have also identified some horses with moderate to severe myopia (−1.5 to −3.5 D) that show a reluctance to jump,

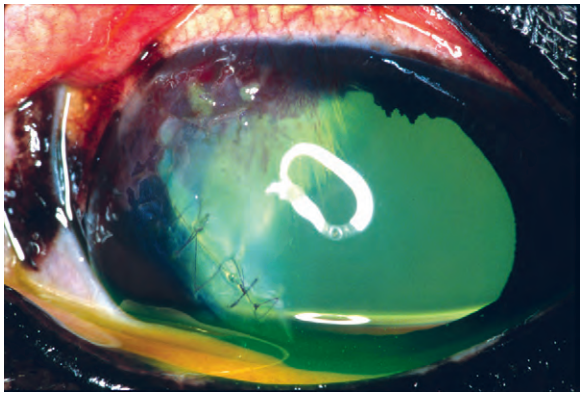


Figure 11-37. Corneal astigmatism resulting from a corneal laceration. Although the visual axis was clear and the horse had a good menace response, vision was undoubtedly distorted, as evidenced by the deformation of the normally circular flash artifact into an irregular ellipse. Such a marked distortion would alter how the light passing through this region landed on the retina. (Courtesy Dr. Ellison Bentley.)

and some horses spook excessively in response to benign objects in their environment. However, these observations must still be considered anecdotal because a causative relationship was not established beyond doubt in these patients. Unfortunately, despite an increase in the number of veterinary professionals specifically trained in comparative ophthalmology, very little progress has been made in the critical assessment of visual performance in horses. Little has been done to dispel Uberreiter's statement that "it is by no means proved that errors of refraction are the cause of shying in horses."[169] Nevertheless, it is unreasonable to argue that refractive errors would not affect visual performance, because this is a fundamental component of the physics of every optical system, and one needs to look no further than the human experience in which refractive errors, if uncorrected, would debilitate a significant portion of the human population.

Although corrective lenses are not widely used in horses, this is the result of failure to recognize refractive errors in horses, not because such devices cannot be manufactured. In general, it seems reasonable to perform retinoscopy or some other technique for determining the presence of refractive errors in every horse presented for evaluation of a questionable vision problem, when the cause is not obvious after routine ophthalmic examination. Refraction should also be considered in the ophthalmic prepurchase examination of performance horses.

Perhaps the most obvious situation in which a refractive error would affect visual performance is after cataract extraction. The equine eye without a lens (aphakia) has been reported to have a refractive error between +8 and +10.5 D.[92,98] Practically, this means that in air, a convex^{+} lens of between 8 and 10.5 D power would have to be placed in front of the eye for the horse with aphakia to accurately visualize an object placed 20 or more feet from the eye. It is well recognized in humans, and has been proven in dogs, that a predictable decrease in resolving power of the eye occurs with optical defocus.[83] In the dog, mimicking aphakia by placing concave^{-} lenses in front of the eye reduces visual acuity from approximately 20/65 to worse than 20/800.[83] Defocusing the equine eye results in a similar loss of approximately one cycle per degree (CPD) of visual acuity for each diopter of defocus.[10] If one assumes the visual acuity of the healthy horse is approximately 10 CPD[160] (Snellen equivalent of approximately 20/60 [see Table 11-1]), and the refractive error of a horse with aphakia is −9.5 D, then the predicted visual acuity of the horse with aphakia would be 0.5 CPD (20/1200 Snellen equivalent). A previous report on the visual performance of a foal with aphakia suggests that the equine eye may not experience a marked decrement in visual performance according to an analysis of the physical constants of the equine optical system and the horse's retinal structure.[92] However, the preceding calculations would suggest that the foal in that report was not required to perform visually challenging tasks and that, like many animals, it adapted to a state of constant visual defocus, most likely through adaptation of its other senses. An animal with 20/1200 vision can still determine the locations of a stall door and a fence border but by no means should be considered to have "good vision."

Though horses undergoing cataract extraction would clearly benefit optically from the placement of an appropriately designed intraocular lens, the ability of the current commercially available lenses to return the eye to emmetropia is unclear. Both 14-D and 18-D intraocular lenses are currently available.[78,170,171] So what information should the veterinary ophthalmologist offer the owner of a horse who is considering cataract extraction? The owner should be informed that if the horse has advanced cataracts, it will experience a marked improvement in its visual abilities after surgery. If an intraocular lens is not placed after cataract surgery, the owner should be informed that the horse will be markedly farsighted, meaning that there is no object in the horse's visual environment that is not severely defocused (many owners mistakenly believe that the term *farsighted* means the ability to see far-away objects well). Although most horses will adapt extremely well to this condition and develop strategies that emphasize use of their other senses, at no time after surgery will an animal have anything that approximates normal vision. It has also been noted that some horses with aphakia have reduced vision at night and what appears to be reduced contrast sensitivity as evidenced by difficulties seeing dark steers in dim light.[172,173] Whether the animal is to be used for riding is up to the owner, but the following caveats should always be provided. How well the horse does after cataract extraction will depend on its temperament, its level of training, and the skill of the rider. A well-trained blind horse and a skilled rider can do amazingly well. However, a horse with aphakia is more likely to misinterpret visual cues, and under no circumstances should the animal be ridden by inexperienced riders or ridden in potentially dangerous situations (e.g., trail riding along cliffs). Any rider getting on the horse should also be informed of its visual disability.

Finally, although Rocky Mountain horses with cornea globosa might be suspected to have marked refractive errors, one study demonstrated no such shift in refractive state.[174] In this study, retinoscopy, keratometry, phacometry, and ultrasonography were used to analyze the refractive components of the eye. Although anterior chamber depth was greater in the horses with cornea globosa (and might reasonably be expected to be associated with a shift in refractive state), this finding was offset by the thinner anterior-posterior lens thickness and a more shallow vitreous chamber depth.[174] It is not clear whether this finding represents an attempt by the eye during development to compensate for the anterior segment abnormalities

(emmetropization), but it does serve to illustrate that careful analysis of the eye as a whole is necessary to properly evaluate the effect ocular abnormalities may have on vision.

ORBITAL DISORDERS

In addition to the obvious disease state, orbital disorders have the ability to induce diplopia, or double vision, if the two eyes can no longer move in a conjugate fashion. Such diplopia may be constantly present or may occur in certain gazes or positions if the movement of the globe is limited in one direction but not others. Undoubtedly this condition is present in many horses with orbital disorders, and it has a considerable impact on the animal's ability to perform visually directed tasks. In humans, diplopia is frequently quite debilitating, and some people prefer to be monocular rather than to have diplopia. Because a method of determining whether diplopia is present is not readily available for horses, patients with mild diplopia likely remain undiagnosed, and the impact this disorder may have on their vision is not appreciated. Similarly, orbital surgical procedures that result in the loss of orbital fat but preserve the globe (as may occur after excision of a squamous cell carcinoma that invaded the orbit or a severe eyelid laceration with prolapse of orbital fat) may also induce diplopia if the globe is not properly supported and oriented.

CORNEAL DISORDERS

Of all the diseases the veterinarian is called on to treat, those affecting the cornea may be the most likely to have long-term consequences for an animal's vision. All corneal opacities (scar, infiltrate, deposit, pigment, vessels, edema, foreign body, and loss of stromal substance caused by trauma or septic/nonseptic ulceration) can substantially impair vision, and therapies should be directed at minimizing their magnitude if the eye is to perform optimally. Simply getting an ulcer to heal should not be the goal of therapy; instead, the goal should be to achieve healing with the greatest preservation of the visual potential of the eye. Although a conjunctival flap may result in a septic axial corneal ulcer healing faster than if medical therapy alone were used, it should be done only with the knowledge that it also results in a significant permanent corneal opacity because the conjunctiva does not have the same optical clarity as the cornea. If the sole purpose of the therapy is globe preservation, the procedure that is selected becomes largely irrelevant as long as the structural integrity of the corneoscleral shell is maintained. In the ideal setting, therapy should be chosen that will result in the least impediment to vision in the long run. In this regard, a corneoscleral transposition that maintains greater transparency of the axial cornea, intensive medical therapy, or perhaps limited débridement and application of cyanoacrylate tissue adhesive may be preferable to a conjunctival flap or a tectonic corneal transplant. Corneal opacities may reduce the amount of light entering the eye (example: pigment or diffuse dense scarring), or they may scatter light in the case of edema and deposits, thereby resulting in glare or halos around objects as reflected points of light are further distorted into blobs. Very dense opacities may result in a scotoma or blind spot. Astigmatism is a common consequence of corneal disorders that result in scarring or alterations in the corneal curvature. As noted previously in this chapter, the presence of a menace response does not indicate that the animal with corneal disease has normal vision.

IRIS CYSTS

Iris cysts are observed frequently in horses and, though rare, have been reported to be associated with visual impairment.[175] Visual impairment can occur with the presence of large cysts or single to multiple free-floating cysts in the anterior chamber. Gilger et al.[175] reported on eight equine patients that were examined because of visual impairment (n = 5), decreased jumping performance (n = 2), or head shaking (n = 1). Laser treatment of the iris cysts resolved the clinical signs in all eight horses.

LENS DISORDERS

Aside from the obvious impact of cataracts on vision (Fig. 11-38), lens subluxation can also significantly alter visual performance, because light is unequally focused on the retina by the regions in which the lens is and is not present. Spherical aberration may also become extreme not only because the more highly curved equatorial region of the lens now assumes a more axial position but also because loss of zonular attachments allows the lens to assume a more spherical shape in those regions. This relaxation may result in myopia, and if the lens is displaced anteriorly, myopia will also occur. Tilting of the lens may cause marked irregular astigmatism. Monocular "double vision" may also result when the lens is partly in and partly out of the pupil. The visual disturbance may be dynamic

Figure 11-38. Simulated vision through an incipient axial cataract near the posterior nodal point. **A,** Normal view. **B,** Simulated view with a cataract.

in nature if the lens moves with head movements. If the lens is completely luxated posteriorly, it will result in an aphakic refractive error and also behave as a very large vitreal floater as it casts shadows on the retina.

GLAUCOMA

Increased intraocular pressure is associated with numerous visual defects, not the least of which is the complete loss of light perception in advanced cases. Earlier in the process, many other, more subtle, alterations in vision occur (Fig. 11-39). The equine optic nerve is relatively unique in that it contains a substantial portion of large-diameter optic nerve fibers,[49] and these fibers are the most susceptible to injury as intraocular pressure increases.[176] Such fibers are especially involved in motion detection, stereopsis, and sensitivity to dim light, suggesting that horses in the early stages of glaucoma may have abnormalities in these areas as well.[176] Humans with glaucoma also have reduced contrast sensitivity,[177] reduced ability to detect flickering lights,[178] impaired dark adaptation,[179] increased glare disability,[179] and abnormal color vision, especially in the blue-yellow pathway[180] but also in the red-green pathway.[181] In humans with early glaucoma, the reduced contrast sensitivity associated with the disease is more of an impediment to everyday real-life visual performance than is reduced visual acuity associated with the disease.[177] In view of the heavy reliance of the horse on the blue-yellow pathway, it seems possible that glaucoma in this species may result in significantly impaired color vision. Buphthalmia also increases the axial length of the globe and induces myopia if vision remains.

Figure 11-39. Simulated vision of a horse with glaucoma. **A,** Normal view. **B,** Simulated view with glaucoma.

Glaucomatous visual-field losses seen on perimetry testing are well recognized in humans[182] and undoubtedly occur in horses as well, although the ability to detect such losses is limited by the lack of a standardized method of evaluating the animal's visual field. These changes often represent more advanced disease than the visual abnormalities previously discussed. Humans experience a number of visual-field defects, including a generalized central and peripheral depression of the visual field, localized paracentral blind spots (scotomas), and isolated peripheral to midperipheral defects on the nasal side that progress to form arcuate defects above and eventually below the central visual field.[182] Humans, and undoubtedly horses, with reduced peripheral vision tend to trip over or bump into objects more frequently and have difficulty performing certain outdoor mobility tasks.[179] In very advanced stages, peripheral vision is lost, and only the central visual field remains (see Fig. 11-39). Eventually, even the ability to perceive light is lost.

PRESUMED VISUALLY MEDIATED BEHAVIORAL DISORDERS

PHOTIC HEAD SHAKING

Violent shaking of the head and neck may render a horse unsuitable for riding and even make it dangerous to be around.[183,184] This may or may not be associated with exposure to bright light (photic head shaking). In some cases, head shaking was markedly reduced when the animal was placed in a darkened environment, blindfolded, or had eye masks placed over its eyes, suggesting that the amount of incident light plays a significant role in the process.[183,184] For unknown reasons, head shaking can also be brought on by exercise, regardless of the photic environment. There are a number of presumed causes of this condition, many of which are unrelated to the eyes and vision. A thorough workup of these animals should be performed, and otitis media/interna, guttural pouch disease, upper respiratory tract disease, and oral as well as ocular diseases should be ruled out. In photic head shaking, a mechanism similar to light-induced sneezing in humans has been proposed. Optic nerve stimulation may summate with responses in the trigeminal nerve, resulting in sensory abnormalities in the nasal cavity. Sunlight may stimulate parasympathetic activity in the infraorbital nerve or the facial sensory branch of the trigeminal nerve, resulting in irritating nasal sensations that cause the horse to sneeze or rub and "flip" the nose. A favorable response to oral cyproheptadine, an antihistamine serotonin antagonist (0.3 mg/kg twice daily), occurs in most affected horses, and melatonin therapy has also been suggested to be beneficial. Bilateral infraorbital neurectomy can be used for medically refractory cases if infraorbital nerve blocks eliminate the behavior. Because this behavior has been observed in dim light a few minutes after the onset of exercise (P. Miller, C. Murphy, unpublished data), it is feasible that exercise-induced (as opposed to photically induced) alterations in neuronal output may be the true initiating factor in some cases. Head shaking has also been associated anecdotally with iris cysts and vitreal floaters. Horses may also exhibit head shaking as a learned response to avoid performing activities that they deem undesirable. The neurologic pathways underlying photic head shaking remain definitively unexplored,

although the efficacy of cyproheptadine may offer some insight into these pathways.

"SHYING" OR "SPOOKING"

The association of a visual disturbance with shying or spooking appears to be more well defined than the association with head shaking. As described in detail earlier in this chapter, conditions that have been associated with this behavior include refractive errors, iris cysts, vitreal floaters, and lens luxations. Because horses' normally poor peripheral visual acuity only allows detection of movement and brightness over much of the visual field and because they have a prey mentality, even horses with normal vision are likely to adopt the attitude of "run first, ask questions later." Because this behavior is present in every horse to some degree, it may be in part a hard-wired reflex, but experience suggests that it can be substantially modified by proper training and desensitization. Horses with visual abnormalities in one eye may be more easily surprised by objects approaching from that side and react in sometimes surprising or violent ways. Again, with training or establishing a high degree of trust between the horse and rider, these behaviors can be reduced if not eliminated in many animals. The use of blinkers that block out the horse's peripheral field of view may divert its attention from these types of distractions and cause it to focus on objects ahead of it and better seen binocularly. However, some horses seem to respond with increased levels of fear when this is done.

DIFFICULTY MOVING BETWEEN LIGHT AND DARK

Given the comparatively slow rate of excursion of the equine pupillary light reflex and the 30 minutes or more required for equine rhodopsin to fully adapt to dim light, it is not surprising that even modestly rapid shifts from bright to dim environments (and vice versa) would be visually disturbing to a horse. In normal circumstances, the transition from daylight to twilight to nighttime occurs slowly, so there is no need for the animal to rapidly acclimate to varying lighting conditions. Again, to some extent, a prey mentality may play a role in this behavior because inability to fully evaluate the visual environment before entering a trailer, stall, paddock, or other area may provoke anxiety about the unknown. Some horses will move between light and dark environments better if all visual input is controlled. In severe cases of night blindness, in which injury may result from inadvertent collisions with various obstacles, the possibility of retinal disease should be considered. Congenital stationary night blindness is an inherited defect (possibly a sex-linked recessive trait) that may involve abnormalities in the transmission of visual impulses at the level of the middle retina.[70,185-187] It is most common in Appaloosa breeds but is seen in other breeds as well. It is characterized by visual impairment in dim light but relatively normal vision in bright light. Also seen are behavioral uneasiness and unpredictability at night, but ophthalmoscopic examination reveals no abnormalities. Foals may appear to be disorientated, may stare off into space, and may have a bilateral dorsomedial strabismus. It is generally nonprogressive (hence the name *stationary*) and often accompanied by other abnormalities such as chronic posterior segment uveitis. It is diagnosed by abnormalities on electroretinography consisting of decreased scotopic b-wave amplitude and a large, negative, monotonic a-wave.[185-187] Other differential diagnoses include progressive retinal atrophy, which is rare in horses.[188]

SUMMARY

The act of seeing is a complex process that involves not only the eye focusing and detecting light, which may vary in intensity by as much as 40 billion–fold, but also the brain perceiving the resulting image. Because the horse's food is essentially immobile and not particularly challenging to identify or capture, much of the horse's visual capabilities appear to be defensive and devoted to ensuring the animal's survival by more easily identifying potential threats rather than capturing prey (as in the case of a predator). Horses have several adaptations to both dim light (a large cornea and pupil, and a reflective fibrous tapetum lucidum) and bright light (yellow-filtering pigments in the lens and the corpora nigra, which act as "internal visors," and a significant population of cones). They maintain the image on the retina during motion in much the same way as humans do, and like humans, they detect moving objects more easily than stationary ones. Their visual field is enormous (up to 350 degrees) and provides nearly a complete sphere of vision with only a few small blind spots. The degree of binocular overlap (55 to 65 degrees) rivals or exceeds that of dogs, and horses use both monocular and binocular clues to estimate depth, although the binocular depth threshold is five times better than for one eye. From 2 m away, horses can detect a 9-cm difference in depth, which approximates the ability of a cat. Accommodation is limited (less than 2 D), but only small changes by the lens are needed to maintain a focused image on the retina. Although some individuals are greater than or equal to 3 D myopic or hyperopic, the average resting refraction is near emmetropia (normal). Horses possess a visual streak located in the tapetal zone, oriented so it conforms to the projection of the horizon on the retina, and an optic nerve that contains approximately the same number of fibers as a human's. At 20/30 to 20/60, the horse's visual acuity is among the best of the domestic mammals, including predators, and is better than that of many humans. Horses have dichromatic color vision with two cone types: a short wavelength–sensitive (blue) cone with a peak sensitivity of approximately 428 nm and a second cone with a peak sensitivity around 540 nm, which is between the human red and green cones. It is probable that this results in colors appearing as washed-out pastels or sepia, and horses have difficulty in differentiating orange and blue, much like some colorblind men have difficulty differentiating between red and green. Because many predators have also evolved coats that closely match the background in terms of color, and in some cases, visual texture, color may be a relatively poor way for the horse to "break the camouflage" of a predator. Instead, objects can be differentiated from their surroundings if they are suitably different in any one of five different aspects: luminance ("brightness"), motion, texture, binocular disparity (depth), or color. The current inability to clinically recognize anything but the most massive visual impediments in horses is not because the horse is unusually resistant to disorders that impair vision in other species but because of the crudeness of the tools the clinician currently has available to determine how well a particular horse can see.

References

1. Timney B, Keil K: Horses are sensitive to pictorial depth clues, Perception 25:1121–1128, 1996.
2. Galambos R, Juhász G: How patterns of bleached rods and cones become visual perceptual experiences: a proposal, Proc Natl Acad Sci 98:11702–11707, 2001.
3. Green DG: Visual acuity, color vision, and adaptation. In Albert DM, Jakobiec FA, editors: Principles and practice of ophthalmology, Philadelphia, 1994, WB Saunders Co.
4. Livingstone MS, Hubel DH: Psychophysical evidence for separate channels for the perception of form, color, movement, and depth, J Neurosci 7:3416–3468, 1987.
5. Livingstone M, Hubel D: Segregation of form, color, movement and depth: anatomy, physiology, and perception, Science 240:740–749, 1988.
6. Regan D: Early visual processing of spatial form. In Kaufman PL, Alm A, editors: Adler's physiology of the eye: clinical applications, ed 10, St Louis, 2003, Mosby.
7. Carroll J, Murphy CJ, Neitz M, et al: Photopigment basis for dichromatic color vision in the horse, J Vis 1:80–87, 2001.
8. Hart NS, Hunt DM: Avian visual pigments: characteristics, spectral tuning, and evolution, Am Nat 169(Suppl):S7–S26, 2007.
9. Sakmar TP: Color vision. In Kaufman PL, Alm A, editors: Adler's physiology of the eye: clinical applications, ed 10, St Louis, 2003, Mosby.
10. Ver Hoeve JN, Neitz J, Murphy CJ: Horse sense: electrophysiologic measures of equine vision, Invest Ophthalmol Vis Sci 40:s22, 1999.
11. Livingstone M: Luminance and night vision. In Livingstone M, editor: Vision and art: the biology of seeing, New York, 2002, Harry N. Abrams Inc.
12. Palmer DA: Rod-cone mechanisms underlying the Purkinje shift, Nature 262:601–603, 1976.
13. Lu C, Fender DH: The interaction of color and luminance in stereoscopic vision, Invest Ophthalmol 11:482–490, 1972.
14. Rodieck RW: The first steps in seeing, Sunderland, Mass, 1998, Sinauer Associates.
15. Warrant EJ: Seeing better at night: life style, eye design and the optimum strategy of spatial and temporal summation, Vis Res 39:1611–1630, 1999.
16. Harman AM, Moore S, Hoskins R, et al: Horse vision and an explanation for the visual behavior originally explained by the "ramp retina," Equine Vet J 31:384–390, 1999.
17. Hebel R: Distribution of retinal ganglion cells in five mammalian species (pig, sheep, ox, horse, dog), Anat Embryol 150:45–51, 1976.
18. Wouters L, De Moor A: Ultrastructure of the pigment epithelium and the photoreceptors in the retina of the horse, Am J Vet Res 40:1066–1071, 1979.
19. Hecht S, Shlaer S, Pirenne MH: Energy, quanta, and vision, J Gen Physiol 25:819–840, 1942.
20. Davis JL, Stewart T, Brazik E, et al: The effect of topical administration of atropine sulfate on the normal equine pupil: influence of age, breed and gender, Vet Ophthalmol 6:329–332, 2003.
21. Roth LS, Balkenius A, Kelber A: The absolute threshold of colour vision in the horse, PLoS One 3:e3711. Epub 2008.
22. Dowling J: Neural and photochemical mechanisms of visual adaptation, J Gen Physiol 46:1287–1301, 1963.
23. Soemmerring DW: De Ocularum hominis animaliumque sectione horizontali commentatio, Vandenhoeck et Ruprecht, 1818, Gottingen.
24. Walls GL: The vertebrate eye and its adaptive radiation, New York, 1963, Hafner Publishing.
25. Plummer CE, Ramsey DT, Hauptman JG: Assessment of corneal thickness, intraocular pressure, optical corneal diameter, and axial globe dimensions in Miniature horses, Am J Vet Res 64:661–665, 2003.
26. Ramsey DT, Hauptman JG, Peterson-Jones SM: Corneal thickness, intraocular pressure, and optical corneal diameter in Rocky Mountain horses with cornea globosa or clinically normal corneas, Am J Vet Res 60:1317–1321, 1999.
27. Hammond P, Mouat GS: The relationship between feline pupil size and luminance, Exp Brain Res 59:485–490, 1985.
28. Miller PE, Nelson MJ, Rhaesa SL: Effects of topical administration of 0.5% apraclonidine on intraocular pressure, pupil size, and heart rate in clinically normal dogs, Am J Vet Res 57:79–82, 1996.
29. Murphy CJ, Howland HC: On the gecko pupil and Scheiner's disc, Vis Res 26:815–817, 1986.
30. Schmidt-Morand D: Vision in the animal kingdom, Vet Int 1:3–32, 1992.
31. Findlay JB, Barclay PF, Brett M, et al: The structure of mammalian rod opsins, Vis Res 24:1501–1508, 1984.
32. Jacobs GH, Deegan JF 2nd, Crognale MA, et al: Photopigments of dogs and foxes and their implications for canid vision, Vis Neurosci 10:173–180, 1993.
33. Kemp CM, Jacobson SG: Rhodopsin levels in the central retina of normal miniature poodles and those with progressive rod-cone degeneration, Exp Eye Res 54:947–956, 1992.
34. Parkes JH, Aquirre G, Rockey JH, et al: Progressive rod-cone degeneration in the dog: characterization of the visual pigment, Invest Ophthalmol Vis Sci 23:674–678, 1982.
35. Bernstein MH, Pease DC: Electron microscopy of the tapetum lucidum of the cat, J Biophys Biochem Cytol 5:35–40, 1959.
36. Braekevelt CR: Morphology of the tapetum fibrosum in the eye of domestic sheep, Can J Zool 61:1109–1115, 1983.
37. Coles JA: Some reflective properties of the tapetum lucidum of the cat's eye, J Physiol 212:393–409, 1971.
38. Elliott JH, Futterman S: Fluorescence in the tapetum of the cat's eye. Identification, assay and localization of riboflavin in the tapetum and a proposed mechanism by which it may facilitate vision, Arch Ophthalmol 70:531–534, 1963.
39. Pedler C: The fine structure of the tapetum cellulosum, Exp Eye Res 2:189–195, 1963.
40. Pirie A: Crystals of riboflavin making up the tapetum lucidum in the eye of a lemur, Nature 183:985–986, 1959.
41. Pirie A: The chemistry and structure of the tapetum lucidum in animals. In Graham-Jones O, editor: Aspects of comparative ophthalmologys, Oxford, 1966, Pergamon Pres.
42. Weale RA: The spectral reflectivity of the cat's tapetum measured in situ, J Physiol 119:30–42, 1953.
43. Ezeh PI, et al: Utilizing an optokinetic device in assessing the functional visual acuity of the dog, Prog Vet Neurol 1:427–432, 1990.
44. Gunter R: The absolute threshold for vision in the cat, J Physiol 114:8–15, 1951.
45. Hanggi EB, Ingersol JF: Stimulus discrimination by horses under scoptic conditions, Behav Proc Apr 21, 2009.
46. Murphy CJ, Johnson C, Howard D, et al: Spectral transmission properties of the equine lens, Proc Am Coll Vet Ophthalmol 24:82, 1993.
47. Wolffsohn JS, Cochrane AL, Khoo H, et al: Contrast is enhanced by yellow lenses because of selective reduction of short-wavelength light, Optom Vis Sci 77:73–81, 2000.
48. Zigman S, Paxhia T: The nature and properties of squirrel lens yellow pigment, Exp Eye Res 47:819–824, 1988.
49. Brooks DE, Blocker TL, Samuelson DA, et al: Histomorphometry of the optic nerves of normal horses and horses with glaucoma, Vet Comp Ophthalmol 5:193–210, 1995.
50. Guo X, Sugita S: Topography of ganglion cells in the retina of the horse, J Vet Med Sci 62:1145–1150, 2000.
51. Berkley MA, Warmath DS, Tunkl JE: Movement discrimination capacities in the cat, J Comp Physiol Psychol 92:463–473, 1978.
52. Pasternak T, Merigan WH: Movement detection by cats: invariance with direction and target configuration, J Comp Physiol Psychol 94:943–952, 1980.
53. Miller NR: The neural control of eye movements. In Miller NR, Newman NJ, editors: Walsh and Hoyt's clinical neuro-ophthalmology, 4th ed, Baltimore, 1985, Williams & Wilkins.
54. Robinson DA: The biology of eye movements. In Albert DM, Jakobiec FA, editors: Principles and practice of ophthalmology, Philadelphia, 1994, WB Saunders.
55. Schor CM: Neural control of eye movements. In Kaufman PL, Alm A editors: Adler's physiology of the eye, ed 10, St Louis, 2003, Mosby.
56. Kardon R: The pupil. In Kaufman PL, Alm A, editors: Adler's physiology of the eye, 10th ed, St Louis, 2003, Mosby.
57. Duke-Elder S: System of ophthalmology, vol 1, The eye in evolution, St Louis, 1958, Mosby.
58. Peichl L: Topography of ganglion cells in the dog and wolf retina, J Comp Neurol 324:603–620, 1992.
59. Sherman SM, Wilson JR: Behavioral and morphological evidence for binocular competition in the postnatal development of the dog's visual system, J Comp Neurol 161:183–195, 1975.
60. Tychsen L: Binocular vision. In Hart WM, editor: Adler's physiology of the eye: clinical application, ed 9, St Louis, 1992, Mosby.

61. McFadden SA: The binocular depth stereoacuity of the pigeon and its relation to the anatomical resolving power of the eye, Vis Res 27:1967–1980, 1987.
62. Pettigrew JD: The evolution of binocular vision. In Pettigrew JD, Sanderson KJ, Levick WR, editors: Visual neuroscience, Cambridge, 1986, Cambridge University Press.
63. Cumming BG, Parker AJ: Binocular mechanisms for detecting motion-in-depth, Vis Res 34:483–495, 1994.
64. McKee SP: The spatial requirements for fine stereoacuity, Vis Res 23:191–198, 1983.
65. Packwood J, Gordon B: Stereopsis in normal domestic cat, Siamese cat, and cat raised with alternating monocular occlusion, J Neurophysiol 38:1485–1499, 1975.
66. Finley B: Horse racing; one-eyed colt shows derby promise. The New York Times, page D7, March 6, 2004.
67. Timney B, Keil K, Schultz L: The use of monocular depth clues by horse, Invest Ophthalmol Vis Sci 33(Suppl):1368, 1992.
68. Timney B, Keil K: Local and global stereopsis in the horse, Vis Res 39:1861–1867, 1999.
69. Brooks DE: Ophthalmology for the equine practitioner, Jackson, WY, 2002, Teton NewMedia.
70. Timney B, Macuda T: Vision and hearing in horses, J Am Vet Med Assoc 218:1567–1574, 2001.
71. Saslow CA: Factors affecting stimulus visibility for horses, Appl Anim Behav Sci 61:273–284, 1999.
72. Bartoš L, Bartošová J, Starostová L: Position of the head is not associated with changes in horse vision, Eq Vet J 40:599–601, 2008.
73. Westheimer G: Detection of disparity motion by the human observer, Optom Vis Sci 67:627–630, 1990.
74. Cumming BG: The relationship between stereoacuity and stereomotion thresholds, Perception 24:105–114, 1995.
75. Harris JM, Rushton SK: Poor visibility of motion in depth is due to early motion averaging, Vis Res 43:385–392, 2003.
76. Timney B: Effects of brief monocular deprivation on binocular depth perception in the cat: a sensitive period for the loss of stereopsis, Vis Neurosci 5:273–280, 1990.
77. Borish IM: Clinical refraction, vol 1, ed 3, Chicago, 1975, The Professional Press Inc.
78. Westheimer G: Visual acuity. In Kaufman PL, Alm A editors: Adler's physiology of the eye, ed 10, St Louis, 2003, Mosby.
79. Timney B, Keil K: Visual discrimination learning and resolution acuity in the horse, Invest Ophthalmol Vis Sci 31(Suppl):323, 1990.
80. Wadensten L: The use of flicker electroretinography in the human eye: observations on clinical cases, Acta Ophthalmol 34:311–340, 1956.
81. Blake R, Cool SJ, Crawford MLJ: Visual resolution in the cat, Vis Res 14:1211–1217, 1974.
82. Miller PE, Murphy CJ: Vision in dogs, J Am Vet Med Assoc 207:1623–1634, 1995.
83. Murphy CJ, Mutti DO, Zadnik K, et al: Effect of optical defocus on visual acuity in the dog, Am J Vet Res 58:414–418, 1997.
84. Hall CA, Cassaday HJ, Derrington AM: The effect of stimulus height on visual discrimination in horses, J Anim Sci 81:1715–1720, 2003.
85. Holladay JT: Proper method for calculating average visual acuity, J Refract Surg 13:388–391, 1997.
86. Miller D: Physiologic optics and refraction. In Kaufman PL, Alm A, editors: Adler's physiology of the eye, ed 10, St Louis, 2003, Mosby.
87. Schwiegerling J: Theoretical limits to visual performance, Surv Ophthalmol 45:139–146, 2000.
88. Westheimer G: Optical properties of vertebrate eyes. In Organs Fuortes MGF, editor: Physiology of photoreceptor, New York, 1972, Springer-Verlag.
89. Bogler BD: Unterludjungen über die säufigkeit des auftretens von augenerkrankungen und deren refiduen bei militärpferden, Z Veterinarkunde (1.Heft):11–22, 1906.
90. Cottier R: Ein refraktometer für tieraugen. Archiv für Wissenschaftliche und praktische tierheilkunde, Berlin 78:395–413, 1943.
91. Dubar MJ, Thieulin MG: L'état de refraction des yeux des mamifères domestiques, Rev Gen Med Vet 36:561–566, 1927.
92. Farrall H, Handscombe C: Follow-up report of a case of surgical aphakia with an analysis of equine visual function, Equine Vet J Suppl 10:91–93, 1990.
93. Knill LM, Eagleton RD, Harver E: Physical optics of the equine eye, Am J Vet Res 38:735–737, 1997.
94. Lang W, Barrett JW: The refractive character of the eyes of mammalia, R Lond Ophthalmic Hosp Rep 11:103–129, 1886.
95. Roberts SM: Equine vision and optics, Vet Clin North Am Equine Pract 8:451–457, 1992.
96. Sivak JG, Allen DB: An evaluation of the "ramp" retina of the horse eye, Vis Res 15:1353–1356, 1975.
97. Smith S, Goldman L: Color discrimination in horses, Appl Anim Behav Sci 62:13–25, 1999.
98. Stuhr C, Abrams G, Bullimore M, et al: The normal refractive state of the equine, Proc Am Coll Vet Ophthalmol 30:74, 1999.
99. Tervoert FW: Untersuchungen über den astigmatismus des pferdeauges [dissertation], Holland, 1914, Hohen veterinär-medizinischen fakultät der universität Bern, pp 1–121.
100. Wouters L, De Moor A: Retinoscopische refraktiebepaling bij het paard, Vlaams Diereneeskd Tijdschr 47:445–454, 1978.
101. Coile DC, O'Keefe LP: Schematic eyes for domestic animals, Ophthalmic Physiol Opt 8:215–220, 1988.
102. Kubai MA, Bentley E, Miller PE, et al: Refractive state of eyes and association between ametropia and breed in dogs, Am J Vet Res 69:946–951, 2008.
103. Murphy CJ, Zadnik K, Mannis M: Myopia and refractive error in dogs, Invest Ophthalmol Vis Sci 33:2459–2463, 1992.
104. Mutti DO, Murphy CJ, Zadnik K: A naturally occurring model of vitreous chamber-based myopia in the Labrador Retriever, Invest Ophthalmol Vis Sci 40:1577–1584, 1999.
105. Howland HC: Physiological optics. In Albert DM, Jakobiec FA, editors: Principles and practice of ophthalmology, Philadelphia, 1994, WB Saunders.
106. Glasser A, Kaufman PL: Accommodation and presbyopia. In Kaufman PL, Alm A, editors: Adler's physiology of the eye, ed 10, St Louis, 2003, Mosby.
107. Murphy CJ, Howland HC: The optics of comparative ophthalmoscopy, Vis Res 27:599, 1987.
108. Bayer J: Augenheiklunde, Vienna, 1914, Braumueller. Cited by Samuelson DA: Ophthalmic anatomy. In Gellatt KN, editor: Veterinary ophthalmology, ed 3, Philadelphia, 1999, Lippincott Williams & Wilkins.
109. Lancon MR, Miller D: Corneal hydration, visual acuity and glare sensitivity, Arch Ophthalmol 90:227, 1973.
110. Sivak JG: The accommodative significance of the "ramp" retina of the eye of the stingray, Vis Res 16:945, 1976.
111. Rohen JW, Kaufman PL, Eichhorn M, et al: Functional morphology of accommodation in the raccoon, Exp Eye Res 48:523, 1989.
112. Murphy CJ, Howland HC: Owl eyes: accommodation, corneal curvature, and refractive state, J Comp Physiol 151:277–284, 1983.
113. Murphy CJ, Howland HC, Kwiecinski GG, et al: Visual accommodation in the flying fox *(Pteropus giganteus)*, Vis Res 23:617–620, 1983.
114. Tscherning M: Accommodation. In Weiland D, editor: Physiologic optics, ed 2, Philadelphia, 1904, The Keystone.
115. Schachar RA, Cudmore DP, Black TD: Experimental support for Schachar's hypothesis of accommodation, Ann Ophthalmol 25:404–409, 1993.
116. Schachar RA: Cause and treatment of presbyopia with a method for increasing the amplitude of accommodation, Ann Ophthalmol 24:445–447, 1992.
117. Aggarwala KR, Kruger ES, Mathews S, et al: Spectral bandwidth and ocular accommodation, J Opt Soc Am A Opt Image Sci Vis 12:450–455, 1995.
118. Aggarwala KR, Nowbotsing S, Kruger PB: Accommodation to monochromatic and white-light targets, Invest Ophthalmol Vis Sci 36:2695–2705, 1995.
119. Kruger PB, Mathews S, Aggarwala KR, et al: Chromatic aberration and ocular focus: Fincham revisited, Vis Res 33:1397–1411, 1993.
120. Hoffmann ML, Zrenner E, Langhof HJ: The effect of the pupil as aperture and field stop on the various components of the human electroretinogram, Albrecht Von Graefes Arch Klin Exp Ophthalmol 206:237–245, 1978.
121. Murphy CJ, Howland HC: The functional significance of crescent-shaped pupils and multiple pupillary apertures, J Exp Zool Suppl 5:22–28, 1991.
122. Harkness L: Chameleons use accommodative cues to judge distance, Nature 267:346–349, 1977.
123. Harkness L, Bennet-Clark HC: The deep fovea as a focus indicator, Nature 272:814–816, 1978.

124. Guo X, Sugita S: Quantitative analysis of the organization of the inner nuclear layer of the horse retina, J Vet Med Sci 64:847–849, 2002.
125. Stone J: A quantitative analysis of the distribution of ganglion cells in the cat's retina, J Comp Neurol 124:337–352, 1965.
126. Sandmann D, Boycott BB Peichl L: Blue-cone horizontal cells in the retinae of horses and other Equidae, J Neurosci 16:3381–3396, 1996.
127. Masland RH: Cell mosaics and neurotransmitters. In Albert DM, Jakobiec FA, editors: Principles and practice of ophthalmology, Philadelphia, 1994, WB Saunders.
128. Chao TI, Grosche J, Friedrich KJ, et al: Comparative studies on mammalian Muller (retinal glial) cells, J Neurocytol 26:439–454, 1997.
129. Sharma RK, Ehinger BEJ: Development and structure of the retina. In Kaufman PL, Alm A, editors: Adler's physiology of the eye, ed 10, St Louis, 2003, Mosby.
130. Norcia AM, Wesemann W, Manny RE: Electrophysiological correlates of vernier and relative motion mechanisms in human visual cortex, Vis Neurosci 16:1123–1131, 1999.
131. Shapley R, Victor J: Hyperacuity in cat retinal ganglion cells, Science 231:999–1002, 1986.
132. Skottun BC: Hyperacuity and the estimated positional accuracy of a theoretical simple cell, Vis Res 40:3117–3120, 2000.
133. Swindale NV, Cynader MS: Vernier acuity of neurones in cat visual cortex, Nature 319:591–593, 1986.
134. Altes RA: Ubiquity of hyperacuity, J Acoustical Soc Am 85:943–952, 1989.
135. Murphy KM, Mitchell DE: Vernier acuity of normal and visually deprived cats, Vis Res 31:253–266, 1991.
136. Hanggi EB: Interocular transfer of learning in horses *(Equus caballus)*, J Equine Vet Sci 19:518–523, 1999.
137. Hanggi EB: Categorization learning in horses *(Equus caballus)*, J Comp Psychol 113:243–252, 1999.
138. Hanggi EB: Discrimination learning based on relative size concepts in horses *(Equus caballus)*, Appl Anim Behav Sci 83:201–213, 2003.
139. Hanggi EB: Equine cognition and perception: understanding the horse. In: Fujita K, Itakura S, editors: diversity of cognition: evolution, development, domestication, and pathology, Kyoto, 2006, Kyoto University Press, pp 98–118.
140. Hanggi EB, Ingersoll JF: Long-term memory for categories and concepts in horses *(Equus caballus)*, Anim Cogn 12:451–462, 2009.
141. Pfungst O: Clever Hans (The horse of Mr. von Osten): A contribution to experimental animal and human psychology (Trans. C. L. Rahn), New York, 1911, Henry Holt (Originally published in German, 1907).
142. Hubel DH, Wiesel TN: Receptive fields, binocular interaction and functional architecture in the cat's visual cortex, J. Physiol 160:106–154, 1962.
143. Hubel DH: Evolution of ideas on the primary visual cortex, 1955–1978: a biased historical account. From Nobel Lectures, Physiology or Medicine 1981–1990, Editor-in-Charge Tore Frängsmyr, Editor Jan Lindsten, Singapore, 1993, World Scientific Publishing Co.
144. Priebe NJ, Ferster D: Inhibition, spike threshold, and stimulus selectivity in primary visual cortex, Neuron 28:482–497, 2008.
145. Jacobs GH: The distribution and nature of color vision among the mammals, Biol Rev 68:413–471, 1993.
146. Jacobs GH: Colour vision in animals, Endeavour 7:137–140, 1983.
147. Regan BC, Julliot C, Simmen B, et al: Fruits, foliage and the evolution of primate colour vision, Philos Trans R Soc Lond B Biol Sci 356:229v283, 2001.
148. Carroll J, Neitz J, Neitz M: Estimates of L:M cone ratio from ERG flicker photometry and genetics, J Vis 2:531–542, 2002.
149. Grzimek VB: Versuche über das Farbsehen von Pflanzenesssern. 1. Das farbige Sehen (und die Sehscharfe) von Pferden, Z Tierpsychol 9:23–29, 1952.
150. Macuda T, Timney B: The spectral sensitivity of the horse, Invest Ophthalmol Vis Sci 39:S162, 1998.
151. Pick DF, Lovell G, Brown S, et al: Equine color perception revisited, Appl Anim Behav Sci 42:61–65, 1994.
152. Jacobs GH, Neitz J: Polymorphism of the middle wavelength cone in two species of South American monkey: *Cebus apella* and *Callicebus molach*, Vis Res 27:1263–1268, 1987.
153. Neitz J, Jacobs GH: Polymorphism of the long-wavelength cone in normal human color vision, Nature 323:623–625, 1986.
154. Neitz M, Neitz J: Molecular genetics of color vision and color vision defects, Arch Ophthalmol 118:691–700, 2000.
155. Yokoyama S, Radlwimmer FB: The molecular genetics of red and green color vision in mammals, Genetics 153:919–932, 1999.
156. Stockman A, Sharpe LT: Human cone spectral sensitivities: a progress report, Vis Res 38:3193–3206, 1998.
157. Curcio CA, Sloan KR, Kalina RE, et al: Human photoreceptor topography, J Comp Neurol 292:497–523, 1990.
158. Wikler KC, Rakic P: Distribution of photoreceptor subtypes in the retina of diurnal and nocturnal primates, J Neurosci 10:3390–3401, 1990.
159. Hurvich LM: Color vision, Sunderland, MA, 1981, Sinauer Associates.
160. Blackmore TL, Foster TM, Sumpter CE, et al: An investigation of colour discrimination with horses (*Equus caballus*), Behav Processes 78:387–396, 2008.
161. Hanggi EB, Ingersoll JF, Waggoner TL: Color vision in horses *(Equus caballus)*: deficiencies identified using a pseudoisochromatic plate test, J Comp Psychol 121:65–72, 2007.
162. Roth LS, Balkenius A, Kelber A: Colour perception in a dichromat, J Exp Biol 210:2795–2800, 2007.
163. Hall CA, Cassaday HJ: An investigation into the effect of floor colour on the behaviour of the horse, J Appl Anim Behav Sci 99:301–314, 2006.
164. Hall CA, Cassaday HJ, Vincent CJ, et al: Cone excitation ratios correlate with color discrimination performance in the horse (*Equus caballus*), J Comp Psychol 4:438–448, 2006.
165. Wachtler T, Dohrmann U, Hertel R: Modeling color percepts of dichromats, Vis Res 44:2843–2855, 2004.
166. Verhulst S, Maes FW: Scotopic vision in colour-blinds, Vis Res 38:3387–3390, 1998.
167. Morgan MJ, Adam A, Mollon JD: Dichromats detect colour-camouflaged objects that are not detected by trichromats, Proc R Soc Lond B Biol Sci 248:291–295, 1992.
168. Simunovic MP, Regan BC, Mollon JD: Is color vision deficiency an advantage under scotopic conditions? Invest Ophthalmol Vis Sci 42:3357–3364, 2001.
169. Ubbereiter O: Examination of the eye and eye operations in animals, Adv Vet Sci 5:1–80, 1959.
170. McMullen RJJ, Gilger BC: Keratometry, biometry and prediction of intraocular lens power in the equine eye, Vet Ophthalmol 2006; 9:357–360.
171. Townsend WM, Jacobi S, Petersen-Jones SM, et al: Phacoemulsification and implantation of a +14 diopter foldable intraocular lens in an adult horse, Vet Ophthalmol 10:407, 2007.
172. Dziezyc J, Millichamp NJ, Keller CB: Use of phacofragmentation for cataract removal in horses: 12 cases (1985–1989), J Am Vet Med Assoc 198:1774–1778, 1991.
173. Whitely RD, Moore CP, Slone DE: Cataract surgery in the horse: a review, Equine Vet J (Suppl 2):127–134, 1983.
174. Ramsey DT, Mutti DO, Zadnik K, et al: Refractive error in Rocky Mountain horses with corneal globosa and with normal corneas, Proc Am Coll Vet Ophthalmol 30:82, 1999.
175. Gilger BC, Davidson MG, Nadelstein B, et al: Neodymium:yttrium-aluminum-garnet laser treatment of cystic granula iridica in horses: eight cases (1988–1996), J Am Vet Med Assoc 211:341–343, 1997.
176. Shabana N, Cornilleau PV, Carkeet A, et al: Motion perception in glaucoma patients: a review, Surv Ophthalmol 48:92–106, 2003.
177. Hawkins AS, Szlyk JP, Ardickas Z, et al: Comparison of contrast sensitivity, visual acuity, and Humphrey visual field testing in patients with glaucoma, J Glaucoma 12:134–138, 2003.
178. Pearson P, Swanson WH, Fellman RL: Chromatic and achromatic defects in patients with progressing glaucoma, Vis Res 41:1215–1227, 2001.
179. Nelson P, Aspinall P, Papasouliotis O, et al: Quality of life in glaucoma and its relation to visual function, J Glaucoma 12:139–150, 2003.
180. Johnson CA, Sample PA, Cioffi GA, et al: Structure and function evaluation (SAFE). I. Criteria of glaucomatous visual field loss using standard automated perimetry (SAP) and short-wavelength automated perimetry (SWAP), Am J Ophthalmol 134:177–185, 2002.
181. Castelo-Branco M, Faria P, Forjaz, et al: Simultaneous comparison of relative damage to chromatic pathways in ocular hypertension and glaucoma: correlation with clinical measures, Invest Ophthalmol Vis Sci 45:499–505, 2004.
182. Drake MV: Glaucomatous visual field loss. In Albert DM, Jakobiec FA, editors: Principles and practice of ophthalmology, Philadelphia, 1994, WB Saunders.

183. Madigan JE, Kortz G, Murphy C, et al: Photic headshaking in the horse: 7 cases, Equine Vet J 27:306–311, 1995.
184. Wilkins PA: Cyproheptadine: medical treatment for photic head-shakers, Compend Contin Educ Pract Vet 19:98–111, 1997.
185. Rebhun WC, Loew ER, Riis RC, et al: Clinical manifestations of night blindness in the Appaloosa horse, Contin Educ Pract Vet 6:S103–S106, 1984.
186. Witzel DA, Riis RC, Rebhun WC, et al: Night blindness in the appaloosa: sibling occurrence, J Equine Med Surg 1:383–386, 1977.
187. Witzel DA, Smith EL, Wilson RD, et al: Congenital stationary night blindness: an animal model, Invest Ophthalmol Vis Sci 17:788–795, 1978.
188. Rebhun WC: Retinal and optic nerve diseases, Vet Clin North Am 8:587–608, 1992.

Chapter 12

Inherited Ocular Disorders

Simon M. Petersen-Jones
Susan Ewart

Hereditary eye diseases have been described in several breeds of horses (Table 12-1), but few have been studied in the same detail as similar disorders in other species such as humans, mice, and dogs. With the recent publication of the deoxyribonucleic acid (DNA) sequence of the equine genome[1] coupled with the existing linkage maps[2] and radiation hybrid maps,[3] the molecular tools are now in place to facilitate the investigation of equine genetic traits. Such research will lead to the identification of disease-causing gene mutations and development of DNA-based tests to screen for them. This chapter will cover some basic concepts about the genome and describe the steps that may be taken to further our understanding of hereditary eye disease.

THE EQUINE GENOME

The horse has 31 pairs of autosomal chromosomes plus two sex chromosomes. Every animal normally has two copies of each autosomal chromosome and two sex chromosomes (XX for females and XY for males), so the diploid number—the number of chromosomes in every cell nucleus, with the exception of the gametes—is 64.

GENES

Genes, which are sections of DNA that code for protein production, are positioned on the chromosomes. Because there are two copies of each autosomal chromosome, there are two copies of each section of DNA, including coding and noncoding sections. Each copy is known as an *allele*. The coding portions of the genes, known as *exons*, are interspersed by noncoding sections called *introns*. A messenger ribonucleic acid (mRNA) copy is made from the nuclear DNA to allow for the expression of a gene. The mRNA leaves the cell nucleus and is translated into amino acids within the protein-manufacturing machinery of the cytoplasm. As the mRNA is created, the noncoding introns are spliced out, resulting in an mRNA that is an uninterrupted code for protein production. Some noncoding portions of the DNA on the chromosomes are *promoters* for genes. Promoters control gene expression and respond to elements to increase or decrease expression. They also control factors such as tissue specificity of expression. Other noncoding regions that make up a large proportion of the genome have no known function.

The number of genes predicted to be present in the horse genome is about 20,000, which is similar to the estimates for other mammals, including humans. The majority of these genes are *orthologous*, meaning they are similar to genes in different species, having arisen in a common ancestor. Not only can genes be similar between species, but there is often similarity between genes within a species. Genes that have similar nucleotide structure are categorized into *families*. Members of a gene family may code for similar proteins or be expressed at different times during development, although in some instances, gene function is not similar within gene family members. Gene family expansion occurs within a species when a family of genes holds high evolutionary significance for that species. Several such interesting gene family expansions were noted by Wade et al. (2009) in the equine genome.[1] Along with the expansion of keratin family genes, predicted to be important for hoof development, was the gene family expansion related to vision. The opsin family of genes had more than twofold as many gene paralogs (or duplications) in horses as in humans, with 21 gene family members for photoreception in the horse, compared to nine in humans. This gene family expansion may relate to the importance of vision in prey species.

Table 12-1 | **Suspected Hereditary Eye Defects in Horses**

DEFECT	MODE OF INHERITANCE AND GENETIC BASIS	BREED(S)	REFERENCES
Entropion	Unknown—multifactorial likely	Thoroughbred	4
Multiple congenital ocular malformations syndrome (MCOA) likened to anterior segment dysgenesis; severity varies, posterior segment lesions also present	Semidominant; mapped to ECA6 in regions of *PMEL17* gene (mutation in gene causes silver coat color)	Rocky Mountain horse, Miniature horse, others (Mountain Pleasure horse, Kentucky Saddle horse)	5-10
Aniridia (associated with cataract and in some cases dermoids)	Autosomal dominant suggested	Belgian Draft horse, Thoroughbred, Quarter Horse	11-14
Congenital glaucoma (associated with anterior segment dysgenesis)	Unknown	Thoroughbred, Standardbred	15-17
Congenital nuclear cataract	Autosomal dominant	Morgan horse, Thoroughbred	18,19
Congenital cataract	Unknown	Belgian Draft horse, Thoroughbred, Quarter Horse	20,21
Congenital stationary night blindness (also abnormal head and eye position and microphthalmos)	Autosomal recessive; mapped to ECA1 to region of *TRPM1* gene	Appaloosa, Paso Fino	22-27
Optic nerve coloboma	Unknown	Quarter Horse	28
Retinal degeneration	Unknown	Thoroughbred predisposition	29

MEIOSIS AND LINKAGE DISEQUILIBRIUM

During the formation of gametes by meiosis, there is an exchange of material between the maternally and paternally derived chromosomes. After duplication of the DNA of the chromosomes to form two chromatids for each chromosome, the maternally derived and paternally derived copies of each chromosome are paired. There is then exchange of material (crossing over) between one chromatid of each chromosome and its pair (Fig. 12-1). When genes are on separate chromosomes, there is random assortment of genetic material during meiosis, as stated in Mendel's law of independent assortment (Mendel's second principle). Such genes are "unlinked." However, when two genes are close together on the same chromosome, they are more likely to remain together and not be separated during meiosis. Two such genes are described as being "linked" and are considered to be in linkage disequilibrium (LD). LD can be used to investigate how close together two linked genetic loci (for example, a gene or other DNA marker) on a chromosome are. The size of LD blocks in horses is reported to be greater than in humans and smaller than in dogs.[1] Linkage disequilibrium was similar across multiple horse breeds with the exception of the Thoroughbred, which had higher LD due to its history of a few founders and closed breeding structure. The closer two sections of DNA are on the chromosome, the less frequently they will become separated during meiosis.

The genetic distance separating loci is measured in centimorgans (cM). Two markers are 1 cM apart when they separate during meiosis (i.e., a recombination event between them occurs) at a frequency of 1%. Genetic distance in centimorgans does not directly relate to physical distances (measured in base pairs of DNA, usually kilobases or megabases), because the rate of crossover (recombination) between paired chromosomes during meiosis is not uniform along the length of the chromosome. It also differs between the sexes. In humans, on average, 1 cM is equivalent to about 1 megabasepair of DNA.

GENETIC VARIATION

Naturally occurring variations in DNA (or more accurately individual alleles) between individuals are found across the genome. Although a few of the variations are responsible for diseases (and are called *mutations*), and others account for the normal hereditary variability within the population, many others are in noncoding regions of DNA and have no apparent influence on phenotype. The polymorphisms in DNA that are used for mapping include microsatellites and single-nucleotide polymorphisms (SNPs, pronounced "snips") or other small variations in DNA such as insertions or deletions (indels) of short sections of DNA. These variations in DNA are inherited in a simple mendelian fashion and are spread across the genome. Microsatellites are regions of DNA where typically two or more nucleotides are repeated several times (Fig. 12-2). The number of repeats is variable (polymorphic). This variation in number of repeats is stable and inherited in a mendelian fashion. Dinucleotide (two base pair) repeats are most commonly used for mapping purposes, although trinucleotide and tetranucleotide repeats are also used. More than two versions (alleles) of a microsatellite can be found within a population. However, because each animal has two of each autosomal chromosome (one paternally derived and the other maternally derived), each animal will have two copies of each autosomal microsatellite. For example, for one particular microsatellite, one animal may have one copy (allele) with 20 repeats and another copy with 19 repeats. Offspring from that animal will receive one of those alleles (i.e., either the 19-repeat allele or the 20-repeat allele); the other allele will derive from the other parent. Ascertainment of which versions of a microsatellite an animal has requires the use of polymerase chain reaction (PCR) to amplify that particular microsatellite. Each microsatellite has a unique DNA sequence that flanks it, and primers for PCR are designed from that unique DNA sequence, allowing the amplification of only the portion of DNA of interest. The amplified microsatellite is then subjected to electrophoresis to ascertain the size of the two alleles (which is dependent on the number of repeats) the animal being tested has.

SNPs (Fig. 12-3) are variations at a single nucleotide, and typically only two versions of each SNP exist in the population. This means they are less powerful for mapping than microsatellites, which often have more than two alleles in a population. The advantage of SNPs is that they occur very frequently across

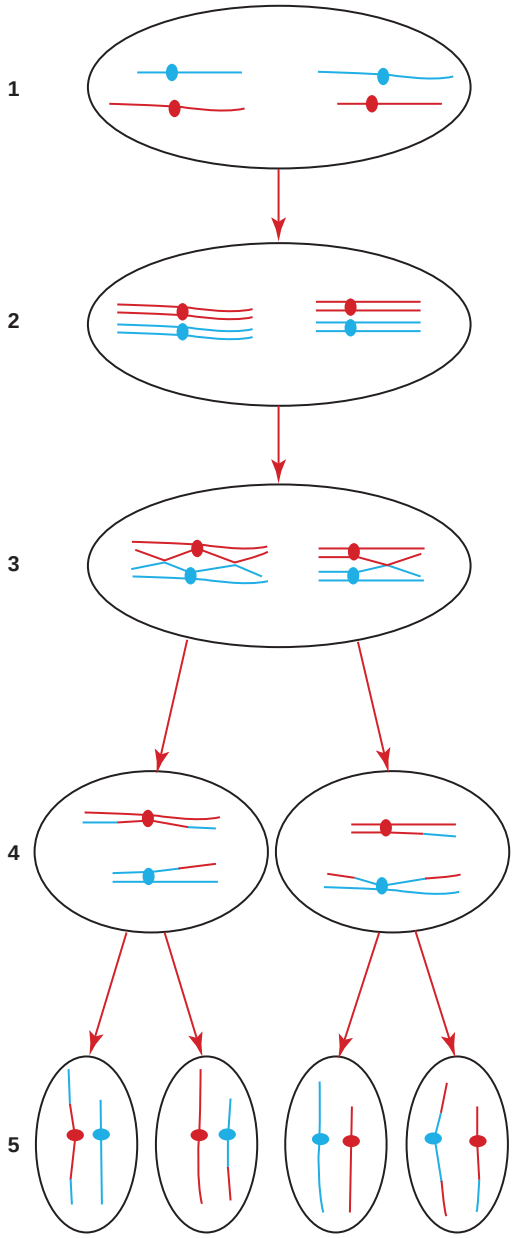


Figure 12-1. In this diagram of meiosis in the male, the cell has two pairs of chromosomes. Maternally derived chromosomes are red, and paternally derived ones are blue. *1,* Cell with a diploid (2n) number of chromosomes (n). Each chromosome has one chromatid. The cell is 2n, 2c. *2,* Maternally and paternally derived versions of each chromosome pair together. DNA replications have occurred, duplicating each chromatid. The cell is now 2n, 4c. *3,* Crossover between one chromatid of each pair of chromosomes is occurring. One chromosome pair has two crossover points, and the other has one crossover point. *4,* The cell divides (meiosis I—reductive division) to produce two cells, each containing one copy of each chromosome, with each copy having two chromatids (1n, 2c). Note the exchanged chromosomal material between maternally and paternally derived chromosomes. *5,* Meiosis II, the final division to produce the gametes. Each gamete has one copy of each chromosome, and each chromosome has one chromatid (1n, 1c). Note the recombination of material within the chromosomes in comparison with the paternally and maternally derived chromosomes.

the genome. Sequence analysis of 11 common horse breed sets, as well as a set of individuals representing 24 other breeds and equids (donkey and Przewalskii horse), has identified over 1.1 million SNPs in the equine genome, at an average frequency of 1 SNP per 2000 basepairs.[1] These variants will be useful for mapping traits within and between horse breeds.

There are several methods of genotyping an individual animal for an SNP or establishing which version(s) of the SNP are present. The EquineSNP50 Genotyping BeadChip, available from Illumina Inc. (San Diego, CA), contains over 54,000 evenly spaced SNPs derived from the EquCab2.0 sequence assembly. Utilizing this technology allows for the simultaneous genotyping of all 54,000 SNPs. It can be used for whole-genome screening to allow mapping of genetic disease, but a more dense array of at least 100,000 SNPs will be required for comprehensive genome-wide association analyses (see later). Methods of genotyping individual SNPs include using techniques such as DNA sequencing, restriction length polymorphism analysis, denaturing high-performance liquid chromatography (HPLC), and fluorogenic 5′ nuclease (TaqMan) assays.[30-32]

GENOME SEQUENCE

The genomes of several species, including the horse, have now been sequenced (see http://www.ncbi.nlm.nih.gov/Genomes/index.html for updated information). *Sequencing* a genome is the determination of the exact order of all nucleotides for every chromosome in the species being sequenced. While there is extensive similarity in the DNA sequence between species, there is much to be gained by having a precise and detailed blueprint for the species of interest. The Horse Genome Project began in 1995 as an international collaboration with the intent of defining the DNA sequence of domestic horses. The resultant recently reported equine genome sequence is a tremendous tool that will assist researchers to more efficiently uncover the genetic basis of heritable conditions in horses.[1] Wade et al. (2009) sequenced the DNA of a thoroughbred mare with 6.8× coverage.[1] *Coverage* is an indication of sequencing redundancy, which is important to ensure accurate capture of the nucleotide data. An average coverage of 6.8× means that the chance of each segment of DNA being "read" at least 4 times is about 90%. This was a massive undertaking; it required 2.88 × 10^7 separate sequence reads to achieve this coverage. The human genome sequencing project provides an estimated 8× to 9× coverage of each chromosome. The size of the equine genome is estimated to be between 2.5 to 2.7 gigabasepairs (Gb), which is intermediate to the size of the human and bovine genomes (2.9 Gb) and the canine genome (2.5 Gb).

INVESTIGATION OF HEREDITARY EYE DISEASE

CHARACTERIZATION OF THE DISEASE PHENOTYPE

The first stage in the investigation of a suspected hereditary eye disease is a thorough and accurate description of the phenotype. The animal in which the disease state is first identified is called the *proband*. The proband and related animals, including unaffected animals, should be examined and monitored over time to establish the range of ages at onset and rate of progression

Figure 12-2. Diagram of a microsatellite. In this theoretical example, there are 14 CA repeats (shown in red). Note that the DNA sequence flanking either side of the microsatellite is unique, and polymerase chain reaction primers may be designed from the region to amplify the microsatellite.

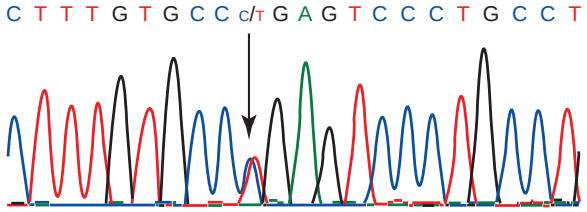


Figure 12-3. DNA sequencing chromogram showing a single nucleotide polymorphism (SNP). This example is the result of direct sequencing of a polymerase chain reaction (PCR) product. The animal from which this DNA was amplified is heterozygous for the SNP *(arrow)*. Each colored peak represents one of the four bases that makes up DNA (*A*, adenine; *C*, cytosine; *G*, guanine; and *T*, thymine). An arrow indicates the position of the SNP. One allele of this animal has a C at this position; the other alleles have a T there. The PCR product is an equal mix of the amplification of both alleles.

of the disease. There can be considerable variation in phenotype between individual animals with disease caused by the same gene mutation. This variability can be due to environmental influences or background genetic variations. Such variation can affect severity of disease, age at onset, and rate of progression. An extreme example of this variability is incomplete penetrance, whereby the genetic feature is not expressed in some individuals but is expressed in others. The percentage of genetically affected animals that express the phenotype gives the percentage penetrance. Phenotype variability and incomplete penetrance can complicate the investigation of a genetic trait and attempts to establish a mode of inheritance. Misdiagnosis and the occurrence of phenocopies can also confound attempts to investigate hereditary diseases. Phenocopies are animals with an environmentally induced disease that mimics a known hereditary disease.

As an accurate description of a disease phenotype is established and related animals are screened for the presence of the disease, a family tree (pedigree) displaying the disease status can be created. Ideally, this should span two or more generations and include several related animals. With a sufficiently extensive pedigree and accurate phenotyping, it may be possible to prove the mode of inheritance of the disease. For an equine ophthalmic example of pedigree analysis, see the article by Ewart et al.[9]

ESTABLISHING A MODE OF INHERITANCE

Although analysis of a pedigree to establish a mode of inheritance may seem straightforward, in practice it is not always possible to conclusively prove the mode of inheritance. The features of each particular mode of inheritance are described in the following sections.

AUTOSOMAL RECESSIVE

In autosomal recessive inheritance, the causal gene mutation lies on an autosome. Both alleles must be mutant for the disease phenotype to be expressed. Animals with one diseased and one normal allele (heterozygous for the mutation) do not express the disease phenotype and are described as *carriers*. When the incidence of carriers is low in a population, the odds of two carriers being mated are low. The offspring from a mating between two heterozygous animals have a one in four chance of being homozygous for the mutation and thus expressing the disease phenotype. Because carriers of autosomal recessive traits are phenotypically normal, the disease tends to skip generations (unless the mutant allele becomes very common in the population), and each occurrence of the disease may appear to be an isolated case. Eradication of autosomal recessive traits from a population is difficult because of the occurrence of phenotypically normal heterozygous carriers. Test mating with a known affected animal can be used to identify carriers, but in horses this is not usually a practical proposition. Once the genetic mutation that underlies the defect is identified, a DNA-based test can be developed and used to identify carrier animals.

AUTOSOMAL DOMINANT

In autosomal dominant inheritance, the causal genetic mutation lies on an autosome. The presence of one copy of the mutant allele causes the disease phenotype. On average, 50% of the offspring from a cross between a healthy animal and an affected animal will have the disease. In contrast to the autosomal recessive mode of inheritance, the disease does not skip generations unless the trait is less than 100% penetrant. As described previously, incomplete penetrance is said to occur when less than 100% of individuals with the mutant allele have the disease trait.

X-LINKED RECESSIVE

In X-linked recessive inheritance, the causal gene mutation lies on the X chromosome. The disease is primarily expressed in male animals that inherit an X chromosome with the mutant gene from their dams. In the event that both X chromosomes of a female animal have the mutant allele, that female will have the disease. This would be very uncommon unless the mutant allele occurred at a high frequency in the population. All female offspring from an affected male will be carriers of the mutant allele. Male offspring from a carrier female crossed with a healthy male will have a 50% chance of being affected, and the female offspring will have a 50% chance of being carriers.

X-LINKED DOMINANT

In X-linked dominant inheritance, the causal gene mutation lies on the X chromosome. This is a less common form of inheritance than the previously described forms. Both males and females are affected. The male offspring of an affected male will never be affected (unless the dam is affected). Female offspring of affected males will always be affected. Both male

and female offspring of an affected female will have a 50% chance of being affected (unless the affected female is homozygous for the mutant allele, but this would be uncommon). Heterozygous females may have a less severe phenotype than males or homozygous affected females. This is because in each cell, only one of the X chromosomes is active; the other is inactivated and can be seen as the Barr body. The process by which one X chromosome is inactivated is called *random X chromosome inactivation* and occurs during embryonic development. Once one X chromosome is inactivated in a cell, all daughter cells from that cell will have the same X chromosome inactivated. Because this process occurs during embryonic development, the result is that patches of tissues (derived from the same parental cell) will have the same X chromosome inactivated. This explains why heterozygous females can have a less severe manifestation of an X-linked dominant trait than males.

MITOCHONDRIAL INHERITANCE

Mitochondria within eukaryotic cells contain their own genomes. It is hypothesized that mitochondria arose from aerobic bacteria that were engulfed by evolving eukaryotes. Mitochondria are only transmitted in the ova, not in the sperm, so each animal inherits mitochondria from the dam only. Diseases resulting from defects in mitochondrial DNA are therefore maternally inherited.

METHODS OF IDENTIFYING DISEASE-CAUSING GENETIC MUTATIONS

The ultimate aim is to identify the actual genetic mutation that causes the disease under investigation so that a DNA-based test can be developed to help eradicate the condition. One approach is to use linkage mapping to identify the approximate chromosomal location of the disease locus. Then with knowledge of the positions of genes across the genome, genes that are present on that part of the chromosome can be investigated to determine whether they are mutated in affected animals.

An alternative to the linkage approach is the *candidate gene approach,* which can be successful if there is very strong evidence from detailed investigations of the phenotype and comparisons with very similar conditions in other species suggesting that the causal mutation may lie in one of a few *candidate genes*. This approach can be used if insufficient DNA samples have been collected for the mapping approach.

LINKAGE MAPPING OF A GENETIC DEFECT

Identification (i.e., mapping) of the chromosomal location of any given trait requires a minimum set of polymorphic DNA markers spread across the genome. Microsatellites have been widely used in mapping of disease loci. However, SNPs are now being used more commonly, and as a result of the sequencing of the equine genome (see earlier), an equine genotyping BeadChip is available to allow genotyping of over 54,000 SNPs spread across the equine genome.

For the purpose of mapping the disease locus, DNA samples should be available from several members of families in which the disease is segregating, and different generations should be included so there are sufficient meioses within the sample pool. It is very helpful but not essential if the mode of inheritance has been established.

Animals within the pedigree are typed for the polymorphic markers, and a computer program is used to apply a statistical analysis to calculate the probability that each particular marker is linked to the disease locus. The degree of linkage is the LOD (logarithm of the odds) score. Linkage between loci is considered significant when the LOD score is greater than 3. A LOD score of 3 or greater means that the odds are 1000 to 1, or better, in favor of linkage. Such stringent odds (compared with the typical P value of <0.05 selected to indicate significance in most biological statistical analyses) are used because with multiple testing of many markers, the false-positive rate is increased. Once a marker that appears to be linked to the disease locus (i.e., has a high LOD score) is found, then flanking markers are investigated until recombinations are found between linked markers and the disease mutation. The chromosomal region adjacent to the disease-causing mutation site will be identical between disease-affected alleles; this is called *identity by descent* because all affected animals are descended from the founder animal in which the mutation arose. The number of meioses within the pedigree since the occurrence of the mutation is important. The greater the number of meioses, the easier it should be to narrow the confidence interval (the interval in which the disease mutation must lie). Once the disease locus is mapped, further investigations must be undertaken to identify the actual gene containing the disease-causing mutation. This can be a considerable amount of work because in many instances, the confidence interval will remain quite large. Examination of the annotated equine genome sequence, along with comparison of the homologous regions in other species, will allow the development of a list of known genes that are present within the estimated confidence interval. Genes within the confidence interval are described as *positional candidate genes* for the disease under investigation. Consideration of the known function of those genes may suggest that one or more of the genes are particularly good potential candidates for causing the disease. For example, if a retinal disease is being considered, genes within the mapped region that are known to play an important role in retinal function are likely to be good candidates to investigate first. Screening of positional candidate genes to identify the disease-causing mutation may initially consist of sequencing of the coding region of the gene. However, the possibility that a mutation causing the disease is present within a noncoding portion of the gene (e.g., the promoter within introns) should also be considered.

CANDIDATE GENE APPROACH TO IDENTIFY THE MUTATED GENE

A candidate gene approach uses information from the description of the disease phenotype to make an educated guess as to which genes, if mutated, could be responsible. Knowledge of the gene defects that cause very similar diseases in other species can be very helpful when potential candidate genes are selected. Examples in which this approach has been successful include hereditary diseases in which biochemical investigations indicate a failure of a particular biochemical pathway, providing strong evidence that the disease mutation is likely to lie in one of a small number of genes. In contrast, some phenotypically similar eye diseases, such as the progressive retinal

degenerations (e.g., progressive retinal atrophy in dogs, retinitis pigmentosa in humans), have exceptional genetic heterogeneity; that is, similar diseases can be caused by mutations in one of many different genes. This obviously complicates a candidate gene approach.

Once the candidate genes have been selected, the initial step is to determine whether they are linked to the disease locus. Polymorphic markers within or very close to the genes are selected. These can be known markers such as microsatellites or SNPs identified during the sequencing of the equine genome. Once a polymorphic marker(s) is identified within the gene, it can be used to determine whether the gene locus is linked to disease status by genotyping the animals within the pedigree and determining whether the presence of one allele of the marker co-segregates with the mutant allele. If the mode of disease inheritance is known, such studies are easier. For example, for autosomal recessive diseases, the affected animals will be homozygous for the same markers along the chromosome adjacent to the mutation. If the mode of inheritance is unknown, it must be assumed that the disease being investigated has the requirement for the presence of one allele with a particular DNA variation at one major locus. If the study suggests that a candidate gene locus is likely to be associated with the disease under investigation, that gene can be screened in detail for possible disease-causing mutations. This usually involves initially sequencing the exons and junctions between introns and exons. If no likely mutations are found, it is possible that the disease-causing mutation might lie in an adjacent gene (depending on the width of the region that is identical by descent) or within an important but noncoding region of the gene such as a promoter. A candidate gene can be excluded with some certainty if different affected animals are homozygous for different alleles of the marker within or very close to the candidate gene. When such investigations are carried out, the possibility that misdiagnosis of disease status could have been made in one or more animals within the study should also be considered.

ASSOCIATION MAPPING

Complex traits with a genetic basis may result from contributions from several genetic loci as well as a combination of interactions with environmental factors. Attempts to identify the loci that predispose to complex traits require a population study and utilize association mapping. Put simply, comparison of markers between diseased animals (cases) and healthy animals (controls) is made, and an analysis is performed to identify loci that are "associated" with the presence of the disease. This utilizes linkage disequilibrium to track inheritance patterns through the examination of *haplotypes*, which are regions of linked variants. Specifically, haplotypes are the set of DNA sequence variants that are present on a length of a single chromosome. As all nucleated cells have two copies of each chromosome (except gametes), so do all such cells have two copies of each haplotype. An individual may inherit the same haplotype from each parent, or they may have received different haplotypes from each parent, giving them two distinct haplotypes at any given chromosomal location. Haplotypes can be described in terms as short as tens of nucleotides (bases) or as large as tens of thousands of nucleotides. Typically, one or two haplotypes occur commonly in a given chromosomal region making up more than half of the genetic variation present in that region, while the less common haplotypes occur at frequencies of less than 10% to 20%. Because haplotypes generally describe a contiguous stretch of DNA, the variants within a haplotype tend to be inherited together because of their close physical proximity. Thus, haplotype analysis utilizes local LD structure within a chromosomal region to assess genetic associations. Linkage disequilibrium through a haplotype region can be used to increase the efficiency of genotyping, because the genotyped variants in one location can be used to predict or "infer" the genetic variation in a linked location. Similarly, a subset of all variants within a haplotype can be used to "tag" that haplotype and thus reduce the amount of direct genotyping required to assess a chromosomal region. If a haplotype or genotype occurs more commonly in the group of diseased animals compared to well-matched non-diseased animals, then it is considered to be a risk for that disease. Alternatively, if a haplotype or genotype is more common in control animals, it is said to be protective against that disease. The most common finding is of course no association, in which case there is no difference in the frequency the haplotype or genotype occurs in cases and controls. Based on the LD structure in horses and the number of haplotypes within haplotype blocks, it is predicted that at least 100,000 variants need to be analyzed to detect genetic association on a genome-wide scale. However, the current SNP array consists of only 54,000 SNPs.

DNA TESTS FOR GENETIC DISEASE

Once a disease-causing mutation or a very closely linked marker has been identified, a DNA-based diagnostic test for the disease can be developed.

MUTATION DETECTION TESTS

The gold standard DNA-based test is the mutation detection test, which identifies the actual gene mutation. Once the mutation is identified, development of a test to identify the presence of the mutation is generally straightforward. So long as the necessary controls are built into the test protocol and followed, such a test will be 100% accurate and 100% specific. There are several methods of genotyping an animal for a known gene mutation:

- Sequencing of a PCR-amplified portion of the gene that includes the mutation site
- Use of a PCR-restriction enzyme digest test (Fig. 12-4) to show the presence or absence of the mutant allele

Some mutations may introduce or remove a cutting site for an enzyme called a *restriction enzyme*. These enzymes only cut (digest) DNA at sites where a certain sequence of base pairs occurs and not at other sites. If a restriction enzyme cutting site is introduced or removed by the mutation, this can be used to indicate the presence or absence of the mutation. If there is no naturally occurring difference in restriction enzyme cutting between the normal and mutant alleles, one can be engineered by designing a PCR primer that has a mismatch to the actual DNA sequence. Such a primer can still work to prime the PCR, but the products will contain the altered sequence dictated by the primer and therefore the introduced sequence. This altered sequence, in combination with the sequence from the normal and mutant alleles, will lead to a difference in restriction enzyme cutting between normal and mutant alleles. Whether the PCR product is cut by the restriction enzyme can be

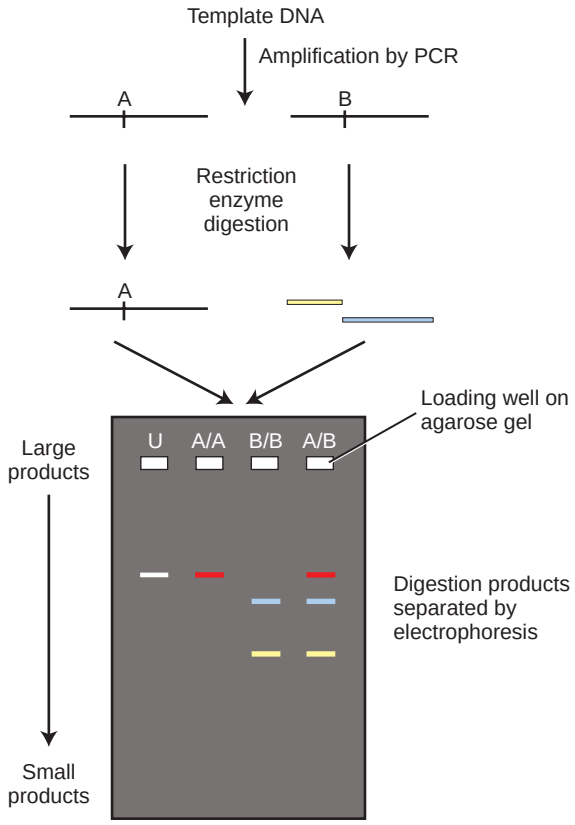


Figure 12-4. Diagram of a polymerase chain reaction–restriction enzyme (PCR-RE) mutation detection test. This example shows amplification of a section of DNA that has two alleles. The position of the single-nucleotide polymorphism (SNP) is marked with *A* and *B*. The allele with the *B* version is cut with the restriction enzyme that with the *B* version is not cut. The initial step is to amplify the DNA of interest by PCR. The resulting products are digested with the restriction enzyme and then size-separated by gel electrophoresis. Key for gel: *U*, PCR product that has not been digested (to show size of uncut product for comparison); *A/A*, result from PCR product from an animal homozygous for the A allele; *B/B*, result from PCR product from an animal homozygous for the B allele; *A/B*, result from PCR product from an animal heterozygous for this allele. Note that the digested DNA and bands on the gel are color-coded for clarity.

demonstrated by separating the products on an agarose gel (see Fig. 12-4). For an example of such an assay, see the study by Petersen-Jones and Entz.[33] Several alternative assays can be used to detect the sequence difference between the mutant and normal alleles; examples include direct sequencing and fluorogenic 5′ nuclease (TaqMan) assays.

GENETIC LINKAGE TESTS

A second form of DNA-based test is the linked marker test, which can be developed once a polymorphic marker that is very closely linked to the mutation site has been identified. A good marker for a genetic test should be very closely linked to the disease locus, and ideally, the version of the marker that segregates with the diseased gene should be uncommon among those animals that do not have the disease-causing mutation. If the version of the marker associated with the disease-causing mutation is common in the healthy (normal) population, this will limit its value for use in a discriminatory diagnostic test. Fig. 12-5 shows the reasons for the limitation with this type of test. Animals homozygous for the version of the marker that is not found with the mutation are highly likely to be homozygous normal for the disease-causing mutation (unless a recombination between marker and disease-causing mutation occurs). One problem with linkage-based tests is explaining their inherent shortcomings to breeders and owners. Another problem is that if the marker and mutation site are not very closely linked, a crossover between the marker and the mutation could occur during meiosis, which would mean that in the animals that inherited the recombinant allele, a different version of the marker would be linked to the disease mutation.

RECENT ADVANCES IN EQUINE GENOME AND HEREDITARY EYE DISEASE

CONGENITAL STATIONARY NIGHT BLINDNESS

The coinheritance of leopard spotting and congenital stationary night blindness in Appaloosa horses has long been established, and the details of the genetic mechanism of these phenotypes are now being unveiled. The leopard-spotting color pattern was mapped by linkage analysis to a 6-cM region of ECA1.[34] A positional candidate gene in this region, transient receptor potential cation channel subfamily M, member 1 *[TRPM1]* (also known as *melostatin 1 [MLSN1]*), was found to be differentially expressed in retinas. In affected horses, retinal expression of *TRPM1* was only 0.05% of the level observed in unaffected horses, and its expression was downregulated to a lesser extent in horses heterozygous for leopard spotting.[27] Wade et al. report a 173-kb haplotype on ECA1 that contained *TRPM1* and was strongly associated with leopard spotting and congenital stationary night blindness.[1] Functional analysis of variants in this haplotype that lie within conserved elements may soon reveal the causative mutation for these phenotypes.

MULTIPLE CONGENITAL OCULAR ANOMALIES SYNDROME

Other coat color and ocular disease relationships have been observed in horses. The silver coat color is a dilution of eumelanin and is common in the Rocky Mountain horse, the breed in which the autosomal dominant multiple congenital ocular malformations (MCOA) phenotype (previously called *anterior segment dysgenesis*) was originally described.[5,7] A linkage analysis followed by targeted sequencing identified a missense mutation in the *PMEL17* gene on ECA6 as the cause of silver coat coloration.[35] A separate linkage analysis mapped the MCOA locus to a small region on ECA6 containing *PMEL17* and several nearby genes.[9] The *PMEL17* missense mutation does not cause ocular phenotypes in all breeds in which it is found, so further analyses, such as comprehensive sequencing through the linked region, are required to establish the MCOA causative mutation.

THE FUTURE

Until now, the literature has a relative paucity of detailed investigations of possible hereditary eye diseases in horses. There are several case reports of horses with conditions known to have a hereditary basis in other species, as well as reports of other conditions that are likely to have a hereditary component

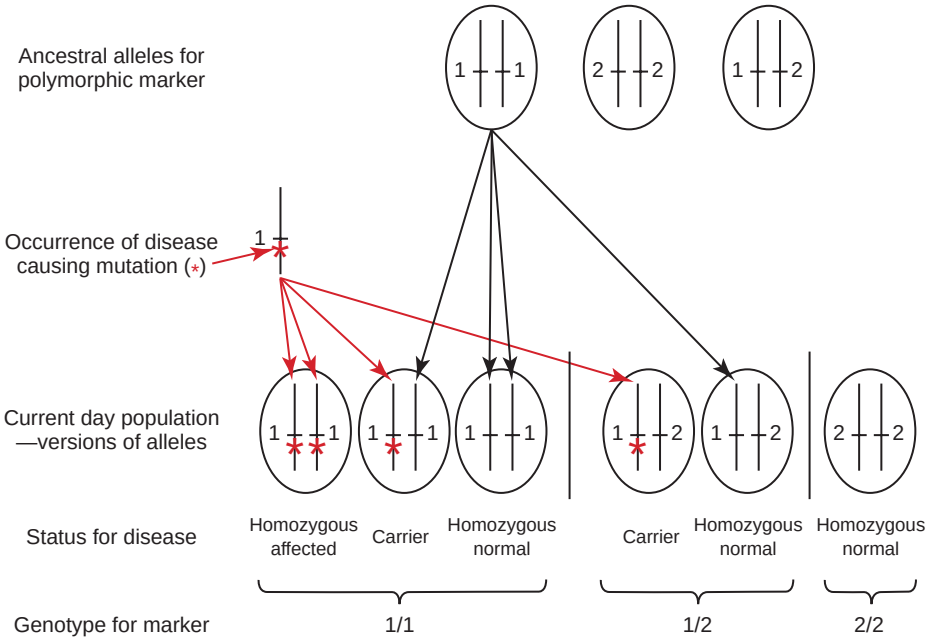


Figure 12-5. Linkage test. Diagram shows why a linkage test does not divide animals into groups by disease status; example is for an autosomal recessive disease. This shows one chromosome with a polymorphic marker that has two alleles (1 or 2). The polymorphism predates the occurrence of the disease-causing mutation. In one animal, a mutation arises in a gene very closely linked to the polymorphic marker. All animals that inherit the diseased allele will also have version 1 of the marker because the mutation arose in a single animal, and all those with the mutant allele inherited it from the founder animal (assuming there are no recombinations between mutation and marker). In the current population, there are animals who inherited version 1 of the marker with a normal copy of the gene that is mutated in the disease (color-coded arrows indicate whether allele 1 was inherited from the founder animal or whether they inherited an ancestral copy of the polymorphism without the mutation). The polymorphism can be used as a linkage-based test. Note that only the disease status of animals with a 2/2 genotype for the marker can be deduced with certainty (again assuming no recombinations between marker and mutation). The frequency of the allele with marker version 1 and no disease mutation in the population will influence how likely it is that an animal that is 1/1 for the marker is homozygous affected for the disease mutation.

but could be multifactorial, either being complex genetic traits or being the result of a combination of environmental influence and genetic predisposition. As understanding of the genome increases, the distinction between strictly genetic disease and strictly environmentally induced disease is blurred. The following are examples of this:

- An animal's genotype influences disease susceptibility. Certain conditions are more common in certain breeds, suggesting a genetic predisposition (e.g., anterior uveitis in the Appaloosa, ocular squamous cell carcinoma in Draft breeds). Furthermore, conditions that might appear to be purely environmental, such as bacterial infections, are influenced by genetic factors (e.g., resistance to bacterial infection has a genetic basis).
- The expression of a genetic disease can be influenced by background genetics (other gene loci that influence expression of the disease locus) and by environmental factors.

Table 12-1 lists some of the ocular conditions with evidence of a strong genetic component. The tools for accurately examining traits of interest in the equine genome have rapidly improved, and the equine genome has been sequenced. Because of these technical advances, the scientific community is now poised to not only identify the DNA changes that underlie traits inherited in a simple mendelian fashion but also more complex traits, such as diseases with polygenic inheritance or reasons for differences in performance and behavior.

References

1. Wade CM, Giulotto E, Sigurdsson S, et al: Genome sequence, comparative analysis, and population genetics of the domestic horse, Science 326:865–867, 2009.
2. Guerin G, Bailey E, Bernoco D, et al: The second generation of the International Equine Gene Mapping Workshop half-sibling linkage map, Anim Genet 34:161–168, 2003.
3. Chowdhary BP, Raudsepp T, Honeycutt D, et al: Construction of a 5000(rad) whole-genome radiation hybrid panel in the horse and generation of a comprehensive and comparative map for ECA11, Mamm Genome 13:89–94, 2002.
4. Roberts SM: Congenital ocular anomalies, Vet Clin North Am Equine Pract 8:459–478, 1992.
5. Ewart SL, Ramsey DT, Xu J, Meyers D: The horse homolog of congenital aniridia conforms to codominant inheritance, J Hered 91:93–98, 2000.
6. Ramsey DT, Ewart SL, Render JA, Latimer CA, et al: Anterior segment dysgenesis of Rocky Mountain horses, Proc Am Coll Vet Ophthalmol 27:46–48, 1996.
7. Ramsey DT, Ewart SL, Render JA, Cook CS, et al: Congenital ocular abnormalities of Rocky Mountain horses, Vet Ophthalmol 2:47–59, 1999.

8. Ramsey DT, Hauptman JG, Petersen-Jones SM: Corneal thickness, intraocular pressure, and optical corneal diameter in Rocky Mountain horses with cornea globosa or normal corneas, Am J Vet Res 60:1317–1321, 1999.
9. Andersson LS, Juras R, Ramsey DT, et al: Equine multiple congenital ocular anomalies maps to a 4.9 megabase interval on horse chromosome 6, BMC Genet 9:88, 2008.
10. Grahn BH, Pinard C, Archer S, Bellone R, et al: Congenital ocular anomalies in purebred and crossbred Rocky and Kentucky Mountain horses in Canada, Can Vet J 49:675–681, 2008.
11. Ueda Y: Aniridia in a thoroughbred horse, Equine Vet J Suppl 29, 1990.
12. Joyce JR, Martin JE, Storts RW, Skow L: Iris hypoplasia (aniridia) accompanied by limbic dermoids and cataracts in a group of related Quarterhorses, Equine Vet J (suppl) 10:26–28, 1990.
13. Ericksson K: Hereditary aniridia with secondary cataract in horses, Nord Vet Med 7:773–793, 1955.
14. Joyce JR: Aniridia in a Quarterhorse, Equine Vet J 15:21–22, 1983.
15. Marrion RM, Grahn BH, Sorden SD, Collier LL: Congential equine glaucoma: clinical and light microscopic findings in two cases, Vet Comp Ophthalmol 7:105–109, 1997.
16. Gelatt KN: Glaucoma and lens luxation in a foal, Vet Med Small Anim Clin 68:261, 1973.
17. Barnett KC, Cottrell BD, Paterson BW, Ricketts SW: Buphthalmos in a Thoroughbred foal, Equine Vet J 20:132–135, 1988.
18. Beech J, Irby N: Inherited nuclear cataracts in the Morgan horse, J Hered 76:371–372, 1985.
19. Beech J, Aguirre G, Gross S: Congenital nuclear cataracts in the Morgan horse, J Am Vet Med Assoc 184:1363–1365, 1984.
20. Huston R, Saperstein G, Leipold HW: Congenital defects of foals, J Equine Med Surg 1:146–161, 1977.
21. Gelatt KN: Congenital and acquired ophthalmic disease in the foal, Anim Eye Res 1–2:15–27, 1993.
22. Witzel DA, Smith EL, Wilson RD, Aguirre GD: Congenital stationary night blindness: an animal model, Invest Ophthalmol Vis Sci 17:788–795, 1978.
23. Joyce JR, Witzel DA: Equine night blindness, J Am Vet Med Assoc 170:878, 880, 1977.
24. Brooks DE: Equine Ophthalmology. In Gelatt KN, editor: Veterinary ophthalmology, ed 3, Philadelphia, 1999, Lippincott, Williams and Wilkins, pp 1053–1116.
25. Witzel DA, Riis RC, Rebhun WC, Hillman RB: Night blindness in the Appaloosa: sibling occurrence, J Equine Med Surg 1:383–386, 1977.
26. Rebhun WC, Loew ER, Riis RC, Laratta LJ: Clinical manifestations of night blindness in the appaloosa horse, Compend Contin Educ Vet 6:S103–S106, 1984.
27. Bellone RR, Brooks SA, Sandmeyer L, et al: Differential gene expression of *TRPM1*, the potential cause of congenital stationary night blindness and coat spotting patterns (LP) in the Appaloosa horse *(Equus caballus)*, Genetics 179:1861–1870, 2008.
28. Wheeler CA, Collier LL: Bilateral colobomas involving the optic discs in a quarterhorse, Equine Vet J Suppl 39–41, 1990.
29. Cutler TJ, Brooks DE, Andrew SE, et al: Disease of the equine posterior segment, Vet Ophthalmol 3:73–82, 2000.
30. Giordano M, Oefner PJ, Underhill PA, et al: Identification by denaturing high-performance liquid chromatography of numerous polymorphisms in a candidate region for multiple sclerosis susceptibility, Genomics 56:247-253, 1999.
31. Underhill PA, Jin L, Lin AA, et al: Detection of numerous Y chromosome biallelic polymorphisms by denaturing high-performance liquid chromatography, Genome Res 7:996-1005, 1997.
32. Livak KJ: Allelic discrimination using fluorogenic probes and the 5′nuclease Assay, Genet Anal 14:143-149, 1999.
33. Petersen-Jones SM, Entz DD: An improved DNA-based test for detection of the codon 616 mutation in the alpha cyclic GMP phosphodiesteraseg ene that causes progressive retinal atrophy in the Cardigan Welsh Corgi, Vet Ophthalmol 5:103-110, 2002.
34. Terry RB, Archer S, Brooks S, Bernoco D, et al: Assignment of the Appaloosa coat colour gene (LP) to equine chromosome 1, Anim Genet 35:134–137, 2004.
35. Brunberg E, Andersson L, Cothran G, Sandberg K, et al: A missense mutation in *PMEL17* is associated with the silver coat color in the horse, BMC Genet 7:46, 2006.

Additional Reading and Resources

http://www.ncbi.nlm.nih.gov/—National Center for Biotechnology Information website. This website provides access to several areas for publications, information on DNA, proteins, and disease databases including the following:
http://www.ncbi.nlm.nih.gov/Genomes/index.html—National Center for Biotechnology Information website for genomes
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=OMIM—Online Mendelian Inheritance in Man, a database of human genes and genetic disorders
http://genome.ucsc.edu/index.html—USCS Genome Bioinformatics (select Genome Browser for horse)
http://www.ornl.gov/sci/techresources/Human_Genome/home.shtml—Human Genome Project Information
http://www.jcvi.org/—The J. Craig Venter Institute web page
http://www.agbase.msstate.edu/—AgBase web page

Equine Genome
http://www.equinegenome.org/Equinegenome.org.html
http://www.nifa.usda.gov/nea/animals/sri/an_breeding_sri_equine.html
http://www.uky.edu/Ag/Horsemap/
http://www.ex.ac.uk/equinet/
http://www.vgl.ucdavis.edu/services/horse.php
http://www.thearkdb.org
http://www.fungen.org/Projects/Horse/Equus%20Project.htm

Chapter 13

Ocular Manifestations of Systemic Disease

Jennifer L. Davis

The ocular examination is greatly underused in the diagnosis of systemic diseases in horses. Ocular clinical signs may provide the practitioner with a shorter list of differential diagnoses and a prognosis. Numerous systemic diseases cause ocular changes in horses. This chapter has two purposes: (1) to allow the equine practitioner to become more aware of the changes that can occur in the eye and be able to use them as diagnostic aids and (2) to enable the veterinary ophthalmologist to recognize the systemic diseases associated with some ocular diseases in the horse.

NEURO-OPHTHALMIC DISEASES

EQUINE PROTOZOAL MYELOENCEPHALITIS

To date, there are no reported visual deficits associated with equine protozoal myeloencephalitis (EPM, *Sarcocystis neurona*), although cerebral lesions could result in blindness.[1] No fundic lesions were seen in an extensive unpublished evaluation of EPM cases (M. Willis, personal communication, 2003). However, if EPM affects the brainstem, cranial nerves (CNs) VII and VIII are usually involved, resulting in facial nerve paralysis (Box 13-1) and vestibular disease.[1] Ocular clinical signs associated with facial nerve paralysis include ptosis, absence of the menace response, and absence of the palpebral reflex (Fig. 13-1). If the parasympathetic nucleus of CN VII is affected, neurogenic keratoconjunctivitis sicca will occur, predisposing the cornea to ulceration and secondary infectious keratitis. Involvement of CN III, IV, and VI may result in unilateral strabismus (Fig. 13-2). The presence of ventrolateral strabismus plus the absence of a pupillary light reflex (PLR) in the stimulated eye, with a normal consensual PLR, indicate an ipsilateral lesion in the oculomotor nerve. If ocular manifestations are present, they are usually accompanied by other cranial

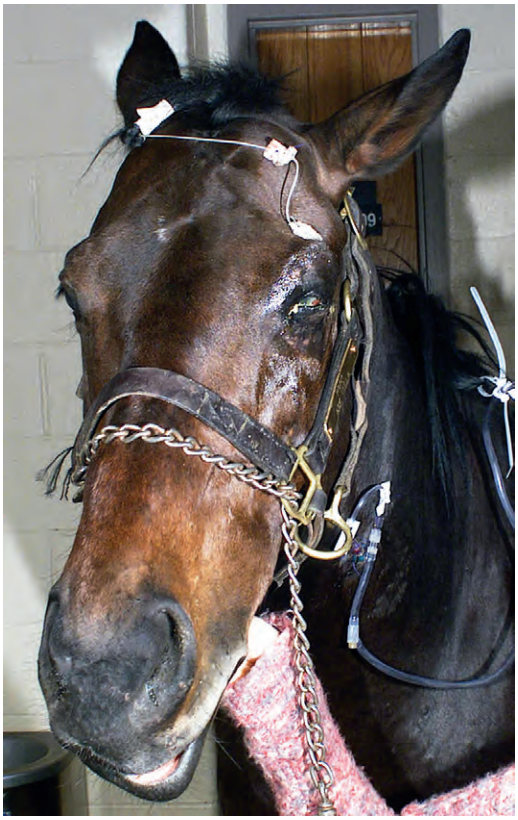


Figure 13-1. Left-sided facial nerve paralysis in a horse.

Box 13-1 | Systemic Illness Causing Facial Nerve Dysfunction

- Equine protozoal myeloencephalitis
- Polyneuritis equi
- Eastern equine encephalomyelitis, Western equine encephalomyelitis, Venezuelan equine encephalomyelitis
- Vestibular disease
- Aspergillosis
- Trauma
- Lyme disease
- Hypothyroidism

nerve deficits. EPM affecting the cervical spinal cord can cause Horner's syndrome (Box 13-2),[2] and clinical signs are listed in the discussion of Horner's syndrome. Other clinical signs associated with EPM include ataxia, (often asymmetrical and worse in the hind limbs), weakness, and muscle atrophy.[1] Some horses may have acute paraplegia or tetraplegia associated with periods of stress such as shipping, pregnancy, or concurrent illness.[3] Diagnosis of EPM is based on typical clinical signs, exclusion of other disease processes, plus the results of immunodiagnostic testing. The most common and reliable immunodiagnostic tests include Western blot or indirect fluorescent antibody test (IFAT) on serum or cerebrospinal fluid (CSF).[4] Positive results on serum titers are only indicative of exposure and cannot be used to diagnose central nervous system (CNS) disease; however, a negative result remains a good means of ruling out

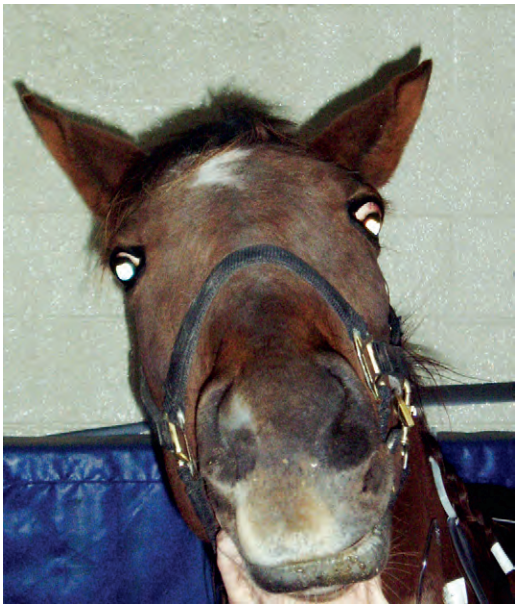


Figure 13-2. Unilateral strabismus secondary to equine protozoal myeloencephalitis in a horse.

Box 13-2 | Equine Protozoal Myeloencephalitis

- Equine protozoal meningitis
- Guttural pouch disease (aspergillosis)
- Polyneuritis equi
- Trauma to the basisphenoid bone
- Esophageal rupture
- Extravasation of an irritating drug (phenylbutazone)
- Trauma

EPM.[5] Positive results on CSF may result from contamination of the sample with red blood cells, so results should be interpreted with caution.[5] One advantage of the IFAT test is that it provides an actual quantitative titer, with serum titers greater than 1:100 and CSF titers greater than 1:5 being more indicative of active disease. Intrathecal production of antibodies without actual invasion of the CNS, or serum-derived antibodies crossing the blood-brain barrier (as occurs with vaccinated horses) are also potential causes of false-positive results. There is no one single ideal test for EPM; the best means of ruling out the disease is a negative result for serum or CSF.

Numerous treatments are licensed in the United States for the treatment of EPM.[6] A combination product of sulfadiazine and pyrimethamine (ReBalance Antiprotozoal Oral Suspension [IVX Animal Health Inc., St. Joseph, MO]) has been used successfully, although treatment is often prolonged, and bone marrow suppression may occur. Newer antiprotozoal drugs include diclazuril, toltrazuril, and ponazuril. Ponazuril (Marquis Antiprotozoal Oral Paste [Bayer Corporation, Shawnee Mission, KS]) is available in the United States and comes in a paste formulation for easy administration. Treatment for 1 or 2 months with these drugs is recommended. Nitazoxanide (Navigator Antiprotozoal Oral Paste [IDEXX Pharmaceuticals, Greensboro, NC]) has also been shown to be effective for the treatment of EPM, but this drug is not often first-line treatment,

owing to its potential for causing severe gastrointestinal side effects. Regardless of which treatment is used, approximately 65% of horses show an improvement in neurologic scores of one to two grades.[1]

EQUINE LEUKOENCEPHALOMALACIA

Blindness (Box 13-3) caused by equine leukoencephalomalacia, also called *blind staggers* or *moldy corn disease*, occurs when the midbrain (cortex-cerebrum) is affected, resulting in central blindness.[7,8] Severe neurologic changes, ataxia, and manic behavior will often accompany the blindness associated with equine leukoencephalomalacia. The disease is caused by chronic ingestion of moldy corn infested with *Fusarium moniliforme* and its associated toxin, fumonisin B1.[9,10] It results in liquefactive necrosis of the white matter in the brain (Fig. 13-3). If one horse on the farm is affected, the other horses have most likely been exposed, and the feed should be checked for presence of the mold. Hepatic enzyme activities—in particular, activity of gamma-glutamyl transferase—are often high in horses exposed to the toxin, and this can be used as a screening test for other horses on the farm.[11] Once neurologic signs have developed, the prognosis is grave. If treatment is attempted, it should consist of supportive care, provision of fluids, and administration of activated charcoal to decrease absorption of the toxin.

Box 13-3 | Equine Leukoencephalomalacia

- Equine leukoencephalomyelitis
- Eastern equine encephalomyelitis, Western equine encephalomyelitis, Venezuelan equine encephalomyelitis
- Thiamine deficiency and plants containing thiaminase
- Equine protozoal myeloencephalitis
- Bacterial meningoencephalitis
- Cryptococcal meningitis
- Ischemic optic neuropathy
- Intracranial neoplasia
- Rabies
- Strangles (brain abscess)
- Aspergillosis
- *Halicephalobus deletrix*
- Vitamin A deficiency
- Trauma
- Optic neuritis
- Plants containing pyrrolizidine alkaloids
- Trypanosomiasis
- Ivermectin toxicosis
- Air embolism

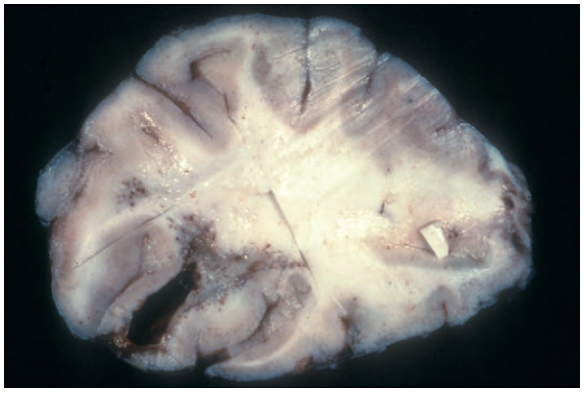


Figure 13-3. Liquefactive necrosis of the white matter in a horse with equine leukoencephalomalacia. (Courtesy Dr. Geoffrey Smith.)

EQUINE MOTOR NEURON DISEASE

Visual deficits are not usually reported with equine motor neuron disease, but approximately 50% of horses with equine motor neuron disease[12] will have characteristic fundic changes caused by ceroid/lipofuscin accumulation in the retinal pigment epithelium, considered pathognomonic for the disease. This dark brown to yellow pigment is deposited in a honeycomb mosaic pattern in the area of the tapetal fundus, with a distinct band of pigment at the tapetal/nontapetal junction (Fig. 13-4). PLRs may be abnormal.[13]

Severe weakness and muscle atrophy and fasciculations are associated with denervation atrophy of type I muscle fibers.[14] Affected horses are not ataxic, and clinical signs actually improve when horses are in motion.[14] The disease usually affects older horses and is slowly progressive. Decreased serum vitamin E levels have been associated with an increased risk of developing the disease and may be related to the pathophysiology, as evidenced by oxidative injury to the spinal cord, particularly in the somatic ventral motor neuron cells.[15,16] Diagnosis is often made on the basis of clinical signs, decreased serum vitamin E levels, increased serum ferritin and hepatic iron concentrations, and findings from electromyography and biopsy of the spinal accessory nerve or sacrodorsalis caudalis muscle.[15-17]

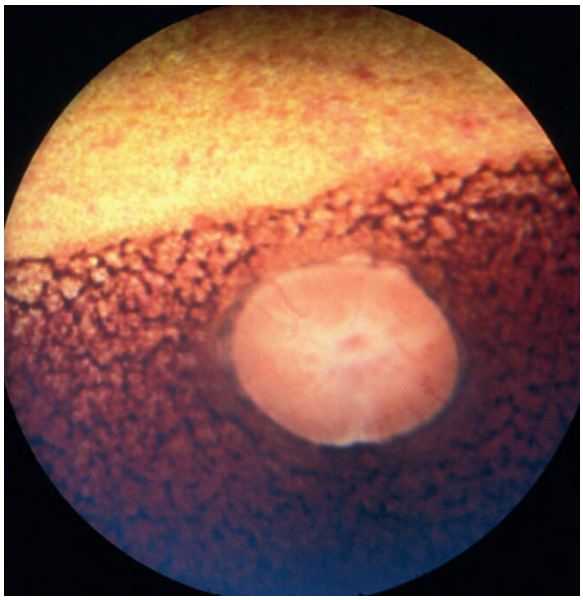


Figure 13-4. Ceroid/lipofuscin accumulation in the retinal pigment epithelium caused by equine lower motor neuron disease. This dark brown to yellow pigment is deposited in a honeycomb mosaic pattern in the area of the tapetal fundus, with a distinct band of pigment at the tapetal/nontapetal junction.

EASTERN EQUINE ENCEPHALOMYELITIS, WESTERN EQUINE ENCEPHALOMYELITIS, AND VENEZUELAN EQUINE ENCEPHALOMYELITIS

Togaviral encephalitides are transmitted by mosquitoes and tend to have a typical geographic distribution according to antigenic variation.[18] Typical clinical signs include fever, conscious proprioceptive deficits, and behavioral changes. Viremia occurs during this period. In the later stages of the disease, progressive signs of cerebral or cerebrocortical and cranial nerve dysfunction can be seen, including blindness; facial, lingual, and pharyngeal paralysis; ataxia; hypermetria; circling; head pressing (Fig. 13-5); and proprioceptive deficits or paresis of the trunk and limbs (see Boxes 13-1 and 13-3).[19] When the brainstem becomes involved, strabismus, nystagmus, pupil dilatation, and head tilt ensue.[20] Diagnosis is based on clinical signs, viral titers, and often, postmortem findings. CSF cytology may reveal a neutrophilic inflammation, and histopathologic examination reveals a nonseptic suppurative inflammatory infiltrate. An immunoglobulin (Ig) M capture enzyme-linked immunosorbent assay (ELISA) may be used to differentiate actual infection from vaccine responses.[21] Treatment involves supportive therapy with fluids, antiinflammatory drugs, and management of the recumbent horse. The mortality rate for Eastern equine encephalitis is the highest and is reported to be 75% to 100%, compared with the mortality rates for Venezuelan equine encephalitis at 40% to 80% and Western equine encephalitis at 20% to 50%.[18] If the horse does recover from the acute phase of the disease, residual neurologic deficits are common, especially with Eastern equine encephalitis. A vaccine that provides adequate protection for 6 to 8 months is available.[22]

SEPTIC MENINGOENCEPHALITIS

Septic meningoencephalitis is rare in adult horses but more common in young foals. In the neonate, hematogenous spread is the most common cause of the disease, but in the adult, it is often a direct extension of infectious agents into the CNS as a result of skull fractures, sinusitis, otitis, or surgical procedures.[23,24] Hematogenous spread may also occur in adult horses as a result of bacterial endocarditis or respiratory disease.[23,25] Clinical signs in foals often begin with stiffness in the neck, photophobia, and hyperesthesia. These signs can then rapidly progress to behavioral changes, cranial nerve deficits, ataxia, coma, seizures, and death. Signs are similar in adult horses but tend to progress slowly over a period of several days.[26] Specific ocular signs that have been reported in horses with bacterial meningoencephalitis include blindness (see Box 13-3), lack of a menace response, lack of a pupillary light response, nystagmus, ventromedial strabismus, decreased palpebral reflex, retraction of the globe, and elevation of the third eyelid.[25,26] Lesions have been reported to be unilateral or bilateral and result from inflammation of the cerebral cortex or individual cranial nerves.[25,26] Diagnosis is made on the basis of findings from CSF cytology, Gram staining, and culture. Treatment can be difficult because of the well-developed blood-brain barrier. Antibiotic choices should be based on findings from culture and sensitivity testing, as well as the physicochemical properties of the drug. In general, lipophilic, nonpolar basic drugs with a broad spectrum of activity and bactericidal action should be considered. In horses that do not respond to typical antibiotic therapies, nonbacterial causes of meningitis should be considered. Fungal infections with *Cryptococcus neoformans*[27] and parasitic infections with *Halicephalobus gingivalis*[28] have also been reported to cause meningitis with concurrent blindness in the horse. Antiinflammatory medications and anticonvulsants are also necessary. The prognosis should be considered guarded in all cases.

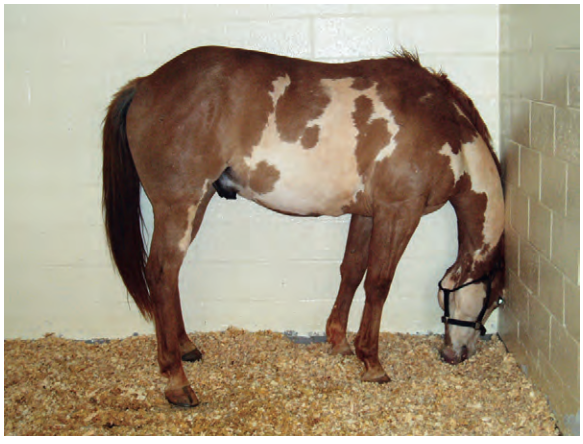


Figure 13-5. Head-pressing behavior in a horse secondary to diffuse cerebral disease with Eastern equine encephalitis.

THIAMINE DEFICIENCY

Thiamine deficiency in the horse can be induced by feeding a diet deficient in thiamine or by the ingestion of thiaminase-containing plants, such as bracken fern *(Pteridium aquilinum)* and horsetail *(Equisetum arvense)*.[7,23] Amprolium has been used experimentally to induce thiamine deficiency.[29] Ataxia, conscious proprioceptive deficits, heart block, bradycardia, blindness, and muscle fasciculations or rhabdomyolysis have all been reported. Electrolyte changes, hyperglycemia, decreased glucose tolerance, and high creatine kinase activities have also been described.[23,30] Supplementation with injectable thiamine is successful in the early stages of the disease.[23] Clinical signs, including blindness, are reversible in the earlier stages of the deficiency.[7]

VESTIBULAR DISEASE

Vestibular disease can be classified as peripheral or central. Peripheral vestibular disease causes head tilt toward the side of the lesion; horizontal or rotary nystagmus, with the fast phase occurring away from the side of the lesion[23]; falling; circling; and asymmetric ataxia without conscious proprioceptive deficits or weakness. Facial nerve paralysis can occur with peripheral disease because of the facial nerve's proximity to the petrous temporal bone. Ipsilateral Horner's syndrome occurs when the postganglionic sympathetic nerves are affected as they course through the petrous temporal bone. Common causes of peripheral vestibular dysfunction include trauma, otitis media, temporohyoid osteoarthropathy, and guttural pouch disease.[31,32]

Central vestibular disease presents in a similar manner; however, conscious proprioceptive deficits, generalized weakness, involvement of multiple cranial nerves, and nystagmus may also be present. Nystagmus may be indistinguishable from peripheral disease but may also be vertical, diagonal, or disconjugate (different in each eye). The direction of the nystagmus may change with head position in horses with central vestibular disease.[33] Paradoxical central vestibular disease may occur with destructive lesions of the cerebellopontine angle or the flocculonodular lobe, resulting in clinical signs contralateral to the lesion.[34] The nuclei of CNs V to XII can be involved; therefore cranial nerve dysfunction, besides dysfunction of CN VII, indicates central disease. In addition, Horner's syndrome is not seen with central vestibular disease. Bilateral vestibular disease is difficult to differentiate from generalized cerebellar disease, and horses with bilateral vestibular disease do not exhibit typical clinical signs. Central vestibular dysfunction is commonly associated with space-occupying lesions such as tumors or abscesses but may also be caused by protozoal, viral, bacterial, or parasitic encephalitides.[31]

Diagnostic techniques for determining the underlying cause of vestibular disease in the horse should include radiographs of the skull (Fig. 13-6), endoscopy of the pharyngeal region and guttural pouches, and possibly magnetic resonance imaging (MRI) or a computed tomography (CT) scan of the head (Fig. 13-7). CSF cytology and ancillary testing for viral or protozoal antibodies are indicated if central disease is suspected. Caloric testing by irrigating the ear canal with cold water and checking for induction of normal horizontal nystagmus can be done, although the test is not always reliable, and most horses will resist the procedure.[35] A decreased or absent reaction indicates the side of the lesion. Brainstem auditory evoked responses are also useful in demonstrating damage to the cochlea and CN VIII and can be used to differentiate between central and peripheral disease.[36,37] The procedure is reliable and repeatable in the sedated horse. Treatment and prognosis should be related to the primary disease process.

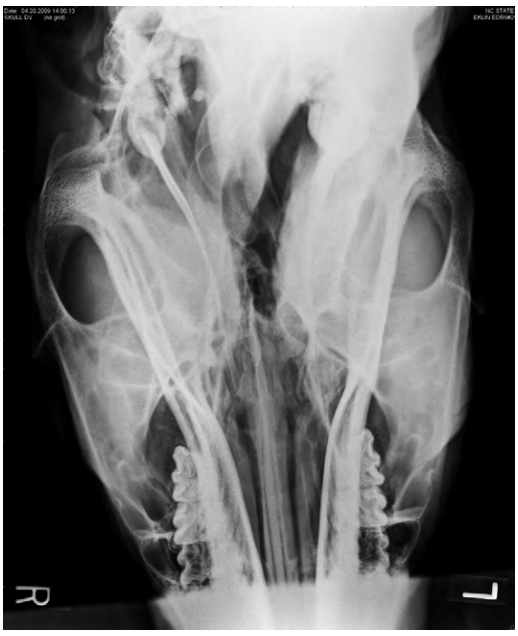


Figure 13-6. Radiograph of a horse with bilateral temporohyoid osteopathy that presented with signs of central vestibular disease.

HORNER'S SYNDROME

Horner's syndrome is caused by damage or denervation along any portion of the sympathetic nervous system. The sympathetic nervous system originates in the hypothalamus (Fig. 13-8). The central sympathetic fibers form the tectotegmentospinal tract (first-order neurons), which descends ipsilaterally through the brainstem and lateral funiculus of the cervical spinal cord to synapse with the preganglionic cell bodies of T1 to T3 or T4. These preganglionic sympathetic neurons (second-order neurons) leave the spinal cord via the segmental ventral roots to the paravertebral sympathetic chain, continue through

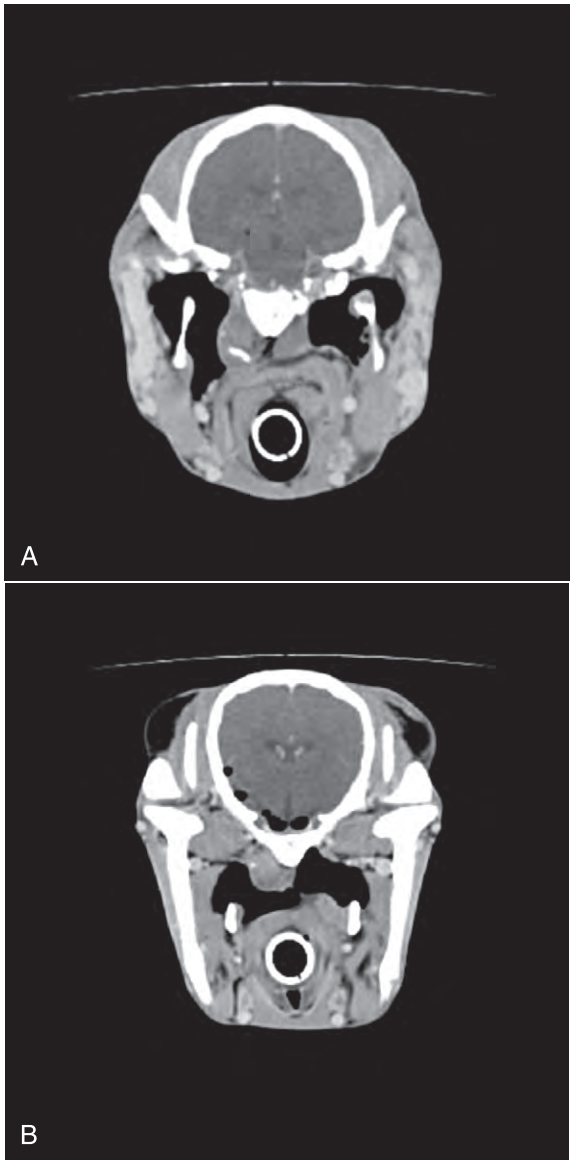


Figure 13-7. **A,** Computed tomography (CT) image of a basisphenoid fracture in a 3-month-old Quarter Horse colt that presented with unilateral vestibular disease secondary to trauma. **B,** Distal CT image from the same foal, showing air within the calvarium.

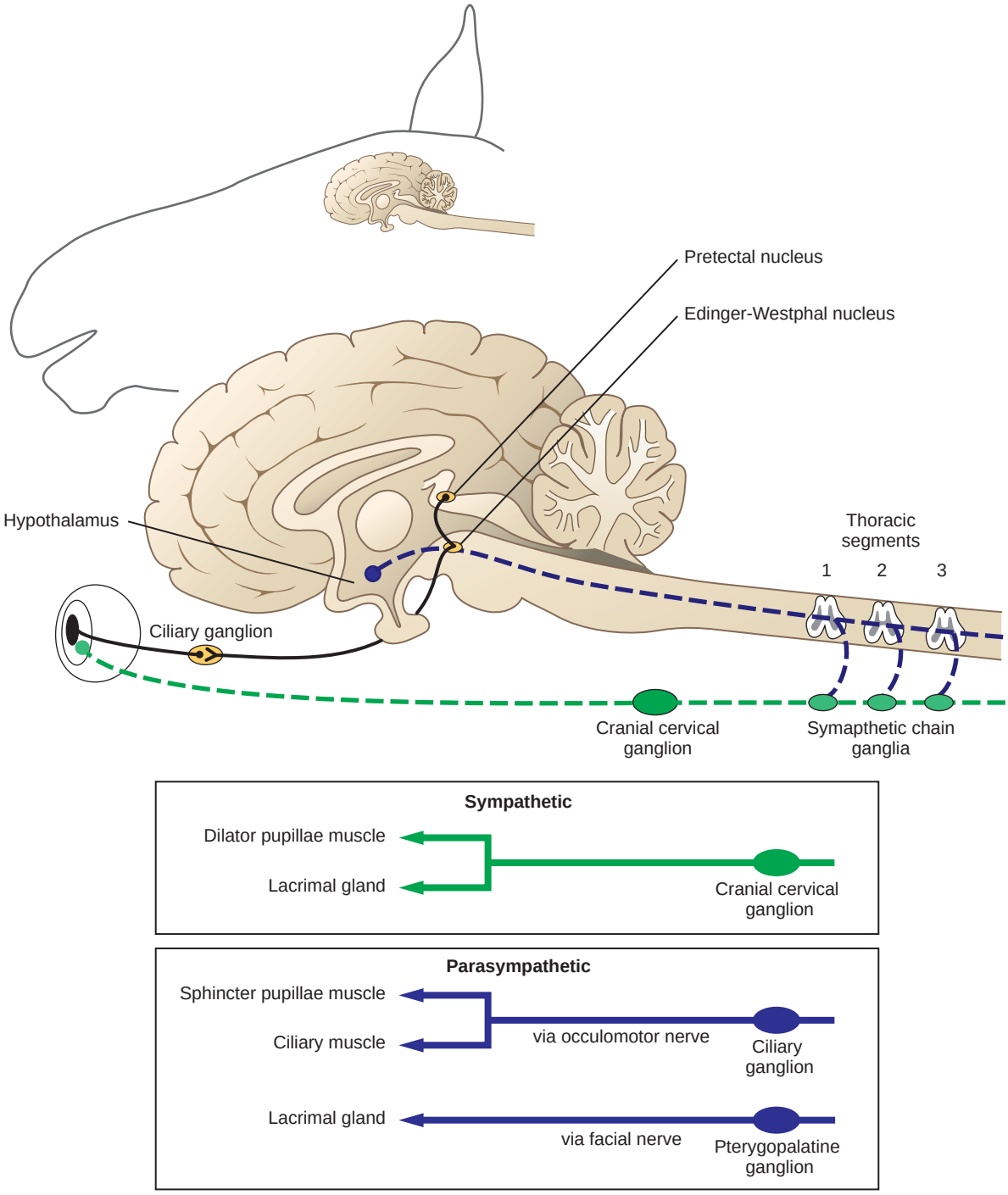


Figure 13-8. Illustration of the sympathetic innervation of the eye.

the brachial plexus, then travel with the vagosympathetic trunk until they synapse at the cranial cervical ganglion caudomedial to the tympanic bulla. The postganglionic fibers (third-order neurons) join the tympanic branch of CN IX (glossopharyngeal nerve) within the middle ear and, in horses, pass over the caudodorsal aspect of the guttural pouch. After the fibers exit the middle ear, they enter the cavernous sinus and join CN V and together continue rostrally in the periorbita (nasociliary nerve) to innervate the orbital smooth muscles, the eyelids (including the third eyelid), and the ciliary body, iris dilator, and iris sphincter muscles.[38,39] Horner's syndrome in horses is most frequently seen as a result of guttural pouch diseases that involve the internal carotid nerve, which is composed of postganglionic sympathetic fibers. Injury to the cranial thoracic spinal cord, brachial plexus avulsions, traumatic lesions, or masses (tumors or abscesses) involving the mediastinum, periorbital tissues, or cervical structures may also cause clinical signs of Horner's syndrome. Iatrogenic Horner's syndrome can occur as a result of ligation of the carotid artery.[39] Causes unique to the horse, besides guttural pouch infections, include

polyneuritis equi syndrome (cauda equina neuritis), EPM affecting the cervical spinal cord, basisphenoid trauma, esophageal rupture, and extravasation of an intravenous drug (e.g., phenylbutazone).[40-42] Clinical signs of Horner's syndrome in horses include ptosis, relative enophthalmos, subtle miosis (anisocoria), regional hyperthermia, and excessive sweating on the ipsilateral side of the face (Fig. 13-9).[40] Cervical sympathetic nerve damage will cause sweating of the neck, congested conjunctival and nasal mucous membranes, and inspiratory stridor. Regional hyperthermia and sweating are thought to be caused by decreased vasomotor tone resulting in vasodilation and increased cutaneous blood flow.[43-45]

The location and cause of the lesion will determine which of the clinical signs are present, and the location will determine what diagnostic tests should be performed. Often, location may provide the prognosis. Phenylephrine (2% or 10%) or 1:1000 epinephrine is more readily available than hydroxyamphetamine or cocaine for the pharmacologic localization of efferent sympathetic lesions. In addition, although cocaine will confirm the presence of a sympathetic deficit, it will not localize the lesion. Hydroxyamphetamine is an indirect-acting sympathomimetic agent that causes endogenous release of norepinephrine from the adrenergic nerve endings. After instillation of topical hydroxyamphetamine, central and preganglionic lesions will have normal mydriasis, and postganglionic lesions will have incomplete to no mydriasis compared with the normal eye. Phenylephrine and epinephrine are direct-acting sympathomimetic drugs that will result in mydriasis within 5 to 8 minutes in postganglionic lesions. This is due to denervation hypersensitivity of the effector cells.[39] One drop of phenylephrine or epinephrine is applied to each eye (the normal eye is used for comparison), and care should be taken to use the same amount in each eye because the response is dose dependent. If hydroxyamphetamine is used before administration of phenylephrine or epinephrine, a 24-hour washout period between the two tests is necessary. If a lesion localizes to the postganglionic arm of the pathway, endoscopy of the pharynx and guttural pouch should be performed.[39] CT is another diagnostic option when it is available.

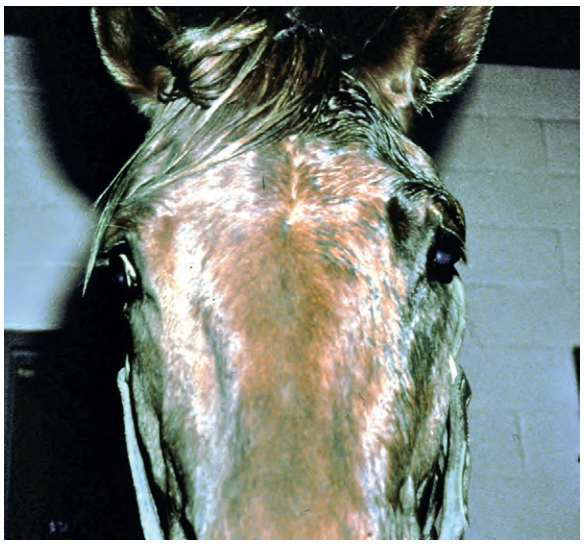


Figure 13-9. Clinical signs of Horner's syndrome in horses include ptosis, relative enophthalmos, subtle miosis (anisocoria), regional hyperthermia, and excessive sweating on the ipsilateral side of the face. (Courtesy Dr. David Wilkie.)

TETANUS

Tetanus most often occurs after infection of a wound with *Clostridium tetani*, an anaerobic, motile, gram-positive, nonencapsulated spore-forming bacteria ubiquitous in soils worldwide.[39,46] The bacteria produce at least three toxins responsible for the clinical signs of the disease: tetanospasmin, tetanolysin, and a nonspasmogenic toxin. Tetanospasmin is responsible for the clinical signs typically associated with tetanus and is thought to work by inhibiting release of glycine and gamma-aminobutyric acid, the main inhibitory neurotransmitters in the CNS.[23] Tetanolysin causes local tissue necrosis, which helps promote bacterial proliferation, and the nonspasmogenic toxin produces overstimulation of the sympathetic nervous system.

The characteristic ocular sign in horses is "flashing" third eyelids (Box 13-4). *Flashing* refers to the rapid protrusion and retraction of the third eyelids coupled with eyeball retraction, usually in response to a menacing gesture.[39] Concurrent clinical signs often include lameness and a stiff gait that progresses to generalized spasticity and severe muscular rigidity. Sensory stimulation can produce muscle spasms, leading to recumbency and the sawhorse stance typical of tetanus. Ocular signs of advanced tetanus include ventrolateral strabismus and fixed, dilated pupils with normal vision.[39] Death usually occurs as a result of involvement of the respiratory tract muscles, leading to hypoxemia, and cardiac failure caused by systemic hypertension.[47] The principles of therapy center around providing muscle relaxation through the use of phenothiazine tranquilizers, barbiturates, or benzodiazepines; preventing self-trauma by providing adequate bedding and good footing; decreasing external stimulation; and preventing further toxin absorption or binding by cleaning and débriding the wound, administration of appropriate antibiotics including high doses of penicillin, and administration of commercially available tetanus antitoxin locally in the wound, intramuscularly, or intrathecally. The prognosis for horses with tetanus is poor, with a mortality rate of 80%. Prevention with annual administration of a tetanus toxoid vaccine is safe and effective and should be recommended for all horses on a routine basis and especially before surgical procedures. Administration of tetanus antitoxin has been associated with the development of acute necrotic hepatitis (Theiler's disease), and its use should be limited to horses at high risk for developing tetanus and those showing clinical signs.[48]

BOTULISM

The clinical signs of botulism are caused by a neurotoxin elicited from the anaerobic bacteria, *Clostridium botulinum*. The

Box 13-4 | Systemic Illness Causing Elevated Nictitating Membrane

- Septic meningoencephalitis
- Hyperkalemic periodic paralysis
- Rabies
- Tetanus (flashing nictitating membrane)

toxin blocks the release of acetylcholine from the presynaptic peripheral cholinergic neurons, resulting in a neuromuscular blockade and generalized muscular weakness.[49] Botulinum toxin is considered to be one of the most potent known toxins, and horses are more sensitive to the toxin than most other species. Three causes of botulism occur in horses: ingestion of preformed toxin, ingestion of spores (toxicoinfectious botulism or shaker foal syndrome), and contamination of a wound.

Ocular signs associated with botulism include enophthalmos caused by retractor bulbi spasm, upper eyelid ptosis,[50] and mydriasis with slow PLRs.[51] Aside from the ocular signs, horses may be presented with limb weakness and ataxia that begins caudally and progresses cranially, decreased tail and anal tone, bladder paralysis, weakness of the tongue, and dysphagia. Colic may be present as a result of progressive ileus. Foals are most often presented in recumbency and, when forced to stand, will show generalized muscle tremors because of severe weakness. Death occurs as a result of paralysis of the intercostal muscles and the diaphragm. Diagnosis of botulism is typically made by demonstration of the preformed toxin or *C. botulinum* spores in feed, serum, wounds, or gastrointestinal contents of affected horses.[52] The mouse inoculation test commonly used in other species is not sensitive enough as the sole diagnostic test in the horse, because the amount of toxin necessary to kill a horse may not be enough to kill a mouse. Diagnosis is frequently made by the exclusion of other neurologic diseases. Results of hematologic analysis are often normal in these horses, with the exception of an elevated P_{CO_2}. Treatment consists of supportive care, ventilatory support, and administration of botulinum antitoxin. Aminoglycoside and tetracycline antibiotics should not be used because they can potentiate neuromuscular blockade. The antitoxin should be specific for the type of botulism involved, although the type is frequently not known. The most common type of botulism in North America is type B, although types C and A have been reported. A polyvalent antiserum is available, but the cost is prohibitive for most horse owners. Antitoxins are only effective against unbound toxin and must be given early in the course of the disease to be beneficial. The prognosis in all cases of botulism should be guarded. Vaccines against type B botulism are commercially available and are recommended on farms where the disease is endemic.

TRYPANOSOMIASIS

Trypanosoma evansi is a protozoal parasite that causes a chronic wasting syndrome in horses and numerous other species, including cattle and dogs. Less frequently, it can cause a severe encephalitis or myeloencephalitis with asymmetric leukoencephalomalacia, edema, demyelination, and lymphoplasmacytic perivascular cuffing.[53] Neurologic signs reported include ataxia, blindness, nystagmus, head tilt, circling, head pressing, proprioceptive deficits, and hyperexcitability leading to obtundity and death.[53,54] The use of subtherapeutic doses of antitrypanosomal drugs, such as diminazene aceturate, may clear the organism from peripheral tissues but appears to predispose the animal to developing CNS infection. Introduction of naïve animals into endemic areas may also account for the severity of signs seen with the neurologic disease. Serology or polymerase chain reaction (PCR) can be used for diagnosis. Once horses develop neurologic signs, the prognosis is grave.

PHOTIC HEAD SHAKING

No visual abnormalities are associated with photic head shaking.[39,55] The underlying cause of head shaking in most horses is unknown. Proposed causes include iris cysts,[39] guttural pouch disease, nasal and dental disease, middle ear disorders, and ear mite infestation *(Trombicula autumnalis)*. A thorough examination should include endoscopy and radiography of the guttural pouches and upper airways and complete ophthalmic, otoscopic, and dental examinations.[56] A more detailed examination should include observation of the horse during exercise and at rest with a fitted nasal mask and tinted contact lenses, as well as during anesthesia of the infraorbital and posterior ethmoidal branches of the trigeminal nerve.[57] Medical management may include administration of cyproheptadine, an antiserotonergic drug thought to decrease neuropathic pain, with or without concurrent administration of carbamazepine, a drug related structurally to the tricyclic antidepressants, which is thought to reduce nerve impulses in the trigeminal nerve and has been used frequently for the treatment of trigeminal neuropathy in humans.[57,58] Additional procedures that have been recommended include posterior ethmoid nerve sclerosis and infraorbital neurectomies, although significant adverse effects may be associated with these procedures.[56,57]

ISCHEMIC OPTIC NEUROPATHY

Epistaxis caused by guttural pouch mycosis can be treated with arterial occlusion of the internal carotid, external carotid, and greater palatine arteries. This treatment can result in sudden irreversible blindness of the eye on the affected side. Clinical lesions include congestion of the optic nerve head and involvement of the nerve fiber layer (see Chapter 9).[59] Severe blood loss can result in bilateral blindness caused by an unknown mechanism.[60]

INTRACRANIAL NEOPLASIA

Intracranial neoplasia is rare in the horse. Clinical signs usually relate to the size and location of the tumor and whether metastasis has occurred. Exophthalmos, ocular discharge, and facial deformity may be observed with masses involving the sinuses or nasal passages.[61-65] Unilateral blindness, ventrolateral strabismus, and a lack of physiologic nystagmus have been described in a horse with intracranial neoplasia that involved the retrobulbar space.[66] These lesions were thought to be due to involvement of CNs II, III, and IV and possibly CN VI through compression by a space-occupying mass or metastasis of the tumor to involve the peripheral nerves. An immune-mediated paraneoplastic peripheral neuropathy may also have contributed to the dysfunction of these peripheral nerves.[66] CSF cytology, radiography, endoscopy of the nasal passages, and CT or MRI can all be used to assist in making the diagnosis.[66] A prognosis should be determined according to the extent and nature of the lesion and the possibility for surgical removal or adjunctive therapy.

POLYNEURITIS EQUI

Polyneuritis equi is a chronic disease characterized initially by hyperesthesia, followed by progressive hypoesthesia and sub-

sequent paralysis of regions innervated by the corresponding nerve roots. Common areas affected include the tail; anus and perineal area; bladder; and CNs V, VII, and VIII, although other cranial nerves may be affected.[67] CNs VII and VIII are more commonly affected than CN V.[38] Facial nerve paralysis and decreased tear production can occur with secondary corneal disease.[68] Colic, as a result of fecal retention and bladder distension, is a common clinical sign. The cause is unknown, but a viral or immune-mediated etiology has been proposed. This is supported by the presence of antibodies to P2 myelin protein that are found in some horses with the disease.[69] This antibody has also been found in horses with equine herpesvirus 1 (EHV-1) and adenovirus infections, however, and should only be considered as a supportive test. Other diagnostic tests should include a complete blood count, which often shows signs of chronic inflammation (mature neutrophilia with hyperfibrinogenemia), and CSF cytology, which may be normal or may show high white blood cell counts or protein levels.[69,70] The definitive diagnosis is often made at necropsy. Histopathologic examination may reveal inflammation and infiltration of the extradural or intradural nerve roots.[71] Treatment with steroids may improve clinical signs in the early stages of the disease, but the lesions are progressive, and euthanasia is often required.

VIRAL DISEASES

EQUINE VIRAL ARTERITIS

Equine viral arteritis is caused by a togavirus and is spread by aerosolization and inhalation or through sexual contact. Carrier stallions are considered responsible for maintaining the disease in the population and may shed the virus in their semen for months to years.[72] Outbreaks have occurred in New Mexico (2006) and France (2007) that highlight the potential for the quick dissemination of the disease among breeding farms.[73] There are two major syndromes associated with equine viral arteritis in the horse: a respiratory syndrome and an abortion syndrome. Many cases are asymptomatic, but clinical signs may include pyrexia, upper respiratory tract disease, severe edema, and abortion 3 to 8 weeks after infection with the virus.[74] The disease is often fatal in neonatal foals. Ocular signs include serous to mucoid ocular discharge, supraorbital and periorbital edema, conjunctivitis, corneal opacity, and photophobia (Box 13-5). The pathophysiology involves a necrotizing vasculitis, mainly of the small arteries in the muscle tissue of affected animals.[75] Diagnosis is based on seroconversion, virus isolation, or results of PCR.[72] Leukopenia with a lymphopenia is a consistent finding on hematologic analysis. There is no specific treatment. Prevention involves vaccination of mares and prepubertal stallions and routine testing of breeding stallions. Freezing of the semen will not deactivate the virus, and both freshly collected and frozen semen are considered infective.[75]

Box 13-5 | Systemic Illness Causing Conjunctival Disease

- Equine viral arteritis
- Equine herpesvirus 2 (EHV-2)
- African horse sickness (chemosis)
- Equine influenza
- Equine granulocytic ehrlichiosis
- Babesiosis
- Epizootic lymphangitis
- Onchocerciasis
- Habronema
- Pemphigus
- Neonatal isoerythrolysis (icterus)
- Cushing's disease

EQUINE INFECTIOUS ANEMIA

Equine infectious anemia (EIA) is caused by a nononcogenic retrovirus that produces an immune-mediated hemolytic anemia in affected horses.[76] The disease originally presents as an acute syndrome characterized by fever, anorexia, depression, and petechial hemorrhages caused by thrombocytopenia. Thrombocytopenia can have associated ocular lesions, including conjunctival and intraocular hemorrhages. Choroiditis has also been documented with EIA.[77] Anemia develops in the subacute to chronic stage, and horses with EIA may have a recrudescence of the disease. Chronic carriers have also been described, and these horses are clinically healthy and hematologically normal. Diagnosis is most frequently made by the Coggins test; the result is positive as early as 10 days after infection and remains positive as a result of chronic antigenic stimulation from the virus.[76] No treatment or vaccine is available for EIA, and infected horses are considered contagious. The disease must be reported, and euthanasia is recommended.

RABIES

Rabies is caused by a neurotropic rhabdovirus that affects most warm-blooded mammals. The disease is rapidly progressive after a variable incubation period, and it is invariably fatal. Early clinical signs are nonspecific and often include muzzle fasciculations, behavioral changes, hindlimb lameness or paresis, colic, and pharyngeal paralysis.[78,79] Recumbency, convulsions, head pressing, and circling may occur as terminal events.[23] Ocular signs are rare and include blindness, prolapse of the third eyelid, nystagmus, and strabismus, most likely caused by diffuse cerebrocortical edema and hemorrhage.[77-79] The retinal ganglion cells may be susceptible to infection.[50] There is no treatment available for rabid animals, and euthanasia is recommended. Appropriate caution should be taken with all animals with neurologic signs, especially those horses that have not been vaccinated for rabies. The most reliable diagnostic test is the fluorescent antibody test performed on brain tissue.[78]

AFRICAN HORSE SICKNESS

African horse sickness is not present in North America but is endemic in sub-Saharan Africa. The virus is a noncontagious, arthropod-borne orbivirus that affects all Equidae; however, mules, donkeys, and zebras are less susceptible than horses.[80] Four forms of the disease are recognized: the pulmonary or peracute form, the cardiac or subacute form, the mixed form, and a milder horse sickness fever.[81] The mixed form is the one most commonly diagnosed and has clinical signs from both the pulmonary and cardiac forms of the disease, which may include

pyrexia; tachypnea; sweating; cough; mucosal congestion; pleural effusion; and pulmonary, interfascial, and subcutaneous edema.[80] Bulging of the supraorbital fossae (Fig. 13-10) occurs in 10% to 20% of cases, but it is a hallmark sign considered diagnostic for the disease (Box 13-6). This is likely due to retrobulbar edema and increased vascular pressure. Another possible ocular sign is marked chemosis (conjunctival edema).[82] The mortality rate is between 50% and 95%. Diagnosis is based on virus isolation or neutralization and serology. Prevention involves quarantine of affected animals and vaccination of animals in endemic areas.[83]

Box 13-6 | Systemic Illness Causing Exophthalmos

- Neoplasia
- African horse sickness (bulging of supraorbital fossa)
- Echinococcosis
- Cryptococcosis

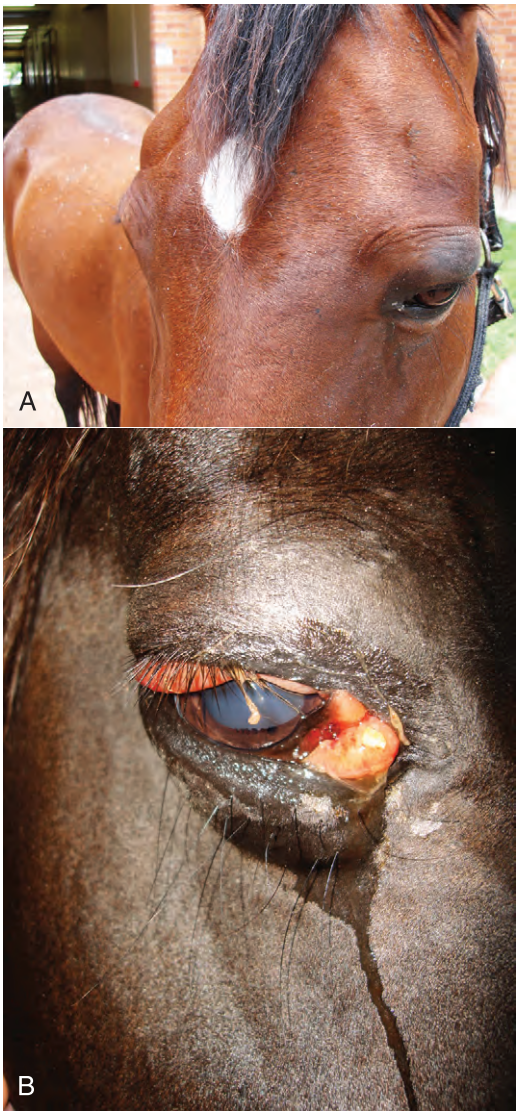


Figure 13-10. **A,** Bulging of the supraorbital fossae in a horse with African horse sickness (AHS). **B,** Marked chemosis in a horse with AHS. (Courtesy Prof. Montague N. Saulez.)

EQUINE HERPESVIRUS

Equine herpesvirus 1 (EHV-1) is a common cause of upper respiratory tract infection, abortion, and neurologic disease in horses. Respiratory signs are more common in young horses and show horses and include fever, cough, and a mucoid nasal discharge that may progress to mucopurulent discharge with secondary bacterial infections. Abortions tend to occur after the seventh month of gestation and are sudden, without premonitory signs.[84] Stillbirths may also occur, and foals born alive are often weak, have severe interstitial pneumonia, and typically die within the first few days of life. The neurologic form of EHV-1 frequently presents with hindlimb ataxia, decreased tail and anal tone, and fecal and urinary retention. Signs may progress to the forelimbs, and horses may eventually become recumbent, which indicates a poor prognosis.

Ocular signs associated with EHV-1 or EHV-4 include hyperemia of the conjunctiva or sclera. Experimental infection of a foal with EHV-1 led to signs of severe visual dysfunction and chorioretinitis 28 days after exposure.[85] Ophthalmic exam revealed severe degeneration of the neurosensory retina, retinal pigmented epithelium, and choroidal layers, with EHV-1 DNA present in the ocular tissues. This lesion has not been reported in naturally occurring infection. Infection with the neuropathic strain of EHV-1 may result in diffuse cerebral dysfunction and cranial nerve involvement.

Treatment with the antiviral drug valacyclovir has been evaluated, but its benefits are questionable, and it remains cost prohibitive at this time.[86] Supportive care including antiinflammatory treatments, stall rest, and adequate nursing for horses with the neurologic form of the disease is recommended. Commercial vaccines against EHV-1 and EHV-4 are available, although protection is only short lived, and the vaccines may not protect against the neurologic form of the disease.

EHV-2 is a cytomegalovirus not known to cause disease by itself but considered important in the pathogenesis of other diseases through immunosuppression or possible transactivation of EHV-1.[87-89] The virus has been detected in pulmonary macrophages of up to 90% of horses with chronic pulmonary disease.[90] There are numerous reports of ocular signs associated with EHV-2, including serous to mucopurulent ocular discharge, conjunctival hyperemia and chemosis, superficial dendritic-type corneal lesions, which may be linear or punctate, and corneal edema and vascularization (Fig. 13-11).[7,91] Response to topical antiviral medications is often favorable.[92,93] Topical application of interferon and oral administration of L-lysine may be helpful (see Chapter 5 for more information).

ADENOVIRUS

The most frequent manifestation of adenovirus in the horse is as a lower respiratory tract pathogen in foals with severe combined immunodeficiency.[94,95] The virus has also been coisolated from foals with diarrhea caused by rotavirus.[96] It is not considered a pathogen in nonimmunocompromised animals. Bronchopneumonia is accompanied by mucopurulent nasal and ocular discharge. Conjunctival epithelial cells are histologically

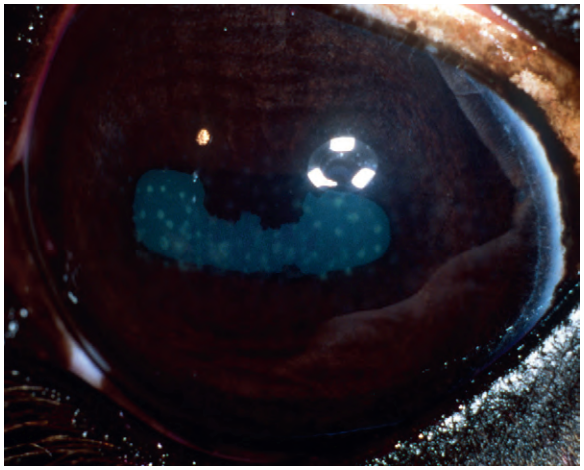


Figure 13-11. Left eye of a 4-year-old Warmblood stallion with equine herpesvirus 2 (EHV-2) keratitis. There are multiple focal, punctate white lesions in the superficial cornea that are rose bengal positive and fluorescein positive. (Courtesy Dr. Stacy Andrew.)

necrotic with intranuclear inclusions, and a neutrophilic infiltrate is present in the uveal vasculature, which is consistent with panuveitis.[7,97]

EQUINE INFLUENZA

Clinical signs of equine influenza virus are virtually indistinguishable from those of upper respiratory tract disease caused by EHV-1 and EHV-4. Fever, cough, and a serous or mucoid nasal and ocular discharge are often present along with conjunctival hyperemia (see Box 13-5).[7] The disease most often affects young horses, and there is usually a history of travel or introduction of a new horse into the herd. The virus spreads extremely rapidly, with an onset of fever within 2 to 3 days, which may last for up to 10 days, and a harsh, dry cough, which may persist for 2 to 3 weeks.[98] Treatment consists of supportive therapy, administration of nonsteroidal antiinflammatory drugs (NSAIDs), and stall rest for several weeks after resolution of clinical signs. Immunity after natural infection may last for more than 1 year; however, immunity after vaccination usually only lasts for 2 to 3 months because of antigenic drift in the virus.[98,99] The modified live intranasal vaccine may provide extended immunity (>6 months) and has proven effective in challenge studies.[100] Studies have shown that early vaccination may actually decrease the immune response, and therefore it is recommended that the initial vaccination not take place until the foal is 8 months old. The mortality rate is very low unless the patient is debilitated or secondary infections such as myositis or pneumonia develop.

WEST NILE VIRUS

West Nile virus encephalitis is caused by a flavivirus with a worldwide distribution. It is considered endemic in Europe, Africa, Asia, and the Middle East. It was not introduced into the Western Hemisphere until 1999; however, it has spread rapidly across North America, and outbreaks have now been reported in almost every state in the United States, as well as in most provinces in Canada. The disease affects horses, humans, and susceptible bird populations. Cases in dogs, cats, camelids, and squirrels have also been reported.[101] The virus is spread by arthropod vectors, notably *Culex* sp. and *Aedes* sp. mosquitoes.[102] The normal life cycle includes birds and mosquitoes, with horses and humans considered to be dead-end hosts.[103]

Clinical signs vary widely, depending on the portion of the CNS affected, and some horses may be asymptomatic even after experimental infection.[104] The most common neurologic sign in horses is hindlimb ataxia or paresis.[105] In one retrospective study, fever was noted in 65% of the cases.[105] Muscle fasciculations are also commonly noted and are thought to be due to either muscular weakness or lesions of the basal ganglia, as documented in humans.[106] Other clinical signs include dysmetria, depressed mentation, cranial nerve abnormalities, anorexia, bruxism, ptyalism, seizures, and recumbency.[105,107] The most common ophthalmic clinical sign of West Nile virus is unilateral or bilateral facial nerve paralysis (see Fig. 13-1 and Box 13-1). Loss of menace response is also reported, although its pathogenesis was not mentioned.[105] In an outbreak of West Nile encephalitis in Italy, mild keratitis, possibly caused by recumbency, and protrusion of the third eyelid were noted in horses that recovered from the disease.[107] Unreported manifestations of West Nile virus including blindness, presumably caused by encephalitis, have been diagnosed at one institution (Dr. Ramiro Toribio, personal communication, 2003). In humans, the virus has been reported to cause optic neuritis, uveitis, and chorioretinitis.[108,109]

Diagnosis of West Nile virus is typically made by IgM capture ELISA of serum or CSF. This test has the advantage of differentiating between an acute infection and a vaccine response; however, hemagglutination inhibition is considered a more sensitive test.[110] CSF cytology may show xanthochromia with or without an increased protein.[105] Treatment is supportive with antiinflammatory therapies, such as NSAIDs, steroids, and dimethyl sulfoxide, which are used to decrease cerebral edema. A hyperimmune plasma labeled for use in horses with West Nile virus encephalitis has also been recommended. There are currently three vaccines available for use in horses: an inactivated whole virus vaccine, a recombinant vector vaccine, and a modified live chimera vaccine.[111,112] The incidence of the disease in horses is decreasing, which may be due to naturally acquired immunity or the prudent use of vaccinations. The mortality rate is around 30% in horses that do not become recumbent and may be as high as 71% in horses that are unable to rise.[105]

BACTERIAL AND RICKETTSIAL DISEASES

NEONATAL SEPTICEMIA

Neonatal septicemia is frequently associated with prematurity or dysmaturity, placental insufficiency, or failure of passive transfer. The foal is often healthy at birth, but signs of septicemia develop within the first 24 to 48 hours. Clinical signs vary widely but often include transient fever or hypothermia, loss of suckle, mild to severe depression, constipation or diarrhea, and bacterial seeding of other organs, including the joints, the lungs, and the umbilicus, as well as the eye. The earliest sign of septic uveitis is a green hue to the iris caused by fibrin seeping from the uveal vessels (Fig. 13-12). With progression, classic signs of uveitis are present: miosis, hypotony, aqueous

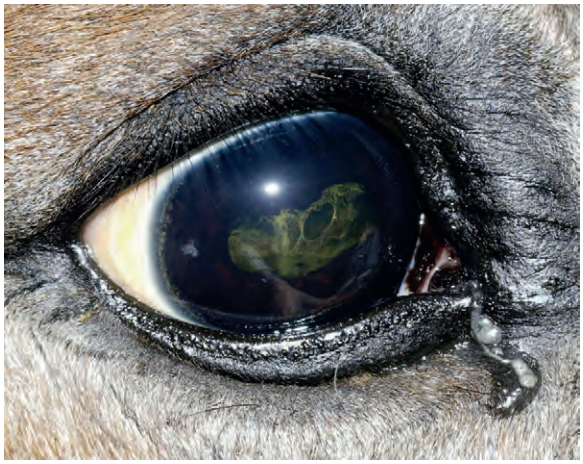


Figure 13-12. Acute uveitis associated with neonatal septicemia. The earliest sign of septic uveitis is a green hue to the iris caused by fibrin seeping from the uveal vessels.

Figure 13-13. Seventeen-year-old Tennessee Walking horse gelding with retropharyngeal swelling characteristic of strangles. The classic presentation of strangles involves acute onset of fever and nasal discharge, with swelling and abscessation of the retropharyngeal and submandibular lymph nodes.

flare, hypopyon, hyphema, hyperemia of the conjunctival and ciliary vessels, and deep peripheral corneal vascularization. Most cases will present bilaterally. If the foal survives, the prognosis for vision is good.[113] Diagnosis is based on clinical signs, hematologic analysis, and a positive blood culture. Treatment includes appropriate antibiotic therapy, administration of colostrum or hyperimmune plasma, gastroprotectants, treatment of endotoxemia, fluid and nutritional support, flushing of joints or removal of an infected umbilicus if necessary, and general supportive care for recumbent foals, including appropriate ventilatory support. Gram-negative bacteria are frequently isolated from foals with sepsis, and initial antibiotic therapy should include broad-spectrum antibiotics with good gram-negative coverage while results of culture and sensitivity are pending. Prognosis often depends on the initial response to treatment and the development of secondary complications.

STRANGLES

Strangles is a common disease caused by *Streptococcus equi* var. *equi*, a gram-positive bacteria with a predilection for lymph tissue. The classic presentation of strangles involves acute onset of fever and nasal discharge, with swelling and abscessation of the retropharyngeal and submandibular lymph nodes (Fig. 13-13). Initial ocular signs include serous discharge followed by mucopurulent discharge; panophthalmitis[114] and chorioretinitis[115] have also been reported. In a separate case, blindness was caused by a brain abscess.[116] Diagnosis is based on culture of the abscess fluid or PCR of nasopharyngeal or guttural pouch washes. The disease is highly contagious and spreads through direct contact or aerosolization or by fomites. In rare instances, horses with long-term carrier status have been described and may serve as reservoirs that can introduce the disease into naïve herds.[117] Recent evidence suggests that horses may carry the bacteria for extended periods in the guttural pouch and can maintain infections within a herd through this route.[118] Culture and/or PCR of the guttural pouch may be a more sensitive method of identifying carriers of the disease than the pharyngeal swabs that were recommended in the past.

Treatment of strangles remains controversial. Recommendations on the use of antibiotics depend on the stage of the disease. Horses that are at risk for exposure to strangles but do not yet have a fever or any other clinical signs will often benefit from vaccination with or without a short course of antibiotics. Horses that have been exposed and are already exhibiting fever and anorexia should not be vaccinated, and antibiotic administration at this time must be prolonged because horses may be more susceptible to the disease once the therapy is stopped. Many veterinarians recommend letting the disease run its course, rather than administering antibiotics at this stage. Once a horse has abscesses in the lymph nodes, antibiotics are thought to only prolong the course of the disease. Rupture and drainage of the lymph nodes should be encouraged by hot packing the area or establishing open drainage. NSAIDs may be given at this time if the horse has a high fever or is not eating or drinking well. Horses that have complications from strangles should be treated with appropriate antibiotics. Penicillin or ceftiofur are the antibiotics of choice for treating infections with *Streptococcus equi*. The organism may also be sensitive to tetracyclines, chloramphenicol, and trimethoprim-sulfa, although culture and sensitivity testing are recommended if one of these drugs is to be used.

Complications associated with strangles include acute upper airway obstruction, bastard strangles, guttural pouch empyema, and purpura hemorrhagica. The enlarged lymph nodes and associated pharyngeal swelling may occlude the upper airway, necessitating an emergency tracheostomy. Once a patent airway has been established, the lymph nodes should be drained to further improve airflow. The term *bastard strangles* refers to spread of the infection to distal sites, including the cranial mediastinal, mesenteric, and inguinal lymph nodes or other organs such as the lungs, liver, kidneys, and brain.[119] This form of the disease is often difficult to treat and requires long-term antibiotic therapy unless a discrete abscess is found and can be successfully removed or drained. Guttural pouch empyema may result from rupture of the retropharyngeal lymph node directly into the pouch, or it may be a consequence of hematogenous spread. Daily lavage of the guttural pouches and establishment of ventral drainage for the abscess are often suc-

cessful in clearing the organism, although surgical drainage of the affected pouch or pouches may be necessary. Instillation of a gel containing sodium penicillin into the affected pouches may shorten the course of the disease.[120] Purpura hemorrhagica is an immune-mediated leukocytoclastic vasculitis that causes mucosal petechiation and severe edema of the head, limbs, and ventral abdomen (Fig. 13-14). Clinical signs usually develop 2 to 4 weeks after acute infection, although they have also been documented to occur after vaccination with products containing the M protein of *Streptococcus equi* in horses exposed to the disease that did not have clinical infection or horses that have recovered from the disease and are reexposed.[121] Anemia, neutrophilia, hyperproteinemia caused by a hyperglobulinemia, hyperfibrinogenemia, high muscle enzyme levels, and azotemia are frequently noted.[121-123] The azotemia may be prerenal, or it may be a result of glomerulonephritis caused by immune complex deposition in the kidneys.[124] Treatment consists of corticosteroids, antibiotics (preferably intravenous potassium penicillin), bandaging of the lower limbs to help decrease the edema, and supportive care with treatment of any secondary infections. The prognosis is good if horses are treated early and aggressively.[121] Cellulitis, myositis, sloughing of the skin, laminitis, diarrhea, and pneumonia may all occur as a result of purpura and should carry a poor prognosis. Other less common complications associated with strangles include rhabdomyolysis and myositis, endocarditis, myocarditis, laryngeal hemiplegia, bronchopneumonia, and septicemia.

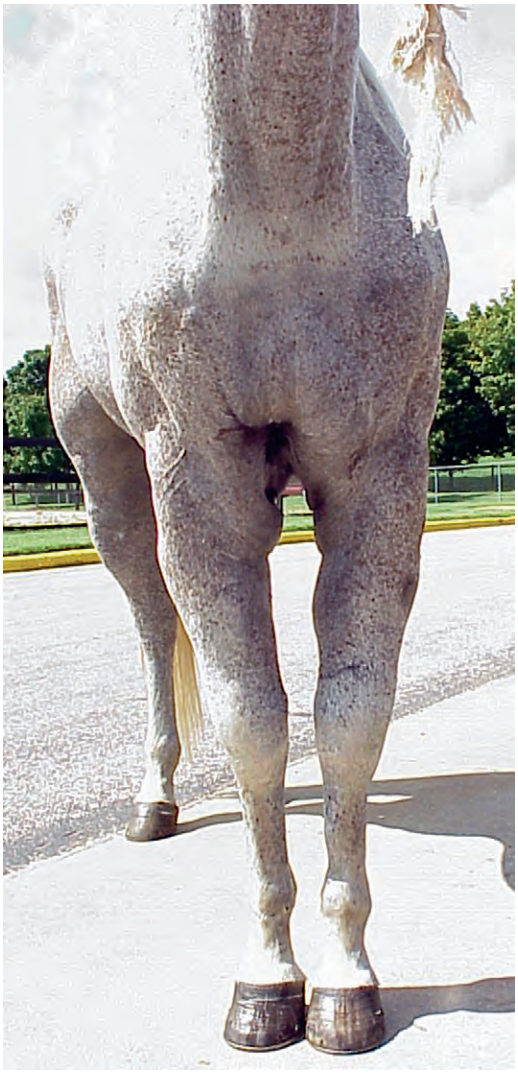


Figure 13-14. Twelve-year-old Quarter Horse gelding with severe vasculitis attributed to purpura hemorrhagica that developed 2 months after he recovered from an episode of strangles. Purpura hemorrhagica is an immune-mediated leukocytoclastic vasculitis that causes mucosal petechiation and severe edema of the head, limbs, and ventral abdomen.

RHODOCOCCUS EQUI

Ocular manifestations of *Rhodococcus equi* infection typically include uveitis and hyphema and may relate to septicemia or immune-mediated causes (Box 13-7).[7] Clinical signs of uveitis include epiphora, blepharospasm, photophobia, corneal edema, conjunctival hyperemia, aqueous flare, hyphema, hypopyon, fibrin in the anterior chamber and/or vitreous, and miosis (Fig. 13-15).[55] The posterior segment may be difficult to examine because of anterior segment changes. Severe infections can present with panuveitis and vitreal abscess formation.[68]

R. equi is a gram-positive pleomorphic bacillus that survives for long periods in the soil. Adult horses are resistant to infection unless an underlying immunodeficiency is present. Young foals exposed to the organism within the first several weeks of

Box 13-7 | Systemic Illness Causing Anterior and/or Posterior Uveitis

- Adenovirus
- Equine infectious anemia
- Neonatal septicemia
- Strangles
- *Rhodococcus equi*
- Lyme disease
- Brucellosis
- Leptospirosis
- Equine granulocytic ehrlichiosis
- Onchocerciasis
- *Setaria* spp.
- *Dirofilaria immitis*
- Mare reproductive loss syndrome

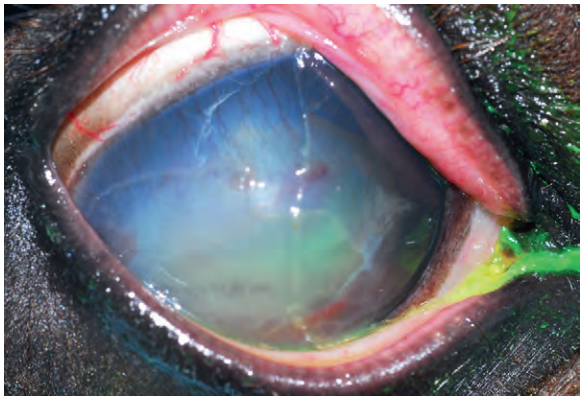


Figure 13-15. Uveitis secondary to *Rhodococcus equi* infection in a 4-month-old Saddlebred colt.

life are most susceptible to disease; however, they do not often show clinical disease until they are between 1 and 6 months of age, with signs of fever, cough, nasal discharge, and varying degrees of respiratory distress.[125] Radiographically, the disease is characterized by the presence of nodules (pyogranulomas) throughout the lungs and areas of consolidation, typically found in the ventral lung fields (Fig. 13-16). Diarrhea, peritonitis, subcutaneous abscessation, joint effusion, osteomyelitis or septic physitis may also be present.[125] Diagnosis can be made on the basis of clinical presentation, radiographic signs, and positive culture or PCR for the organism from transtracheal wash or bronchoalveolar lavage fluid. Blood work and serology can be used as screening tests for other foals on the farm. Neutrophilia and hyperfibrinogenemia will often be present before any clinical signs of the disease.

R. equi tends to form pyogranulomatous lesions that make the disease difficult to treat. The organism can also survive and replicate intracellularly within alveolar macrophages and neutrophils.[126] Historically, treatment has consisted of combination therapy with erythromycin estolate (25 mg/kg orally [PO] every 6 to 8 hours) or erythromycin phosphate (37.5 mg/kg PO every 12 hours) and rifampin (5 to 10 mg/kg PO every 12 hours) for several months. Newer macrolide and azalide antibiotics such as clarithromycin (7.5 mg/kg PO every 12 hours) and azithromycin (10 mg/kg PO every 24 to 48 hours) offer a better choice for therapy, as treatment courses are shortened, less frequent dosing is required, higher intracellular drug concentrations are achieved, and there is a lower incidence of adverse effects.[127] Rifampin is often added to treatments with either clarithromycin or azithromycin as well. Additional supportive therapy such as provision of fluids, nasal insufflation of oxygen, administration of NSAIDs for high fevers, and ulcer prophylaxis may also be necessary. Hyperimmune plasma is available for administration on farms with confirmed cases of *R. equi* infection. The plasma should be administered within the first week of life and has been shown to reduce the incidence of disease.[128] No effective vaccine is available. The prognosis for foals with *R. equi* pneumonia is good so long as treatment is early and aggressive. Antibiotic therapy should be continued until all radiographic evidence of pneumonia has resolved. No significant adverse effects were seen in adult horses that had survived the disease as foals.[129]

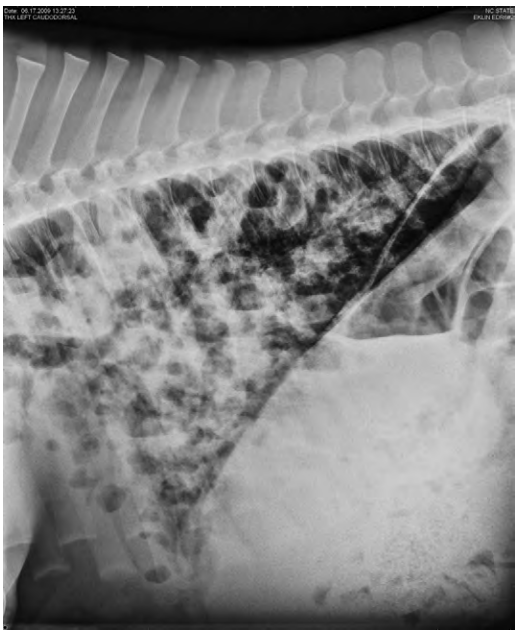


Figure 13-16. Radiograph of multiple pyogranulomas in a severe case of *Rhodococcus equi* infection in a 3-month-old Quarter Horse filly.

LYME DISEASE

Ocular manifestations of Lyme disease are nonspecific and include severe panuveitis and hyphema.[7,68] Spirochetes have been found within eyes with panuveitis, but antibodies to the organisms have not been found.[130] Neurologic disease affecting the eye can include facial nerve paralysis and resulting corneal disease (see Fig. 13-1 and Box 13-1).[131]

Lyme disease is caused by *Borrelia burgdorferi*, a tick-borne bacteria found throughout North America, Europe, and Asia. Western blot, immunofluorescent antibody test, and ELISA are available for serologic testing in horses. In the United States, seroprevalence of the disease varies greatly depending on the region of the country, ranging from 0.2% in Texas to 45% in the Northeast.[132,133] Clinical disease is considered rare. Polysynovitis, arthritis, and reluctance to move in seropositive horses from endemic areas are signs frequently attributed to *B. burgdorferi* infection.[134]

Reproductive dysfunction and neurologic disease have also been associated with Lyme disease.[130,135] Definitive diagnosis of the disease can be difficult because of the high seroprevalence in some areas. A positive response to treatment is considered a useful diagnostic aid in many cases. The organism is typically sensitive to tetracyclines, penicillins, and cephalosporins. Doxycycline (10 mg/kg PO every 12 hours) is considered the antibiotic of choice.

BRUCELLOSIS

Brucella abortus was a significant cause of uveitis (see Box 13-7) in horses until its near-eradication in the 1940s.[136] The organism has not been isolated from ocular tissues in horses with positive serum agglutination titers, so its role in recurrent uveitis is unclear.[136] *B. abortus* is now most frequently implicated as a cause of inflammation of the supraspinous bursa, known as *fistulous withers* in the horse. Initial clinical signs include heat, pain, and swelling over the withers. Eventually, a draining tract forms, and secondary contamination with other bacteria may occur. In one retrospective study of horses with fistulous withers, 37.5% were seropositive for *B. abortus*, and those horses usually had a history of being pastured with cattle and were significantly more likely to have osteomyelitis of the underlying vertebrae than were seronegative horses.[137] Definitive diagnosis is made by culture of the organism, which requires special media and culture conditions.[138] Treatment options include radical surgical excision of the affected area and subcutaneous injections of available cattle vaccines.[137,139] Recurrence after surgery is common, and reactions have been noted with vaccine administration. Brucellosis is a reportable disease, and personnel handling affected animals should wear gloves and masks to avoid exposure. Abortions are not associated with brucellosis in horses.

LEPTOSPIROSIS

Leptospirosis is one of the most commonly associated systemic diseases linked to equine recurrent uveitis (ERU). Experimental infection with leptospiral organisms results in clinical uveitis approximately 1 year after initial inoculation.[140] Blindness often results from chronic ERU that is poorly managed (Fig. 13-17). For a more complete description of ERU and the role of leptospirosis in ERU, see Chapter 8.

Leptospires are spirochete bacteria that are associated with disease in many species. Chronically or subclinically infected animals are the main source for spread of the disease. The *Leptospira interrogans* complex is associated with disease in humans and domestic animals. The serovars most frequently isolated in horses include *L. pomona*, *L. icterohaemorrhagiae*, *L. bratislava*, and *L. autumnalis*.[141] In horses, clinical manifestations aside from uveitis include acute renal failure in foals and stallions, hepatic failure in foals, neonatal deaths, and late-term abortions in mares.[142-145] Diagnosis is based on culture of the organism from blood, tissues, aborted fetuses, or urine. Administration of furosemide may help dislodge the organism from the bladder wall and increase the chance of a positive culture.[146] Dark-field microscopy and serology (ELISA or microscopic agglutination test) may also be useful, because culture is often difficult and may take as long as 6 months.[147] Treatment usually consists of antibiotic therapy with penicillins, tetracyclines, or dihydrostreptomycin, although these antibiotics have not been shown to prevent shedding of leptospires in the urine.[141]

EQUINE GRANULOCYTIC EHRLICHIOSIS

Equine granulocytic ehrlichiosis is caused by a rickettsial organism, *Anaplasma phagocytophilum* (formerly *Ehrlichia equi*), and has recently been discovered to be identical to the causative agent of human granulocytic ehrlichiosis and tick-borne fever of cattle and sheep in Europe.[148] Transmission occurs through *Ixodes* sp. ticks, and experimental transmission with infected tick vectors has been demonstrated.[149] The organism can be found in the cytoplasm of neutrophils and eosinophils of infected horses during the febrile period and can be detected with Giemsa stain or new methylene blue stain. Ocular signs include icteric sclera and petechiation of the bulbar and third eyelid conjunctival mucosa; uveitis may also be present.[150] Systemic clinical signs can include fever, thrombocytopenia, leukopenia, edema of the limbs, mucosal petechiation, icterus, and ataxia. The underlying pathology involves a vasculitis with decreased maturation or release of platelets from the bone marrow.[151] Cardiac arrhythmias may also be seen, possibly as a result of myocardial vasculitis.[134] Clinical signs are less severe in younger horses (<3 years old).[134] Diagnosis is based on clinical presentation, characteristic changes in laboratory blood tests, serology, and demonstration of the organism in buffy coat smears. Treatment with tetracyclines often results in resolution of fever within 12 to 24 hours and resolution of other clinical signs within 7 to 10 days.[134] The prognosis is good in most cases unless complications such as laminitis or secondary bacterial infections occur. No vaccine is currently available, but natural immunity persists for up to 300 days after infection, and no latency or carrier state has been detected.[152]

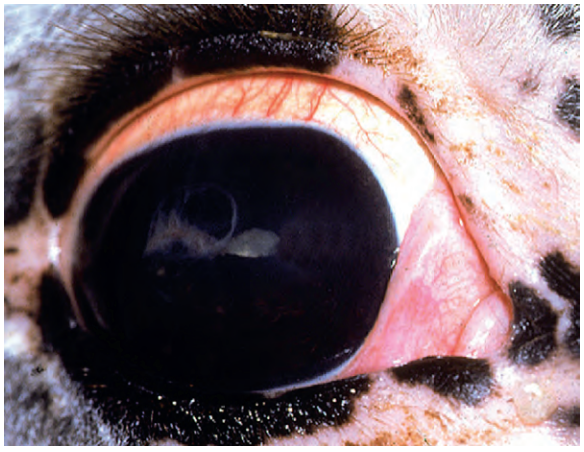


Figure 13-17. Blind and phthisical globe from an Appaloosa horse with chronic equine recurrent uveitis.

PROTOZOAL DISEASES

BABESIOSIS (PIROPLASMOSIS)

Ophthalmic signs of babesiosis include icteric conjunctiva and sclera, blepharoedema, and petechiae and ecchymoses of the conjunctiva, including the third eyelid conjunctiva.[153] Other signs include red-tinged and serous ocular discharge and distension of the supraorbital fossa.[7]

Piroplasmosis is a hemolytic disease of horses caused by *Babesia* sp. The horse is susceptible to two species, *B. caballi*, which is considered endemic in the United States, and *B. equi*. Diagnosis can easily be made from blood smears during the early febrile stages of the disease. *B. caballi* is large and appears as pairs visualized within the red blood cells. *B. equi* is smaller and is found in groups of four.[154,155] A negative complement fixation test result is required before a horse can be imported into the United States. Laboratory findings often seen include hemolytic anemia, jaundice, and hemoglobinuria. The severity of clinical signs (fever, anorexia, depression, ataxia, paresis, icterus, and ocular signs) depends on the organism, and *B. equi* is considered the more pathogenic of the two.[154] Chronic disease may occur, with intermittent fevers and anemia that lasts for months. Treatment involves administration of imidocarb dipropionate (2.2 mg/kg given intramuscularly [IM] every 24 hours for two doses). This has been shown to be reasonably effective for treatment of *B. caballi*, but higher doses for longer periods may be necessary to treat *B. equi*.[156] Adverse effects of imidocarb at higher doses include colic, hypersalivation, diarrhea, and death. Addition of parvaquone or buparvaquone may help with therapy but, when given alone, may cause treated horses to become carriers.[156,157]

TOXOPLASMOSIS

Seroprevalence of antibodies to *Toxoplasma gondii* in horses in the United States ranges from 7% to 10%, but cases of actual clinical disease are rare.[158] Horses fed viable oocysts will have cysts; however, they do not shed the organism.[159] *T. gondii* was originally thought to be the causative agent of EPM, but this has since been disproved. It is a rare cause of abortion in the horse. Horses seem to be resistant to ocular manifestations of

toxoplasmosis. One case of peripapillary and partial optic nerve atrophy in a horse with toxoplasmosis has been reported,[160] but there are no other cases in the literature in which *T. gondii* is cited as the cause of ocular disease in horses. In one study, investigators examined three separate horse populations in India and found that in the few horses with ocular lesions, there was no correlation with positive titers for *T. gondii*.[161] Another study of 71 horses showed that toxoplasmosis was not associated with ERU.[162]

FUNGAL DISEASES

CRYPTOCOCCOSIS

Cryptococcus neoformans is a pathogenic fungus that has been known to infect both healthy horses and those with a history of severe illness. Clinical manifestations include abortion, pneumonia, and less commonly, abdominal abscesses, meningitis, and subcutaneous, nasal, or sinus granulomas.[122,163-166] Ocular signs of equine cryptococcosis have not been reported, although blindness and optic neuritis secondary to meningitis[27] and a retrobulbar mass causing exophthalmos and periorbital distension[167] (see Box 13-6) have been reported. Diagnosis is based on histopathologic evidence of the organism in tissue samples or on cytology, as well as a positive culture. Lung biopsy should be performed to confirm the presence of fungal infection in cases of pneumonia, because fungal organisms have been identified in transtracheal aspirates from healthy horses.[168] Systemic cryptococcosis has a very poor prognosis, and treatment is often not attempted.[164] Cryptococcal organisms are typically sensitive to fluconazole, and this may provide an effective and affordable option if treatment is attempted. Prolonged treatment is recommended and may be as long as 6 months.[27] Abortions caused by *Cryptococcus* spp. usually occur in late gestation and may be associated with infertility.[169]

EPIZOOTIC LYMPHANGITIS

Epizootic lymphangitis is caused by *Histoplasma farciminosum*, a fungal agent found mainly in Africa. It causes cordlike lesions of the subcutaneous lymphatic system or cutaneous pyogranulomas.[170] A conjunctival form of this disease occurs as a result of deposition of the organism on the ocular mucous membranes by biting flies (*Musca* and *Stomoxys* sp.). The initial lesion is a medial canthal swelling that causes purulent discharge and tear eczema.[171] Progression of the disease can result in obstruction and erosion of the lacrimal duct, which can eventually create a fistula between the orbit and the maxillary sinus.[172] Diagnosis is mainly made by cytology and culture, although serologic assays are also available.[170] Amphotericin B is the treatment of choice, and a vaccine is available for horses in endemic areas.

ASPERGILLOSIS

Aspergillus spp. are considered opportunistic fungi that rarely cause disease in nonimmunocompromised horses. Ocular signs of aspergillosis are often manifested as corneal ulceration or abscessation caused by trauma (Fig. 13-18). This manifestation is described in Chapter 5. Aspergillosis is a cause of guttural pouch mycosis, and ocular manifestations can include Horner's syndrome, facial nerve palsy, and blindness caused by ischemic optic neuritis resulting from compression of the optic nerve or chiasm by a granuloma or infarction.[173-177] Other systemic clinical syndromes seen are similar to those described for cryptococcosis. The development of pulmonary aspergillosis has been significantly associated with severe enteritis in the horse, indicating hematogenous spread through a breakdown in the mucosal barrier of the gut wall.[178] The organisms are ubiquitous in the environment, and horses are frequently exposed. Inhalation of the antigen can produce a severe inflammatory reaction in the lungs of horses with recurrent airway obstruction.[179] Late-term abortions can also be seen as a result of aspergillosis. Treatment with systemic antifungal agents may be attempted, but the prognosis is always guarded because of the underlying disease process present and the severity of the lesions.[180] The organism is susceptible to many of the azole antimicrobial drugs, such as ketoconazole, itraconazole, and miconazole; however, it is often resistant to fluconazole. A newer azole drug, voriconazole, may be useful for the treatment of equine aspergillosis, although treatment is cost prohibitive in this species.[181]

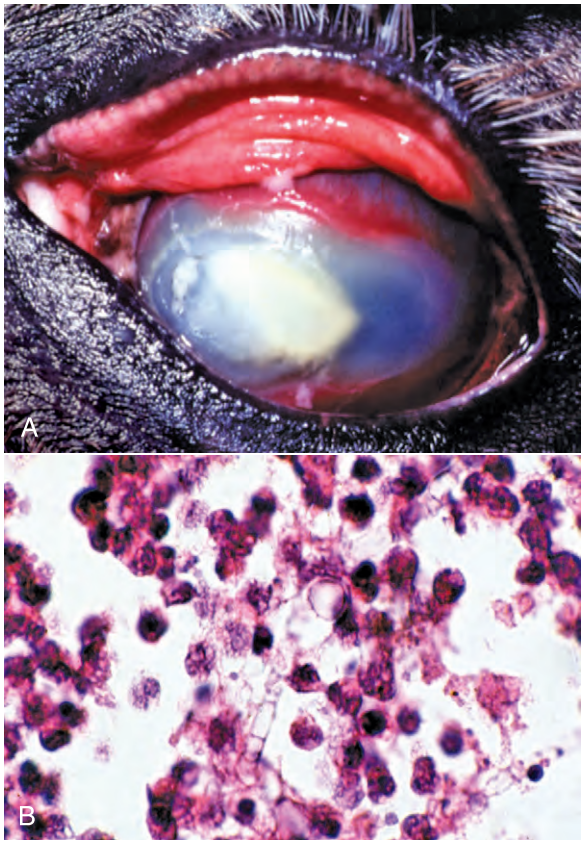


Figure 13-18. **A,** Chronic corneal ulceration and plaque formation typical of *Aspergillus* keratitis. **B,** Cytology sample with septate hyphae typical of *Aspergillus* spp.

PARASITIC DISEASES

ONCHOCERCIASIS

Onchocerca cervicalis is spread by *Culicoides* spp. and is a common cause of dermatitis in horses. Adult parasites live in

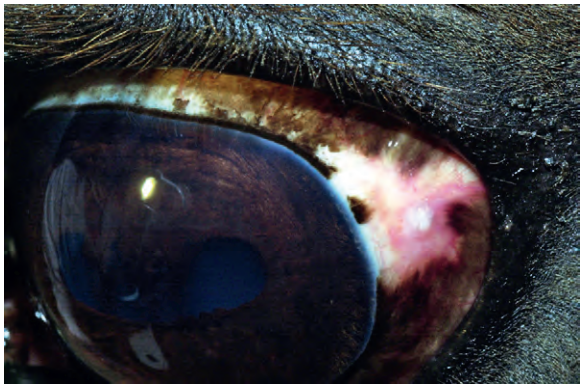


Figure 13-19. The most common ocular lesion evident is depigmentation of the conjunctiva at the temporal limbal region, which is typical of onchocerciasis infection.

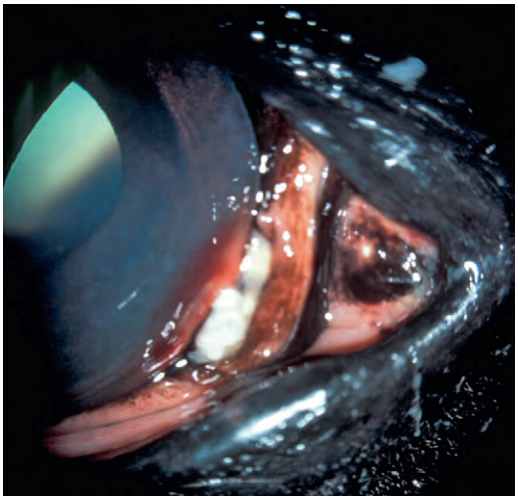


Figure 13-20. Habronemiasis of the medial canthus and third eyelid. (Photograph courtesy Dr. Mike Davidson.)

the nuchal ligament and can produce microfilaria for up to 5 years. The microfilaria then migrate through the subcutaneous tissues, particularly to the ventral midline, base of the mane, proximal forelimbs, and pectoral region. Actual disease is due to an immune reaction to the death of circulating microfilaria that causes a perivascular mononuclear dermatitis.[182] Ocular microfilariae have been reported in horses, and the prevalence varies by geographic location. The eastern United States has the highest prevalence, with 49% of 121 horses affected,[183] and the Midwest has the lowest prevalence, with 11% of 368 horses affected.[184] The most common ocular lesion evident is depigmentation of the conjunctiva at the temporal limbal region (Fig. 13-19).[185] Similar to systemic onchocerciasis, ocular disease is usually due to dead parasites releasing antigens that result in marked inflammation.[184] Other ocular manifestations include conjunctivitis, peripheral keratitis, and anterior and posterior uveitis. Conjunctivitis and keratitis are characterized by chemosis, corneal edema, corneal vascularization, and subepithelial yellow to white corneal opacities.[185] Keratitis is typically seen at the temporal limbus but can extend axially; this results from aberrant migration of the microfilariae that die in the corneal stroma, and keratitis can be accompanied by temporal conjunctivitis and anterior uveitis. Clinical signs of uveitis include epiphora, blepharospasm, miosis, and aqueous flare.[185] Signs of posterior uveitis, including peripapillary chorioretinitis or chorioretinal scarring (i.e., butterfly lesions), are often evident. Although onchocerciasis is often implicated in the pathogenesis of ERU, it is difficult to ascertain the true relevance of this disease because of the prevalence of the parasite in healthy horse populations. Ivermectin is effective in killing the microfilaria, but it will not kill the adult parasites.[186] Treatment may initially worsen clinical signs, and the disease may recur. Lesions are nonseasonal, and older horses are more likely to be infected than younger horses.[182]

CUTANEOUS HABRONEMIASIS

Also known as *summer sores*, cutaneous habronemiasis is caused by aberrant intradermal migration of the larvae of *Habronema* or *Draschia* spp., which are normally found in the stomach. Lesions develop in areas of traumatized skin and are caused by a hypersensitivity reaction to death of the larvae. Granulomas with necrotic centers are typically seen on the lower limbs and the urethral process, as well as the eye; mineralized larvae can often be found in the center of the lesion. Specific common ocular locations for habronemiasis include the eyelids, conjunctiva, lacrimal caruncle, and the third eyelids (Fig. 13-20; also see Chapter 4).[187] Conjunctival lesions are typically located near the medial canthus. Periocular or eyelid lesions have a raised, irregular, yellow appearance, often referred to as *sulfur granules*.[7] Biopsy of the affected area should be performed to aid in diagnosis and rule out other causes of ulcerative skin lesions, such as neoplasia, proud flesh, and bacterial or fungal granulomas.[188] On histopathologic examination, an eosinophilic infiltrate is seen in a fibrous stroma.[189] Treatment consists of an adequate deworming program that includes ivermectin, débridement of the lesions, topical and systemic antiinflammatory therapy, and adequate fly control.[190,191]

SETARIA

Setaria spp. have been documented as a cause of microfilaremia in horses. Systemic clinical signs include poor body condition, depression, stiff gait, and fever. Other clinical signs may be present based on aberrant migration of the parasite to distant sites such as the CNS and eye. *Setaria* spp. have been implicated as a cause of cerebrospinal nematodiasis in horses, sheep, and goats. Cattle are the natural hosts, and the parasites are transmitted to horses through mosquitoes and other blood-sucking insects.[192] Aberrant parasite migration can occur anywhere in the CNS. Spinal cord lesions are more common, and signs include an atonic tail and bladder, ataxia, and conscious proprioceptive deficits.[193] In horses, aberrant migration of *Setaria* into the eye also occurs, resulting in severe intraocular inflammation, photophobia, corneal opacity, blepharospasm and lacrimation.[194-196] Diagnosis can be made based on visualization of the parasite in the aqueous humor and detection of the microfilaria in the blood. Successful removal of the nema-

tode from the anterior chamber has been reported,[197] although complications from the surgery can include phthisis bulbi, corneal edema, and scarring and prolapse of the iris. Treatment with diethylcarbamazine (20 mg/kg IM) has been shown to resolve microfilaremia but requires multiple treatments and has not been documented to kill adult parasites in the eye.[196] A more recent report[195] documented successful treatment of equine ocular microfilariasis caused by *Setaria digitata* in three horses with a single subcutaneous dose of ivermectin (300 mcg/kg). Microfilaremia was resolved by day 7 after treatment, and adult ocular parasites died between 15 and 17 days after treatment. Removal of the dead parasites was not necessary, and all ocular signs had resolved by 90 days after treatment. Antiinflammatory therapy should be instituted along with administration of antiparasitic agents.

DIROFILARIA IMMITIS

Arteriosclerosis secondary to adult *Dirofilaria immitis* parasites in the pulmonary vasculature has been diagnosed in a 20-month-old Quarter Horse stallion.[198] Intraocular migration of *D. immitis* is less common in horses than in carnivores, although successful removal of the nematode from the anterior chamber of a horse has been reported.[199]

ECHINOCOCCUS

Echinococcus granulosus is a small tapeworm. Dogs are the definitive hosts, and horses are considered intermediate hosts. Hydatid cysts with viable protoscolices have been found in the livers of some horses.[200] Exophthalmos is the only reported ocular manifestation of hydatid cyst disease in horses, and it is due to cysts in the orbital tissues. The only definitive treatment is surgical excision, and diagnosis is based on positive histopathologic identification.[201] Cysts are usually an incidental finding at necropsy, but they are of particular concern because they can cause severe disease in humans, who are also intermediate hosts.[202]

HALICEPHALOBUS DELETRIX

Halicephalobus (Micronema) deletrix is a small roundworm that is considered to be saprophytic, but it occasionally acts as a facultative parasite in horses and humans. Common organs affected include the brain, spinal cord, nasal and oral cavities, kidneys, and pituitary gland. Less affected organs include the lymph nodes, heart, lungs, liver, bones, and stomach. As with *Setaria* spp., the neurologic signs depend on the part of the CNS affected. *H. deletrix* is known to have a predilection for the basilar pituitary region of the brain, which may explain the high incidence of blindness reported with this disease.[203] Renal dysfunction caused by larval migration in the renal parenchyma and granulomatous nephritis may be found, often in combination with neurologic signs.[204] Clinical ocular signs include uveitis, granulomatous chorioretinitis, optic neuritis, and blindness.[205,206] Antemortem diagnosis is difficult, and necropsy reveals granulomatous lesions in affected organs. Treatment is often unsuccessful once neurologic signs have been noted. For single peripheral granulomatous lesions, ivermectin and diethylcarbamazine combined with antiinflammatory medications may be useful.[207]

MISCELLANEOUS DISORDERS

NEOPLASIA

Ocular and clinical signs of metastatic neoplasia depend on the site and extent of metastasis. Endoscopy, radiography, CT, ultrasonography, cytology, or biopsy of accessible lesions all aid in the diagnosis of neoplasia in the horse. Chemotherapy and radiation treatment are available, but these treatments are often cost prohibitive and not attempted because of the grave prognosis associated with most tumors.[208,209]

PRIMARY IMMUNODEFICIENCIES

To date, eight primary immunodeficiency diseases have been described in the horse. These include severe combined immunodeficiency, anemia and immunodeficiency of Fell pony foals, agammaglobulinemia, transient hypogammaglobulinemia, selective IgM deficiency, IgG deficiency, selective immunoglobulin deficiency, and common variable immunodeficiency.[95] A primary immunodeficiency disease should be considered in any foal that has an infection with a nonpathogenic organism, fails to respond to adequate therapy for treatment of infections, does not produce a response to a vaccine, has a persistently low leukocyte count or inappropriate numbers of circulating leukocytes, or has unexplained or prolonged fevers.[95] Adenovirus, *Pneumocystis carinii*, *Cryptosporidium parvum*, and *R. equi* are commonly isolated from foals with primary immunodeficiencies. Bronchopneumonia can be caused by adenovirus, enteritis can be caused by *Cryptosporidium parvum*, and arthritis and omphalophlebitis are common.[210] Uveitis can occur as a result of *R. equi*. Once a diagnosis of immunodeficiency is suspected, testing should be performed to classify the disease. Genetic testing for severe combined immunodeficiency in Arabian foals and specific tests for B-cell and T-cell quantification and function are available, including a complete blood cell count, lymph node biopsies, flow cytometry, radial immunodiffusion test for specific immunoglobulins, response to vaccination, intradermal hypersensitivity test, and in vitro blastogenesis.[95] With the exception of transient hypogammaglobulinemia and some cases of IgM deficiency, the prognosis is poor and treatment is unrewarding. Owners of Arabian foals with severe combined immunodeficiency should be cautioned not to breed either mares or stallions because the disease has been proven to be an autosomal recessive trait, and breeding a carrier horse will only perpetuate the disease.

HYPERKALEMIC PERIODIC PARALYSIS

Hyperkalemic periodic paralysis (HYPP) occurs as an autosomal dominant trait in Quarter Horses, American Paint horses, Appaloosas, and Quarter Horse crosses that can trace their lineage back to the Quarter Horse stallion, Impressive.[211] Horses with HYPP tend to be well muscled and, as such, have been preferentially selected in the show ring.[212] The defect involves a point mutation in the sodium channel of the muscle cells that results in a phenylalanine-leucine substitution.[213] When serum potassium levels are increased as a result of exercise, diet, or disease, the sodium channels fail to deactivate, leading to an influx of sodium into muscle cells and an outflow of potassium from the cells. This leads to persistent depolarization and mus-

cular weakness. Horses often appear healthy between attacks. In the early stages of an attack, horses may appear hyperexcitable, sweat profusely, and have focal muscle fasciculations. As the episode progresses, the fasciculations may spread to other muscle groups and produce a generalized weakness, which may result in ataxia, dog sitting, or total recumbency in severe cases.[214,215] The only ocular sign associated with HYPP is retraction of the globe by spasm of the retractor bulbi muscle, resulting in third eyelid elevation.[7] Electromyography may reveal complex repetitive discharges, myotonic potentials, and abnormal fibrillation potentials, even between attacks.[215] Homozygotes experience more frequent and severe episodes and may develop pharyngeal edema or laryngeal paralysis, which may become life threatening, especially in foals.[216] Serum potassium concentrations may or may not be elevated during an attack, but serum creatinine kinase activity is not high unless the horse becomes recumbent. A diagnosis of HYPP can be presumed on the basis of characteristic clinical signs and bloodlines. A DNA test has been developed for definitive diagnosis of the disease. Treatment is aimed at correcting hyperkalemia. Some mild cases may respond to light exercise. Slow intravenous infusion of calcium gluconate, glucose, or sodium bicarbonate can be used to treat a more severe attack. These treatments should be given as a 5% solution in 0.9% sodium chloride and administered to effect. Lactated Ringer's solutions should not be given to horses with HYPP, because they contain potassium. Acetazolamide, a carbonic anhydrase inhibitor that acts as a potassium-wasting diuretic, can be given orally in doses of 2 to 4 mg/kg twice a day as a preventative therapy in horses that experience frequent attacks. A proper diet is also important in preventing attacks. Legume hays such as alfalfa should be avoided, as well as foods containing molasses or oils. Grass hays, oats, corn, wheat, barley, and beet pulp are good alternatives. Medications should be given in corn syrup rather than molasses. Small, frequent feedings and regular exercise may also help decrease the incidence of attacks.

VITAMIN A DEFICIENCY

Vitamin A deficiency is rare in horses grazing pastures or fed good-quality commercially available diets. Those animals that are deficient may show stunted growth, decreased hematopoiesis, or reproductive problems.[217,218] Ocular signs associated with hypovitaminosis A include epiphora and night blindness.[219] In addition, the cornea may become hyperkeratinized, and the conjunctival goblet cells may become atrophied. Chronic vitamin A deficiency can result in complete blindness with dilated unresponsive pupils.[220] Decreased serum concentrations of iron, albumin, and cholesterol may also be observed.[217] Serum retinol concentrations or the retinol dose-response test may be used for diagnosis.[218] Vitamin A supplements are available for horses fed deficient diets.

SYSTEMIC LUPUS ERYTHEMATOSUS

A 2-year-old Standardbred filly with weight loss, alopecia, seborrhea, oral ulceration, lymphadenopathy, and hemolytic anemia with positive Coombs and antinuclear antibody test results was given a diagnosis of systemic lupus erythematosus.[221] A skin biopsy specimen revealed characteristic interface dermatitis with immunoglobulin deposition in the basement membrane. Immunosuppressive therapy was attempted but was not successful. Ocular lesions, though not noted in this report, may include alopecia of the periorbital skin and lesions of the mucocutaneous eyelid margins.[68,222]

PEMPHIGUS

Pemphigus foliaceus is an autoimmune vesiculobullous disorder characterized by intraepidermal acantholysis (loss of cell-cell adhesions), intercellular deposition of IgG and complement on mucocutaneous junctions, and circulating autoantibodies.[223] Appaloosas are predisposed to the disease, although it can occur in other breeds.[224] Clinical signs may wax and wane but initially consist of vesicles or pustules that rapidly progress to crusts and erosions with alopecia, scaling, and epidermal collarettes (Fig. 13-21).[224] Lesions are most commonly seen on the head, ventrum, and limbs, especially around the coronary band. Anorexia, weight loss, edema, fever, and rarely, pruritus may be evident. Pemphigus may affect the eyelids and conjunctiva.[225] Diagnosis is based on the characteristic histologic changes seen on cytologic examination of skin biopsy specimens or vesicular fluid. Treatment consists of immunosuppressive therapy such as corticosteroids (prednisolone, 2 mg/kg given PO every 24 hours, or dexamethasone, 0.2 to 0.5 mg/kg given intravenously every 24 hours initially, then tapered to lowest dose that controls clinical signs) or injectable gold salts (aurothioglucose 1 mg/kg given intramuscularly once a week until a response is seen, then once monthly).[224,226] The prognosis is guarded in adult horses, although in foals and younger horses, the disease may spontaneously regress by 1 year of age.[224]

NEONATAL ISOERYTHROLYSIS

Neonatal isoerythrolysis is a primary immune-mediated hemolytic anemia of foals that occurs when the mare produces antibodies (alloantibodies) against a red blood cell antigen inherited from the stallion (alloantigen) that is not present in the mare.[227] In most cases, the antibodies are directed against the Aa or Qa factor. These antibodies are then passed to the foal in the mare's colostrum, resulting in lysis of the red blood cells and hemagglutination. Before development of these alloantibodies by the mare, the dam must become sensitized to the red blood cell

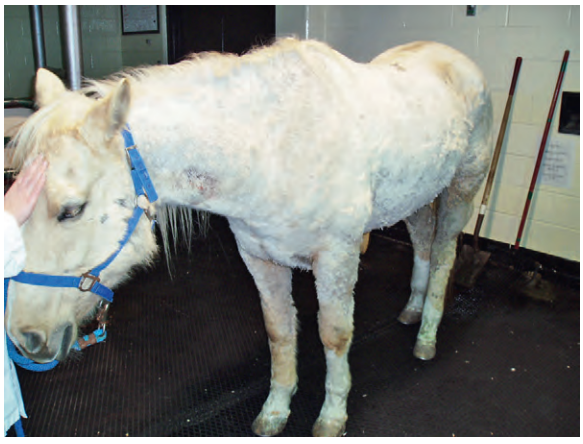


Figure 13-21. Pemphigus foliaceus in a 4-year-old Quarter Horse mare.

factor, either by exposure during a prior pregnancy or blood transfusion, or rarely, by transplacental exposure during the current pregnancy. The foal must have inherited the factor from the sire. The incidence of neonatal isoerythrolysis varies among breeds, with Thoroughbreds and Standardbreds being more likely to have the disease. The incidence may be as high as 10% in mule foals, with antibodies directed against donkey factor, a red blood cell factor unique to mules.[228] Foals are usually healthy at birth, with clinical signs developing 12 to 36 hours after ingestion of colostrum. Weakness, lethargy, loss of suckle, and varying degrees of tachypnea, tachycardia, and dyspnea occur. The mucous membranes, including those of the conjunctivae, are initially pale, then become icteric as the disease progresses. Anemia, hyperbilirubinemia, thrombocytopenia, hemoglobinemia, and hemoglobinuria may be noted on blood tests and urinalysis. Other ocular signs can include conjunctival, episcleral, and intraocular hemorrhages.[68] In severe cases, seizures and death occur as a result of hypoxia.

Diagnosis is made on the basis of a hemolytic crossmatch between the mare's serum or colostrum and the foal's red blood cells, the result of a direct Coombs test, or a saline agglutination crossmatch.[123] Treatment should be aimed at preventing further colostrum absorption, ensuring adequate nutrition, supportive care, and stall rest; nasal oxygen or blood transfusions may be given as necessary.[229] Blood transfusions should be washed red blood cells from the mare or blood from an unrelated gelding. In the case of mules, any unrelated horse is a suitable donor, because horses do not produce the donkey factor. Owners should be educated that the mare should not be bred with the same stallion or other stallions with the same blood factor. If the mare is bred with a stallion that has the same blood factor, the next foal should not be allowed to suckle the mare's colostrum and will need an alternate source of antibodies, such as colostrum from another mare that does not have the alloantibodies or a commercially available hyperimmune plasma solution.

EQUINE CUSHING'S DISEASE

Equine Cushing's disease (ECD) is caused by a dysfunction of the intermediate lobe of the pituitary gland, leading to hyperplasia resulting from a loss of dopaminergic inhibition. This produces an increase in the pro-opiomelanocortin–derived peptides produced in the pituitary, including corticotropin, α-melanocyte–stimulating hormone, endorphin, and corticotropin-like intermediate lobe peptide. Corticotropin, α-melanocyte–stimulating hormone, and endorphin all provide positive feedback to the adrenal glands, resulting in an increased production of glucocorticoids from the adrenal cortex.[230] The hyperplastic pars intermedia may also lead to compression of the adjacent pars distalis and pars nervosa. Clinical signs associated with ECD include polyuria/polydipsia, hirsutism (Fig. 13-22), failure to shed, hyperhidrosis, muscle wasting, recurrent or chronic infections, delayed wound healing, laminitis, parasitism, pseudolactation, seizures, and occasionally, secondary diabetes mellitus or diabetes insipidus.[230,231] Ocular manifestations of Cushing's disease in horses include bulging of the supraorbital fat pad caused by fat redistribution,[232] conjunctival edema, and abnormal vision. Abnormal vision is due to compression of the optic chiasm or cataracts caused by chronic elevated cortisol levels (R. Toribio, personal communication, 2003).

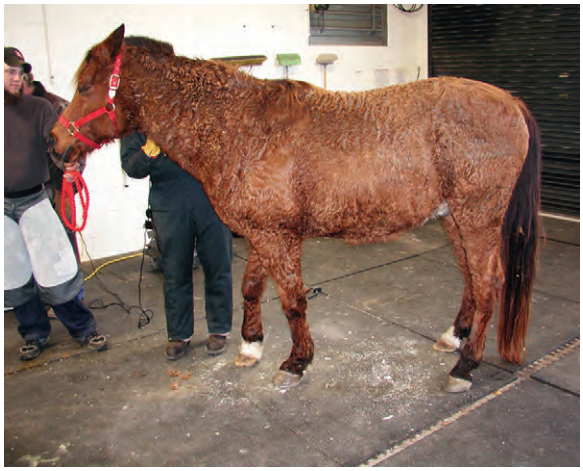


Figure 13-22. Classic haircoat (hirsutism) of equine Cushing's disease on a 28-year-old Quarter Horse.

A diagnosis of ECD is often based on the typical history and clinical signs seen in an older horse. Changes may be noted on hematologic analyses, including a mature neutrophilia, lymphopenia, hyperglycemia, and high alkaline phosphatase activity, although these findings are inconsistent, and the results of blood tests may actually reflect an underlying disease process. Numerous laboratory tests for the definitive diagnosis of ECD are available.[230,231,233,234] Elevations in baseline corticotropin (ACTH) and insulin levels are considered to be good screening tests for ECD but should be used in conjunction with other tests. Additionally, glucose tolerance tests can be used. Horses with ECD will not show an increase in insulin concentrations after intravenous glucose administration. Baseline cortisol levels are not reliable indicators because of the diurnal variation in cortisol secretion found in the horse. The cortisol rhythm test can also be used as a screening test and involves the measurement of cortisol levels in the morning and then again 8 to 10 hours later. Horses with ECD will have less than 30% variation between the two samples. Cortisol levels in horses with ECD will be increased in response to stimulation with thyrotropin-releasing hormone. Corticotropin stimulation tests are not considered reliable indicators of Cushing's disease in horses.

The low-dose dexamethasone suppression test (DST) is considered the gold standard for diagnosis of ECD. This test is the most accurate and reliable indicator of ECD and should be used in all cases unless the horse is having an acute episode of laminitis that may be exacerbated by the administration of steroids. The test can be administered several ways, although the overnight DST is the most widely used procedure because it is the easiest and most convenient test to perform. Blood is collected for measurement of plasma cortisol levels in an EDTA tube immediately before and 19 hours after intramuscular administration of 40 mcg/kg dexamethasone. Horses with ECD will not show any significant decrease in cortisol production. The standard DST is considered more sensitive because it requires the collection of blood samples at 0, 8, 12, 16, 20, and 24 hours after administration of dexamethasone and is less likely to be influenced by diurnal variations in cortisol secretion. Horses may show a seasonal variation in response to dexamethasone suppression testing and ACTH secretion, therefore the time of

year the tests are performed should be taken into account when interpreting the results of such tests.

The treatment of ECD should always include excellent husbandry and preventive medicine. Horses should have proper and consistent farriery, dentistry, vaccination schedules, and parasite control. Proper diet and coat clipping of horses in hot climates are also essential. Many horses can be treated this way without additional therapy. Medical management involves the administration of either dopamine agonists or serotonin antagonists.[232] Pergolide (0.25 to 2 mg/kg PO every 24 hours) is the dopamine agonist most commonly used. Once the horse is receiving the lowest dose that is effective according to the results of the DST and clinical signs, it will need to receive that maintenance dose for the rest of its life. Cyproheptadine (0.25 to 1.2 mg/kg PO every 24 hours) is a serotonin antagonist that has been shown to be useful in the treatment of ECD and may be combined with pergolide in horses that don't respond to conventional therapy. As with pergolide, lifelong treatment is necessary.

HYPOTHYROIDISM

Thyroid gland dysfunction in the adult horse is rare and often misdiagnosed.[235] Treatment of hypothyroidism in horses is often initiated in overweight horses with cresty necks, based on single-point low thyroid hormone levels. However, experimental induction of hypothyroidism in adult horses produces little to no clinical signs, and complete surgical removal of the thyroid gland typically results in mild, nonspecific signs such as cold intolerance, changes in the haircoat, lethargy, exercise intolerance, and decreased feed intake.[236,237] True hypothyroidism can only be documented by use of thyrotropin-releasing hormone (TRH) and thyroid-stimulating hormone (TSH) stimulation testing.

Ocular signs were not noted in any of the horses with experimentally induced hypothyroidism, but there is a report of hypothyroidism and polyneuropathy causing keratoconjunctivitis sicca (KCS) in a horse.[238] The horse presented with bilateral blepharospasm, hyperemic and edematous conjunctiva, and dull corneas and had an abnormal Schirmer tear test. Signs of trigeminal and facial nerve dysfunction were also present, leading to a diagnosis of KCS secondary to damage to the parasympathetic pathways of the facial nerve. The KCS resolved after treatment with levothyroxine.

TRAUMA

Trauma to the head caused by falling over backward and striking the poll or blunt trauma from direct kicks or running forward into a fixed object is frequently associated with neurologic disease. Striking the poll can result in basilar skull fractures involving the nuchal crest, basisphenoid/basioccipital bone, occipital bone, or petrous temporal bone. Trauma to the poll can also result in acute unilateral or bilateral blindness caused by neuropraxia of the intracranial optic nerve.[239] The dural sheath that encases the optic nerve is fused with the periosteum of the optic canal, and traumatic concussive shock waves can cause stretching, shearing, or avulsion of the optic nerve and/or chiasm. Initially, findings on fundic examination may be normal, or intraocular hemorrhage may be seen; but with time, the optic nerve atrophies and the peripapillary retina degenerates (Fig. 13-23).[55,239,240] Damage to the brain and spinal cord may also result, with or without the presence of a fracture. Basilar skull fractures often result in unilateral vestibular signs toward the side of the lesion, and bilateral nystagmus present in the early stages has a fast component away from the side of the lesion, similar to those previously described.[241] In addition, hemorrhage from the nose and ears may be noted. Damage to the region of the petrous temporal bone may result in facial nerve paralysis and/or Horner's syndrome.[7,239] Keratoconjunctivitis sicca secondary to a presumed basilar skull fracture and damage to the lacrimal gland innervation has also been reported in one horse.[242] Diagnosis is based on the history of trauma combined with clinical signs and diagnostic imaging. A radiographic diagnosis may be difficult to establish because of the overlying soft tissue and bony structures. CT is more sensitive, but anesthesia is risky in horses with intracranial hemorrhage and increased intracranial pressure. Treatment is aimed at reducing inflammation in the CNS with corticosteroids, NSAIDs, and dimethyl sulfoxide. Mannitol has also been used for its osmotic effects to help decrease brain and spinal cord edema; however, it may worsen active hemorrhage and should be used with caution. Secondary infectious meningitis may result from skull base fractures; therefore broad-spectrum antibiotic coverage with drugs known to have good CNS penetration is recommended. The horse should be kept in a well-padded stall to prevent additional injury. Prognosis for horses with fractures is poor in most cases, and horses that do recover will often have residual deficits.

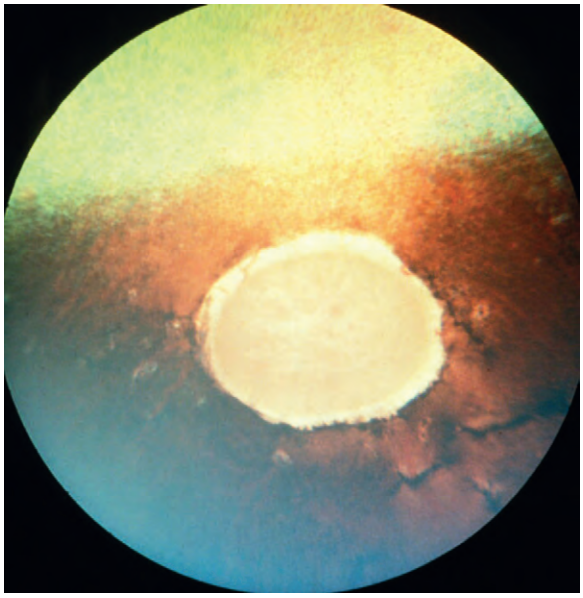


Figure 13-23. Optic nerve atrophy and peripapillary depigmentation 3 months after severe head trauma to the poll and subsequent blindness. Initially, findings on fundic examination may be normal, or intraocular hemorrhage may be seen, but with time, the optic nerve atrophies and the peripapillary retina degenerates.

Clinical signs that follow blunt trauma to the head may occur immediately after the incident or several days later if intracranial hemorrhage or inflammation is present. Depression, cranial nerve deficits, ataxia, and proprioceptive deficits in all four limbs are commonly seen.[243,244] Radiographs should be obtained or CT should be performed to determine whether fractures are

present. If fractures are present, they should be stabilized as soon as possible to prevent further damage. Treatment is similar to that described for basilar skull fractures, and the prognosis should be based on the progression of clinical signs.

AIR EMBOLISM

Venous air embolism via a jugular catheter is a rare cause of disease in adult horses.[245,246] Large volumes of air (>0.25 mL/kg) are necessary to cause clinical signs, although the rate of air embolism may also influence the development of signs. Reports in the literature of two horses with suspected air embolism document severe agitation, pruritus, pulmonary edema, vestibular disease, and blindness. Clinical signs, including blindness, resolved without specific treatment.

OPTIC NEURITIS

Optic neuritis has been reported in association with septicemia, parasite migration, trauma, hemorrhage, anemia, orbital cellulitis, guttural pouch disease, and intraarterial injections of phenylbutazone.[7]

IVERMECTIN TOXICOSIS

An overdose of the avermectin parasiticide, ivermectin, has been reported to cause mydriasis and cortical blindness in adult horses, foals, and other equidae such as mules and zebras.[247,248] Other clinical signs include ataxia, lethargy, depression, recumbency, coma, and potentially death. Young animals may be more sensitive because of an incomplete blood-brain barrier and greater penetration of the drug into the CNS. The mechanism of toxicity is thought to be related to the drug's effects on gamma-aminobutyric acid (GABA). Moxidectin, another avermectin, is also associated with toxicity, particularly in foals. Although blindness has not been specifically associated with toxicity, foals often present comatose, so assessment of vision is difficult.[249] Treatment is mainly supportive; sarmazenil, a benzodiazepine, may speed recovery.[250] Horses that survive the initial toxicity do not appear to have residual visual defects.

MARE REPRODUCTIVE LOSS SYNDROME

In the spring of 2001, and to a lesser degree 2002, a syndrome of early fetal loss, late-term abortions, stillbirths, and neonatal foal deaths occurred in Kentucky, Ohio, West Virginia, and Tennessee.[251] The syndrome was subsequently called *mare reproductive loss syndrome*, or MRLS. Aside from the reproductive losses, epidemics of fibrinous pericarditis and uveitis were also reported in horses of any age, sex, or breed during the same time period. The uveitis is described as peracute, severe exudative endophthalmitis and has been unilateral in all cases. Corneal edema, hemorrhage from the iris, and thick, proteinaceous, tan-yellow exudates are present in the anterior and posterior chambers. Culture and cytology of the affected eyes were negative. Treatment is based on systemic and topical antiinflammatory therapy but may not always be successful. Permanent visual deficits or blindness may result.

The exact cause of MRLS remains a mystery, but there is evidence that links the outbreaks to the presence of the eastern tent caterpillar (ETC). Ingestion of the caterpillars, either in feed or via nasogastric tube, has reproduced abortion in pregnant mares and swine. The ETCs are proposed to produce a toxin that either causes the abortion via effects on hormone production or causes immunosuppression and predisposition to bacterial infection.[252,253] Opportunistic bacteria, such as *Actinobacillus equuli*, have been found in a large proportion of cases of aborted fetuses and fibrinous pericarditis. However, administration of ETCs to horses has not reproduced either the fibrinous pericarditis or the unilateral uveitis. The epidemic of MRLS in Kentucky and the surrounding states appears to be over, but similar abortion storms have been reported in Australia, Florida, and New Jersey between 2004 and 2006. Eastern tent caterpillars were present at each site of the abortion outbreaks.

TOXIC PLANTS

Numerous toxic plants have been associated with ocular changes in the horse. Many of these cause neurologic signs leading to central blindness. Black locust trees *(Robinia pseudoacacia)* are common in the eastern states, and ingestion of the plant may cause gastrointestinal ileus, weakness, ataxia, and blindness. The clinical signs, including blindness, resolve with treatment. Plants containing thiaminases—such as horsetail *(Equisetum arvense)*, kochia weed *(Kochia scoparia)*, and bracken fern *(Pteridium aquilinum)*—can produce cortical blindness as seen with thiamine deficiency. Bracken fern is also associated with retinal degeneration caused by stenosis of the optic vessels and progressive retinal atrophy in sheep, although this has not been reported in horses. The toxic principle involved in the retinal degeneration is ptaquiloside, which also causes myeloid aplasia and bladder tumors in cattle, as well as gastrointestinal tumors in humans.[254,255] Locoweed (*Astragalus* spp.) can produce severe CNS signs in horses and is associated with poor vision.

Numerous other plants can cause cortical blindness by inducing severe hepatic failure. The most common plants associated with this are those containing pyrrolizidine alkaloids, including *Crotalaria* spp., *Amsinckia* spp., and *Senecio* spp. Pyrrolizidine alkaloids cause characteristic changes in the liver, such as megalocytosis, periportal fibrosis, and biliary hyperplasia, which are easily detected on biopsy specimens. The poisoning is usually chronic in nature, although signs of hepatic failure may develop immediately. Icterus of the sclera and mucous membranes often develops as a result of hyperbilirubinemia. Horses with hepatoencephalopathy show signs of depression, ataxia, aimless wandering, circling, head pressing, and blindness. Photophobia may also be present in horses that have secondary photosensitization if they lack pigment in the skin around the eyes or in the third eyelid. Once horses show signs of hepatic failure and encephalopathy, the prognosis is poor. Serum g-glutamyl transferase activity can be used as an early screening test for subclinical hepatic disease in horses grazing pastures with pyrrolizidine alkaloid–containing plants.[256] Other toxic plants associated with hepatic failure and cortical blindness in horses include alsike clover *(Trifolium hybridum)*, buckwheat *(Fagopyrum esculentum)*, and cow cockle *(Vaccaria pyramidata)*. St. John's wort *(Hypericum perforatum)* causes a primary photosensitization and potential photophobia without elevations in liver enzyme levels. Icteric sclera may also be noted in horses with hemolytic anemias and oxidative injury to the red blood cells caused by

ingestion of red maple *(Acer rubrum)* leaves or wild onions (*Allium* spp.).

One of the most common ocular signs of plant toxicity is mydriasis associated with the ingestion of plants containing tropane and other alkaloids. These compounds include atropine, hyoscine (scopolamine), hyoscyamine, and solanine and are found in jimson weed *(Datura stramonium)*, horse nettle *(Solanum carolinense)*, sacred datura *(Datura meteloides*, blindweed *(Convolvulus arvensis)*, nightshade *(Solanum nigrum)*, black henbane *(Hyoscyamus niger)*, buffalo bur *(Solanum rostratum)*, and ground cherry (*Physalis* spp.). The toxins work on the autonomic nervous system and have clinical signs similar to those seen with administration of atropine, including mydriasis, tachycardia, gastrointestinal ileus, and colic. Other toxic compounds have been associated with mydriasis. Oleander *(Nerium oleander)* causes mainly cardiovascular and gastrointestinal effects as a result of cardiac glycoside production, but mydriasis and impaired vision may also be seen. Water hemlock (*Cicuta* spp.) produces cicutoxin, a potent neurotoxin that causes violent convulsions, muscle tremors, and cardiac degeneration, as well as mydriasis. Organophosphate poisoning in horses is rare, but it can cause miotic pupils as it does in other species.

Some plants are not toxic in and of themselves but can produce toxic effects from the molds and fungi associated with them.[257] Yellow sweet clover infected with *Penicillium* or *Aspergillus* spp. can produce dicumarol that, when ingested, interferes with the vitamin K–dependent coagulation factors (II, VII, IX, X). This can lead to a bleeding diathesis in the animal, with hemorrhage into the anterior chamber. Corn infested with *Fusarium* spp. that produce the toxin fumonisin B1 can cause blindness, as discussed previously. Although the major toxic effect seen in horses exposed to black walnut trees (*Juglans nigra*) is a severe acute laminitis, the walnuts, when infected with *Penicillium* spp., may produce penitrem-A, a toxin that causes convulsions, hyperthermia, tachypnea, frequent urination, and mydriasis in many species.

Finally, some plants that produce burs or sharp projections can induce corneal trauma and ulceration. These include burdock (*Arctium* spp.), buffalo bur, and cocklebur (*Xanthium* spp.).

FUTURE RESEARCH

It is likely that diseases other than those described in this chapter can cause changes in the eyes and surrounding structures of the horse. In the future, careful examination of the ocular structures in all horses with systemic diseases may lead to the discovery of more ocular manifestations of disease and potentially useful diagnostic tools for general practitioners as well as ophthalmologists.

References

1. MacKay RJ: Equine protozoal myelitis. In Robinson NE, editor: Current therapy in equine medicine, ed 5, Philadelphia, 2000, Saunders, pp 69–74.
2. Mayhew IG: Horner's syndrome and lesions involving the sympathetic nervous system, Equine Pract 2:44–47, 1980.
3. Saville WJ et al: Analysis of risk factors for the development of equine protozoal myeloencephalitis in horses, J Am Vet Med Assoc 217:1174–1180, 2000.
4. Furr M: Update on EPM diagnosis. Proceedings of the American College of Veterinary Medicine Annual Forum, Montreal, Quebec, Canada; 2009.
5. Daft BM et al: Sensitivity and specificity of Western blot testing of cerebrospinal fluid and serum for diagnosis of equine protozoal myeloencephalitis in horses with and without neurologic abnormalities, J Am Vet Med Assoc 221:1007–1013, 2002.
6. MacKay RJ et al: Equine protozoal myeloencephalitis, Vet Clin North Am Equine Pract 16:405–425, 2000.
7. Stiles J: Ocular manifestations of systemic disease. Part 3. The horse. In Gelatt KN, editor: Veterinary ophthalmology, ed 3, Philadelphia, 1999, Lippincott Williams and Wilkins, pp 1473–1492.
8. De Lahunta A: Small animal neurologic examination and index of diseases of the nervous system. In De Lahunta A, editor: Veterinary neuroanatomy and clinical neurology, Philadelphia, 1983, Saunders, pp 365–387.
9. Wilkins PA et al: A herd outbreak of equine leukoencephalomalacia, Cornell Vet 84:53–59, 1994.
10. Uhlinger C: Clinical and epidemiologic features of an epizootic of equine leukoencephalomalacia, J Am Vet Med Assoc 198:126–128, 1991.
11. Ross PF et al: Experimental equine leukoencephalomalacia, toxic hepatosis, and encephalopathy caused by corn naturally contaminated with fumonisins, J Vet Diagn Invest 5:69–74, 1993.
12. Divers TJ: Spinal cord diseases causing paresis and atrophy in the limbs. In Robinson NE, editor: Current therapy in equine medicine, ed 5, Philadelphia, 2003, Saunders, pp 750–753.
13. Verhulst D, Barnett KC, Mayhew IG: Equine motor neuron disease and retinal degeneration, Equine Vet Educ 13:59–61, 2001.
14. Divers TJ et al: Equine motor neuron disease, Proc Am Coll Vet Intern Med 13:918–921, 1995.
15. De la Rua-Domenech R et al: Association between plasma vitamin E concentration and the risk of equine motor neuron disease, Vet J 154:203–213, 1997.
16. Polack EW et al: Concentrations of trace minerals in the spinal cord of horses with equine motor neuron disease, Am J Vet Res 61:609–611, 2000.
17. Kyles KW et al: Electromyography under caudal epidural anaesthesia as an aid to the diagnosis of equine motor neuron disease, Vet Rec 148:536–538, 2001.
18. Gibbs EPJ: Equine viral encephalitis, Equine Vet J 8:66–71, 1976.
19. Fontaine-Rodgerson G: Viral encephalitides. In Robinson NE, editor: Current therapy in equine medicine, ed 5, Philadelphia, 2003, Saunders, pp 47–50.
20. Schlipf J: Alphavirus and flavivirus encephalitis of horses. In Smith BP, editor: Large animal internal medicine, ed 3, St Louis, 2002, Mosby, pp 888–890.
21. Sahu SP, Alstad AD, Pedersen DD: Diagnosis of Eastern equine encephalomyelitis virus infection in horses by immunoglobulin M and G capture enzyme-linked immunosorbent assay, J Vet Diagn Invest 6:34–38, 1994.
22. Vanderwagen LC et al: A field study of persistence of antibodies in California horses vaccinated against Western, Eastern, and Venezuelan equine encephalomyelitis, Am J Vet Res 36:1567–1571, 1975.
23. Smith MO: Diseases of the nervous system. In Smith BP, editor: Large animal internal medicine, ed 3, St Louis, 2002, Mosby, pp 873–1018.
24. Fjeldborg J, Andresen PH, Svalastoga E: Osteomyelitis secondary to basilar skull fracture in a thoroughbred foal, Equine Pract 19:29–31, 1977.
25. Newton SA: Suspected bacterial meningoencephalitis in two adult horses, Vet Rec 142:665–669, 1998.
26. Santschi EM, Foreman JH: Equine bacterial meningitis. Part I, Compend Contin Educ Pract Vet 11:479–483, 1989.
27. Hart KA, et al: Successful resolution of cryptococcal meningitis and optic neuritis in an adult horse with oral fluconazole, J Vet Intern Med 22(6):1436–1440, 2008.
28. Bryant UK et al: Halicephalobus gingivalis-associated meningoencephalitis in a Thoroughbred foal, J Vet Diagn Invest 18(6):612–615, 2006.
29. Cymbaluk NF, Fretz PB, Loew FM: Amprolium-induced thiamine deficiency in horses: clinical features, Am J Vet Res 39:255–261, 1978.

30. Schryver HF, Hintz HF: Vitamins. In Robinson NE, editor: Current therapy in equine medicine, ed 11, London, 1983, Saunders, 1983, p 84.
31. Moore BR: Vestibular disease. In Reed SM, Bayly WM, editors: Equine internal medicine, Philadelphia, 1998, Saunders, pp 466–473.
32. Newton SA, Knottenbelt DC: Vestibular disease in two horses: a case of mycotic otitis media and a case of temporohyoid osteoarthropathy, Vet Rec 145:142–144, 1999.
33. De Lahunta A: Vestibular system-special proprioception. In De Lahunta A, editor: Veterinary neuroanatomy and clinical neurology, Philadelphia, 1983, Saunders, p 238.
34. Raphel CF: Brain abscess in three horses, J Am Vet Med Assoc 180:874–877, 1982.
35. Watrous BJ: Head tilt in horses, Vet Clin North Am Equine Pract 3:353–370, 1987.
36. Mayhew IG, Washbourne JR: A method of assessing auditory and brainstem function in horses, Br Vet J 146:509–518, 1990.
37. Marshall AE et al: Brainstem auditory evoked response in the diagnosis of inner ear injury in the horse, J Am Vet Med Assoc 178:282–286, 1981.
38. De Lahunta A: Lower motor neuron—general visceral efferent system. In De Lahunta A, editor: Veterinary neuroanatomy and clinical neurology, Philadelphia, 1983, Saunders, pp 115–129.
39. Scagliotti RH: Comparative neuro-ophthalmology. In Gelatt KN, editor: Veterinary ophthalmology, ed 3, Philadelphia, 1999, Lippincott Williams & Wilkins, pp 1307–1400.
40. Firth EC: Horner's syndrome in the horse: experimental induction and case report, Equine Vet J 10:9–13, 1978.
41. Green SL, Cochrane SM, Smith-Maxie L: Horner's syndrome in ten horses, Can Vet J 33:330–333, 1992.
42. Sweeney RW, Sweeney CR: Transient Horner's syndrome following routine intravenous injections in two horses, J Am Vet Med Assoc 185:802–803, 1984.
43. Robertshaw D, Taylor CR: Sweat gland function of the donkey *(Equus acinus)*, J Physiol 205:79–89, 1969.
44. Purohit RC, McCoy MD, Bergfeld WAR: Thermographic diagnosis of Horner's syndrome in the horse, Am J Vet Res 41:1180–1182, 1980.
45. Smith JS, Mayhew IG: Horner's syndrome in large animals, Cornell Vet 67:529–542, 1977.
46. Wilkins CA et al: Occurrence of *Clostridium tetani* in soils and horses, S Afr Med J 73:718–720, 1987.
47. Green SL et al: Tetanus in the horse: a review of 20 cases (1970 to 1990), J Vet Intern Med 8:128–132, 1994.
48. Messer NTT: Serum hepatitis in two brood mares, J Am Vet Med Assoc 204:1790–1792, 1994.
49. Hambleton P: Clostridium botulinum toxins: a general review of involvement in disease, structure, mode of action and preparation for clinical use, J Neurol 239:16–20, 1992.
50. Lavach JD: Systemic disease. In Lavach JD, editor: Large animal ophthalmology, St. Louis, 1990, Mosby, pp 240–251.
51. Whitlock RH: Botulism. In Smith BP, editor: Large animal internal medicine, ed 3, St. Louis, 2002, Mosby, pp 1003–1008.
52. Galey FD: Botulism in the horse, Vet Clin North Am Equine Pract 17:579–588, 2001.
53. Rodrigues A et al: Neuropathology of naturally occurring *Trypanosoma evansi* infection of horses, Vet Pathol 46:251–258, 2009.
54. Berlin D, Loeb E, Baneth G: Disseminated central nervous system disease caused by *Trypanosoma evansi* in a horse, Vet Parasitol 161:316–319, 2009.
55. Brooks DE: Equine ophthalmology. In Gelatt KN, editor: Veterinary ophthalmology, ed 3, Philadelphia, 1999, Lippincott Williams and Wilkins, pp 1053–1116.
56. Madigan JE: Head shaking in horses. In Smith BP, editor: Large animal internal medicine, ed 3, St. Louis, 2002, Mosby, pp 945–946.
57. Newton SA, Knottenbelt DC, Eldridge PR: Headshaking in horses: possible aetiopathogenesis suggested by the results of diagnostic tests and several treatment regimes used in 20 cases, Equine Vet J 32:208–216, 2000.
58. McNamara JO: Drugs effective in the therapy of epilepsies. In Hardman JG, Limbird LE, editors: Goodman and Gilman's the pharmacological basis of therapeutics, ed 10, New York, 2001, McGraw-Hill, pp 521–548.
59. Hardy J, Robertson JT, Wilkie DA: Ischemic optic neuropathy and blindness after arterial occlusion for treatment of guttural pouch mycosis in two horses, J Am Vet Med Assoc 196:1631–1634, 1990.
60. Gelatt KN: Neuroretinopathy in horses, Equine Med Surg 196:1631–1634, 1979.
61. van Maanen C et al: Three cases of carcinoid in the equine nasal cavity and maxillary sinuses: histologic and immunohistochemical features, Vet Pathol 33:92–95, 1996.
62. da Costa P, Merideth R, Sigler R: Cataracts in dogs after long-term ketoconazole therapy, Vet Comp Ophthalmol 6:176–180, 1996.
63. Dixon PM, Head KW: Equine nasal and paranasal sinus tumours. Part 2. A contribution of 28 case reports, Vet J 157:279–294, 1999.
64. Head KW, Dixon PM: Equine nasal and paranasal sinus tumours. Part 1. Review of the literature and tumour classification, Vet J 157:261–278, 1999.
65. Döpke C et al: Metastatic esthesioneuroblastoma in a horse, J Comp Pathol 132:218–222, 2005.
66. Davis JL et al: Nasal adenocarcinoma with diffuse metastases involving the orbit, cerebrum, and multiple cranial nerves in a horse, J Am Vet Med Assoc 221:1460–1463, 2002.
67. Vatistas NJ et al: Polyneuritis equi: a clinical review incorporating a case report of a horse displaying unconventional signs, Prog Vet Neurol 2:67–72, 1991.
68. Lavach JD: Ocular manifestations of systemic diseases, Vet Clin North Am Equine Pract 8:627–636, 1992.
69. Kadlubowski M, Ingram PL: Circulating antibodies to the neurotigenic myelin protein, P2, in neuritis of the cauda equina of the horse, Nature 293:299–300, 1981.
70. Scarratt WK, Jortner BS: Neuritis of the cauda equina in a yearling filly, Compend Contin Educ Pract Vet 7:S197–S202, 1985.
71. Wright JA, Fordyce P, Edington N: Neuritis of the cauda equina in the horse, J Comp Pathol 97:667–675, 1987.
72. Gilbert SA et al: Detection of equine arteritis virus in the semen of carrier stallions by using a sensitive nested PCR assay, J Clin Microbiol 35:2181–2183, 1997.
73. Holyoak GR et al: Equine viral arteritis: current status and prevention, Theriogenology 70:403–414, 2008.
74. Cole JR et al: Transmissibility and abortigenic effect of equine viral arteritis in mares, J Am Vet Med Assoc 189:769–771, 1986.
75. Timoney PJ, McCollum WH: Equine viral arteritis, Vet Clin North Am Equine Pract 9:295–309, 1993.
76. Clabough DL et al: Immune-mediated thrombocytopenia in horses infected with equine infectious anemia virus, J Virol 65:6242–6251, 1991.
77. Hahn CN, Mayhew IG, MacKay RJ: Diseases of multiple or unknown sites. In Colahan PT et al, editors: Equine medicine and surgery, vol 1, St. Louis, 1999, Mosby, pp 884–903.
78. Green SL et al: Rabies in horses: 21 cases (1970–1990), J Am Vet Med Assoc 200:1133–1137, 1992.
79. Hudson LC et al: Clinical presentation of experimentally induced rabies in horses, Zentralbl Veterinarmed B 43:277–285, 1996.
80. House JA: African horse sickness, Vet Clin North Am Equine Pract 9:355–364, 1993.
81. Newsholme SJ: A morphological study of the lesions of African horse sickness, Onderstepoort J Vet Res 50:7–24, 1983.
82. Brown C: Respiratory disease affecting multiple sites: African horse sickness. In Mayhew IG, editor: Equine medicine and surgery, vol 1, ed 5, St. Louis, 1999, Mosby, pp 463–465.
83. House JA et al: Further studies on the efficacy of an inactivated African horse sickness serotype 4 vaccine, Vaccine 12:142–144, 1994.
84. Ostlund EN: The equine herpesviruses, Vet Clin North Am Equine Pract 9:283–294, 1993.
85. Slater JD et al: Chorioretinopathy associated with neuropathology following infection with equine herpesvirus-1, Vet Rec 131:237–239, 1992.
86. Garré B et al: Evaluation of orally administered valacyclovir in experimentally EHV1-infected ponies, Vet Microbiol 135:214–221, 2009.
87. Eagle RC, Font RL, Swercsek TW: Malignant medulloepithelioma of the optic nerve in a horse, Vet Pathol 15:488–494, 1978.
88. Edington N, Welch HM, Griffiths L: The prevalence of latent Equid herpesviruses in the tissues of 40 abattoir horses, Equine Vet J 26:140–142, 1994.
89. Welch HM et al: Latent equid herpesviruses 1 and 4: detection and distinction using the polymerase chain reaction and co-cultivation from lymphoid tissues, J Gen Virol 73:261–268, 1992.
90. Schlocker N, Gerber-Bretscher R, von Fellenberg R: Equine herpesvirus 2 in pulmonary macrophages of horses, Am J Vet Res 56:749–754, 1995.

91. Thein P: The association of EHV-2 infection with keratitis and research on the occurrence of equine coital exanthema (EHV-3) of horses in Germany. Paper presented at the Fourth International Conference of Equine Infectious Diseases, 1976, Lyon, France.
92. Collinson PN et al: Isolation of equine herpesvirus type 2 (equine gammaherpesvirus 2) from foals with keratoconjunctivitis, J Am Vet Med Assoc 205:329–331, 1994.
93. Miller TR et al: Herpetic keratitis in a horse, Equine Vet J 17(suppl 10):15–17, 1990.
94. Perryman LE, McGuire TC, Crawford TB: Maintenance of foals with combined immunodeficiency: causes and control of secondary infections, Am J Vet Res 39:1043–1047, 1978.
95. Davis JL, Jones SL: Equine primary immunodeficiencies, Compend Contin Educ Pract Vet 25:548–556, 2003.
96. Studdert MJ, Blackney MH: Isolation of an adenovirus antigenically distinct from equine adenovirus type 1 from diarrheic foal feces, Am J Vet Res 43:543–544, 1982.
97. McChesney AE, England JJ, Rich LJ: Adenoviral infection in foals, J Am Vet Med Assoc 162:545–549, 1973.
98. Chirnside E, Sinclair R, Mumford JA: Respiratory viral diseases. In Reed SM, Bayly WM, editors: Equine internal medicine, Philadelphia, 1998, Saunders, pp 93–106.
99. Hannant D, Mumford JA, Jessett DM: Duration of circulating antibody and immunity following infection with equine influenza virus, Vet Rec 122:125–128, 1988.
100. Townsend HG et al: Efficacy of a cold-adapted, intranasal, equine influenza vaccine: challenge trials, Equine Vet J 33:637–643, 2001.
101. Centers for Disease Control and Prevention: West Nile virus activity—United States, MMWR Morb Mortal Wkly Rep 2003;52:1132, 2001.
102. Bender K, Thompson FEJ: West Nile virus: a growing challenge, Am J Nurs 103:32–39, 2003.
103. Deubel V et al: Variations in biological features of West Nile viruses, Ann N Y Acad Sci 951:195–206, 2001.
104. Davis BS et al: West Nile virus recombinant DNA vaccine protects mouse and horse from virus challenge and expresses in vitro a noninfectious recombinant antigen that can be used in enzyme-linked immunosorbent assays, J Virol 75:4040–4047, 2001.
105. Porter MB et al: West Nile virus encephalomyelitis in horses: 46 cases (2001), J Am Vet Med Assoc 222:1241–1247, 2003.
106. Solomon T et al: Natural and nosocomial infection in a patient with West Nile encephalitis and extrapyramidal movement disorders, Clin Infect Dis 36:E140–E145, 2003.
107. Autorino GL et al: West Nile virus epidemic in horses, Tuscany region, Italy, Emerg Infect Dis 8:1372–1378, 2002.
108. Anninger WV et al: West Nile virus-associated optic neuritis and chorioretinitis, Am J Ophthalmol 136:1183–1185, 2003.
109. Kuchtey RW et al: Uveitis associated with West Nile virus infection, Arch Ophthalmol 121:1648–1649, 2003.
110. Ostlund EN et al: Equine West Nile encephalitis, United States, Emerg Infect Dis 7:665–669, 2001.
111. Ng T et al: Equine vaccine for West Nile virus, Dev Biol 114:221–227, 2003.
112. Long MT et al: Efficacy, duration, and onset of immunogenicity of a West Nile virus vaccine, live flavivirus chimera, in horses with a clinical disease challenge model, Equine Vet J 39:491–497, 2007.
113. Rebhun WC: Diseases of the uvea. In Mayhew IG, editor: Equine medicine and surgery, vol 2, St. Louis, 1999, Mosby, pp 1253–1260.
114. Barratt-Boyes SM et al: *Streptococcus equi* infection as a cause of panophthalmitis in a horse, Equine Vet Sci 11:229–231, 1991.
115. Roberts SR: Chorioretinitis in a band of horses, J Am Vet Med Assoc 158:2043–2046, 1971.
116. De Lahunta A, Cummings JF: Neuro-ophthalmologic lesions as a cause of visual deficit in dogs and horses, J Am Vet Med Assoc 150:994–1011, 1967.
117. Sweeney CR et al: Description of an epizootic and persistence of *Streptococcus equi* infections in horses, J Am Vet Med Assoc 194:1281–1286, 1989.
118. Fintl C et al: Endoscopic and bacteriological findings in a chronic outbreak of strangles, Vet Rec 147:480–484, 2000.
119. Spoormakers TJ et al: Brain abscesses as a metastatic manifestation of strangles: symptomatology and the use of magnetic resonance imaging as a diagnostic aid, Equine Vet J 35:146–151, 2003.
120. Verheyen K et al: Elimination of guttural pouch infection and inflammation in asymptomatic carriers of *Streptococcus equi*, Equine Vet J 32:527–532, 2000.
121. Pusterla N et al: Purpura haemorrhagica in 53 horses, Vet Rec 153:118–121, 2003.
122. Freeman DE et al: A large frontonasal bone flap for sinus surgery in the horse, Vet Surg 19:122–130, 1990.
123. Morris DD: Disease of the hemolymphatic system, In Reed SM, Bayly WM, editors: Equine internal medicine, Philadelphia, 1998, Saunders; pp 564–566.
124. Roberts MC, Kelly WR: Renal dysfunction in a case of purpura haemorrhagica, Vet Rec 110:114–116, 1982.
125. Ainsworth DM: Rhodococcal infections in foals, Equine Vet Educ 11:191–198, 1999.
126. Johnson JA, Prescott JF, Markham RJF: The pathology of experimental *Corynebacterium equi* infection in foals following intragastric challenge, Vet Pathol 20:450–459, 1983.
127. Davis JL et al: Pharmacokinetics of azithromycin in foals after I.V. and oral dose and disposition into phagocytes, J Vet Pharmacol Ther 25:99–104, 2002.
128. Martens RJ et al: *Rhodococcus equi* foal pneumonia: protective effects of immune plasma in experimentally infected foals, Equine Vet J 21:249–255, 1989.
129. Ainsworth DM et al: Lack of residual lung damage in horses in which *Rhodococcus equi*-induced pneumonia had been diagnosed, Am J Vet Res 54:2115–2120 1993.
130. Burgess EC, Gillette D, Pickett P: Arthritis and panuveitis as a manifestation of *Borrelia burgdorferi* in a Wisconsin pony, J Am Vet Med Assoc 190:1340–1342, 1986.
131. Burgess EC, Mattison M: Encephalitis associated with *Borrelia burgdorferi* infection in a horse, J Am Vet Med Assoc 191:1457–1458, 1987.
132. Magnarelli LA et al: Serologic confirmation of *Ehrlichia equi* and *Borrelia burgdorferi* infections in horses from the northeastern United States, J Am Vet Med Assoc 217:1045–1050, 2000.
133. Cohen ND et al: Seroprevalence of antibodies to *Borrelia burgdorferi* in a population of horses in central Texas, J Am Vet Med Assoc 201:1030–1034, 1992.
134. Madigan JE: Equine ehrlichiosis, Vet Clin North Am Equine Pract 9:423–428, 1993.
135. Sorenson K et al: Lyme disease antibodies in Thoroughbred broodmares correlating to early pregnancy failure, J Equine Vet Sci 10:166–168, 1990.
136. Jones TDC: The relation of brucellosis to periodic ophthalmia in Equidae, Am J Vet Res 1:54–57, 1940.
137. Cohen ND, Carter GK, McMullan WC: Fistulous withers in horses: 24 cases (1984–1990), J Am Vet Med Assoc 201:121–124, 1992.
138. Kowalski JJ: Bacterial and mycotic infections. In Reed SM, Bayly WM, editors: Equine internal medicine, Philadelphia, 1998, Saunders, pp 61–93.
139. Gaughan EM, Fubini SL, Dietze A: Fistulous withers in horses: 14 cases (1978–1987), J Am Vet Med Assoc 193:964–966, 1988.
140. Gilger BC: Equine recurrent uveitis. In Robinson NE, editor: Current therapy in equine medicine, ed 5, Philadelphia, 2003, Saunders; pp 468–473.
141. Bernard WV: Leptospirosis, Vet Clin North Am Equine Pract 9:435–444, 1993.
142. Divers TJ, Byars TD, Shin SJ: Renal dysfunction associated with infection of *Leptospira interrogans* in a horse, J Am Vet Med Assoc 201:1391–1392, 1992.
143. Frazer ML: Acute renal failure from leptospirosis in a foal, Aust Vet J 77:499–500, 1999.
144. Hodgin EC, Miller DA, Lozano F: *Leptospira* abortion in horses, J Vet Diagn Invest 1:283–287, 1989.
145. van den Ingh TS, Hartman EG, Bercovich Z: Clinical *Leptospira interrogans* serogroup Australis serovar Lora infection in a stud farm in The Netherlands, Vet Q 11:175–182, 1989.
146. Nervig RM, Garrett LA: Use of furosemide to obtain bovine urine samples for leptospiral isolation, Am J Vet Res 40:1197–1200, 1979.
147. Theirmann AB: Isolation of leptospires in diagnosis of leptospirosis, Mod Vet Pract 65:758–759, 1984.
148. Maurin M, Bakken JS, Dumler JS: Antibiotic susceptibilities of *Anaplasma (Ehrlichia)* phagocytophilum strains from various geographic areas in the United States, Antimicrob Agents Chemother 47:413–415, 2003.

149. Pusterla N et al: Digenetic trematodes, *Acanthatrium* sp. and *Lecithodendrium* sp., as vectors of *Neorickettsia risticii*, the agent of Potomac horse fever, J Helminthol 77:335–339, 2003.
150. Ziemer EL, Keenan DP, Madigan JE: *Ehrlichia equi* infection in a foal, J Am Vet Med Assoc 190:199–200, 1987.
151. Nyindo MB et al: Immune response of ponies to experimental infection with *Ehrlichia equi,* Am J Vet Res 39:15–18, 1978.
152. Gribble DH: Equine ehrlichiosis, J Am Vet Med Assoc 155:462–469, 1969.
153. Sippel WL, Cooperrider DE, Gainer JH: Equine piroplasmosis in the United States, J Am Vet Med Assoc 141:694–698, 1962.
154. Bruning A: Equine piroplasmosis an update on diagnosis, treatment and prevention, Br Vet J 152:139–151, 1996.
155. de Waal DT: Equine piroplasmosis: a review, Br Vet J 148:6–14, 1992.
156. Kuttler KL, Zaugg JL, Gipson CA: Imidocarb and parvaquone in the treatment of piroplasmosis *(Babesia equi)* in equids, Am J Vet Res 48:1613–1616, 1987.
157. Zaugg JL, Lane VM: Efficacy of buparvaquone as a therapeutic and clearing agent of *Babesia equi* of European origin in horses, Am J Vet Res 53:1396–1399, 1992.
158. Dubey JP et al: Serologic prevalence of *Toxoplasma gondii* in horses slaughtered for food in North America, Vet Parasitol 86:235–238, 1999.
159. Dubey JP: Persistence of encysted *Toxoplasma gondii* in tissues of equids fed oocysts, Am J Vet Res 46:1753–1754, 1985.
160. McDonald DR, Cleary DJ: Toxoplasmosis in the equine, Southwest Vet 23:213–214, 1970.
161. Chhabra MB, Gautam OP: Antibodies to *Toxoplasma gondii* in equids in north India, Equine Vet J 12:146–148, 1980.
162. Alexander CS, Keller H: Atiologie und Vorkommen der periodischen augenentzundung des pferdes iim Raum Berlin, Tierarztl Prax 18:623–627, 1990.
163. Chadna VK et al: Localized subcutaneous cryptococcal granuloma in a horse, Equine Vet J 25:166–168, 1993.
164. Riley CB et al: Cryptococcosis in seven horses, Aust Vet J 69:135–139, 1992.
165. Steckel RR et al: Antemortem diagnosis and treatment of cryptococcal meningitis in a horse, J Am Vet Med Assoc 180:1085–1089, 1982.
166. Blanchard PC, Filkins M: Cryptococcal pneumonia and abortion in an equine fetus, J Am Vet Med Assoc 201:1591–1592, 1992.
167. Scott EA, Duncan JR, McCormack JE: Cryptococcosis involving the postorbital area and frontal sinus in a horse, J Am Vet Med Assoc 165:626–627, 1974.
168. Beech J: Cytology of tracheobronchial aspirates in horses, Vet Pathol 12:157–164, 1975.
169. Ryan MJ, Wyand DS: Cryptococcus as a cause of neonatal pneumonia and abortion in two horses, Vet Pathol 18:270–272, 1981.
170. al-Ani FK: Epizootic lymphangitis in horses: a review of the literature, Rev Sci Tech 18:691–699, 1999.
171. Brown C: Diseases affecting the glandular and tubular lymphatic system: epizootic lymphangitis. In Mayhew IG, editor: Equine medicine and surgery, vol 2, St Louis, 1999, Mosby, pp 2057–2058.
172. Soliman R et al: Ocular histoplasmosis due to *Histoplasma farciminosum* in Egyptian donkeys, Mycoses 34:261–266, 1991.
173. Cook WR: The clinical features of guttural pouch mycosis in the horse, Vet Rec 83:336–345, 1968.
174. Cook WR: The pathology and aetiology of guttural pouch mycosis in the horse, Vet Rec 83:422–428, 1986.
175. Whitley RD, Gelatt KN: Mycotic encephalitis associated with a guttural pouch mycosis. In Gelatt KN, editor: Veterinary ophthalmology, Philadelphia, 1978, Lea and Febiger.
176. Hatziolos BS, Sass B, Albert TF: Blindness in a horse probably caused by gutturomycosis, Zentralbl Veterinarmed 22:362–371, 1975.
177. Hatziolos BS, Sass B, Albert TF: Ocular changes in a horse with gutturomycosis, J Am Vet Med Assoc 167:51–54, 1975.
178. Sweeney CR, Habacker PL: Pulmonary aspergillosis in horses: 29 cases (1974–1997), J Am Vet Med Assoc 214:808–811, 1999.
179. Schmallenbach KH et al: Studies on pulmonary and systemic *Aspergillus fumigatus*-specific IgE and IgG antibodies in horses affected with chronic obstructive pulmonary disease (COPD), Vet Immunol Immunopathol 66:245–256, 1998.
180. Sweeney CR: Fungal pneumonia. In Smith BP, editor: Large animal internal medicine, St. Louis, 1996, Mosby–Year Book, pp 576–577.
181. Roffey SJ et al: The disposition of voriconazole in mouse, rat, rabbit, guinea pig, dog, and human, Drug Metab Dispos 31:731–741, 2003.
182. Schmidt GM et al: Equine onchocerciasis: lesions in the nuchal ligament of midwestern U.S. horses, Vet Pathol 19:16–22, 1982.
183. Lloyd S, Soulsby EJ: Survey for infection with *Onchocerca cervicalis* in horses in eastern United States, Am J Vet Res 39:1962–1963, 1978.
184. Schmidt GM et al: Equine ocular onchocerciasis: histopathologic study, Am J Vet Res 43:1371–1375, 1982.
185. Lavach JD: Parasitic diseases. In Lavach JD, editor: Large animal ophthalmology, St. Louis, 1990, Mosby, pp 252–269.
186. Pollitt CC et al: Treatment of equine onchocerciasis with ivermectin paste, Aust Vet J 63:152–156, 1986.
187. Moore CP: Eyelid and nasolacrimal disease, Vet Clin North Am Equine Pract 8:499–519, 1992.
188. Pusterla N et al: Cutaneous and ocular habronemiasis in horses: 63 cases (1988–2002), J Am Vet Med Assoc 222:978–982, 2003.
189. Mohamed FH et al: Cutaneous habronemiasis in horses and domestic donkeys *(Equus acinus acinus)*, Rev Ele Med Vet Pays Trop 42:535–540, 1990.
190. Fadock VA: Parasitic skin diseases of large animals, Vet Clin North Am 6:3–26, 1984.
191. Campbell WC, Benz GW: Ivermectin: a review of efficacy and safety, J Vet Pharmacol Ther 7:1–16, 1984.
192. Wijesundera WS, Chandrasekharan NV, Karunanayake EH: A sensitive polymerase chain reaction based assay for the detection of *Setaria digitata:* the causative organism of cerebrospinal nematodiasis in goats, sheep and horses, Vet Parasitol 81:225–233, 1999.
193. Frauenfelder HC, Kazacos KR, Lichtenfels JR: Cerebrospinal nematodiasis caused by a filaricide in a horse, J Am Vet Med Assoc 177:359–362, 1980.
194. Levine ND: Nematode parasites of domestic animals and of man, Minneapolis, 1980, Burgess.
195. Muhammad G, Saqib M: Successful treatment of ocular equine microfilariasis (*Setaria* species) with ivermectin, Vet Rec 160:25–26, 2007.
196. Razig SA: A preliminary clinical trial on the use of diethylcarbamazine citrate for the treatment of equine filariasis, Pakistan Vet J 9:93–96, 1989.
197. Jemelka ED: Removal of *Setaria digitata* from the anterior chamber of the equine eye, Vet Med Small Anim Clin 71:673–675, 1976.
198. Thurman JD, Johnson BJ, Lichtenfels JR: Dirofilariasis with arteriosclerosis in a horse, J Am Vet Med Assoc 185:532–533, 1984.
199. Moore CP et al: Equine ocular parasites: a review, Equine Vet J Suppl 2:76–85, 1983.
200. Rezabek GB, Giles RC, Lyons ET: *Echinococcus granulosus* hydatid cysts in the livers of two horses, J Vet Diagn Invest 5:122–125, 1993.
201. Barnett KC, Cottrell BD, Rest JR: Retrobulbar hydatid cyst in the horse, Equine Vet J 20:136–138, 1988.
202. Bryan RT, Schantz PM: Echinococcosis (hydatid disease), J Am Vet Med Assoc 195:1214–1217, 1989.
203. Spalding MG, Greiner EC, Green SL: *Halicephalobus (Micronema) deletrix* infection in two half-sibling foals, J Am Vet Med Assoc 196:1127–1129, 1990.
204. Kinde H et al: *Halicephalobus gingivalis* (*H. deletrix*) infection in two horses in southern California, J Vet Diagn Invest 12:162–165, 2000.
205. Rames DS et al: Ocular *Halicephalobus (Micronema) deletrix* infection in a horse, Vet Pathol 32:540–542, 1995.
206. Jose-Cunilleras E: Verminous encephalomyelitis. In Reed SM, Bayly WM, Sellon DC, editors: Equine internal medicine, St Louis, 2004, Saunders, pp 659–665.
207. Dunn DG et al: Nodular granulomatous posthitis caused by *Halicephalobus* (syn. *Micronema*) sp. in a horse, Vet Pathol 30:207–208, 1993.
208. Theon AP: Radiation therapy in the horse, Vet Clin North Am Equine Pract 14:673–688, 1998.
209. Theon AP: Intralesional and topical chemotherapy and immunotherapy, Vet Clin North Am Equine Pract 14:659–671, 1998.
210. Lunn DP, Horohov DW: Immunodeficiency. In Reed SM, Bayly WM, Sellon DC, editors: Equine internal medicine, St Louis, 1994, Saunders, pp 37–52.
211. Bowling AT, Byrns G, Spier SJ: Evidence for a single pedigree source of the hyperkalemic periodic paralysis susceptibility gene in Quarter Horses, Anim Genet 27:279–281, 1996.
212. Naylor JM: Selection of Quarter Horses affected with hyperkalemic periodic paralysis by show judges, J Am Vet Med Assoc 204:926–928, 1994.

213. Rudolph JA et al: Periodic paralysis in Quarter Horses: a sodium channel mutation disseminated by selective breeding, Nat Genet 2:144–147, 1992.
214. Naylor JM: Equine hyperkalemic periodic paralysis: review and implications, Can Vet J 35:279–285, 1994.
215. Naylor JM: Hyperkalemic periodic paralysis, Vet Clin North Am Equine Pract 13:129–144, 1997.
216. Carr EA et al: Laryngeal and pharyngeal dysfunction in horses homozygous for hyperkalemic periodic paralysis, J Am Vet Med Assoc 209:798–803, 1996.
217. Donoghue S et al: Vitamin A nutrition of the equine: growth, serum biochemistry and hematology, J Nutr 111:365–374, 1981.
218. Greiwe-Crandell KM et al: Seasonal vitamin A depletion in grazing horses is assessed better by the relative dose response test than by serum retinol concentration, J Nutr 125:2711–2716, 1995.
219. Lewis LD: Vitamins for horses, and plant poisoning of horses, Baltimore, 1995, Williams & Wilkins.
220. Howell CE, Hart GH, Ittner NR: Vitamin A deficiency in horses, Am J Vet Res 2:60–74, 1941.
221. Geor RJ et al: Systemic lupus erythematosus in a filly, J Am Vet Med Assoc 197:1489–1492, 1990.
222. Rees CA: Disorders of the skin. In Reed SM, Bayly WM, Sellon DC, editors: Equine internal medicine, ed 2, St Louis, 2004 Saunders, pp 667–720.
223. Kimyai-Asadi A, Jih MH: Paraneoplastic pemphigus, Int J Dermatol 6:367–372, 2001.
224. Fadok VA: An overview of equine dermatoses characterized by scaling and crusting, Vet Clin North Am Equine Pract 11:43–51, 1995.
225. Grassnickel W: Pemphigus and pemphigoid disease in the horse, Monatsh Veterinarmed 15:735–739, 1960.
226. Power HT, McEvoy EO, Manning TO: Use of a gold compound for the treatment of pemphigus foliaceus in a foal, J Am Vet Med Assoc 180:400–403, 1982.
227. Bailey E: Prevalence of anti-red blood cell antibodies in the serum and colostrums of mares and its relationship to neonatal isoerythrolysis, Am J Vet Res 43:1917–1921, 1982.
228. Traub-Dargatz JL et al: Neonatal isoerythrolysis in mule foals, J Am Vet Med Assoc 206:67–70, 1995.
229. Becht JL, Semrad SD: Hematology, blood typing, and immunology of the neonatal foal, Vet Clin North Am Equine Pract 1:91–116, 1985.
230. McCue PM: Cushing's disease, Vet Clin North Am Equine Pract 18:533–543, 2002.
231. Love S: Equine Cushing's disease, Br Vet J 149:139–153, 1993.
232. Donaldson MT et al: Treatment with pergolide or cyproheptadine of pituitary pars intermedia dysfunction (equine Cushing's disease), J Vet Intern Med 16:742–746, 2002.
233. Hillyer MH et al: Diagnosis of hyperadrenocorticism in the horse, Equine Vet Educ 4:131–134, 1992.
234. Dybdal NO et al: Diagnostic testing for pituitary pars intermedia dysfunction in horses, J Am Vet Med Assoc 204:627–632, 1994.
235. Frank N, Sojka J, Messer NT: Equine thyroid dysfunction, Vet Clin North Am Equine Pract 18:305–319, 2002.
236. Johnson PJ et al: Effects of propylthiouracil and bromocriptine on serum concentrations of thyrotrophin and thyroid hormones in normal female horses, Equine Vet J 35:296–301, 2002.
237. Lowe JE et al: Equine hypothyroidism: the long-term effects of thyroidectomy on metabolism and growth in mares and stallions, Cornell Vet 64:276–295, 1974.
238. Schwarz BC, Sallmutter T, Nell B: Keratoconjunctivitis sicca attributable to parasympathetic facial nerve dysfunction associated with hypothyroidism in a horse, J Am Vet Med Assoc 233:1761–1766, 2008.
239. Millichamp NJ: Ocular trauma, Vet Clin North Am Equine Pract 8:521–536, 1992.
240. Martin CL, Kaswan R, Chapman W: Four cases of traumatic optic nerve blindness in the horse, Equine Vet J 18:133–137, 1986.
241. Firth EC: Vestibular disease, and its relationship to facial paralysis in the horse: a clinical study of 7 cases, Aust Vet J 53:560–565, 1977.
242. Reilly L, Beech J: Bilateral keratoconjunctivitis sicca in a horse, Equine Vet J 26:171–172, 1994.
243. Ragle CA: Head trauma, Vet Clin North Am Equine Pract 9:171–183, 1993.
244. Sinha AK, Hendrickson DA, Kannegieter NJ: Head trauma in two horses, Vet Rec 128:518–521, 1991.
245. Holbrook TC, Dechant JE, Crowson CL: Suspected air embolism associated with post-anesthetic pulmonary edema and neurologic sequelae in a horse, Vet Anaesth Analg 34:217–222, 2007.
246. Bradbury LA et al: Suspected venous air embolism in a horse, Vet Rec 156:109–111, 2005.
247. Plummer CE et al: Suspected ivermectin toxicosis in a miniature mule foal causing blindness, Vet Ophthalmol 9:29–32, 2006.
248. Hautekeete LA, Khan SA, Hales WS: Ivermectin toxicosis in a zebra, Vet Hum Toxicol 40:29–31, 1998.
249. Johnson PJ et al: Presumed moxidectin toxicosis in three foals, J Am Vet Med Assoc 214:678–680, 1999.
250. Müller JM et al: The use of sarmazenil in the treatment of a moxidectin intoxication in a foal, J Vet Intern Med 19:348–349, 2005.
251. Sebastian MM et al: REVIEW paper: mare reproductive loss syndrome, Vet Pathol 45:710–722, 2008.
252. Volkmann D et al: Hormone profiles of mares affected by the mare reproductive loss syndrome, Reprod Domest Anim 43:578–583, 2008.
253. Sebastian M et al: The mare reproductive loss syndrome and the eastern tent caterpillar: a toxicokinetic/statistical analysis with clinical, epidemiologic, and mechanistic implications, Vet Ther 4:324–339, 2003.
254. Hirono I et al: Reproduction of progressive retinal degeneration (bright blindness) in sheep by administration of ptaquiloside contained in bracken, J Vet Med Sci 55:979–983, 1993.
255. Shahin M, Smith BL, Prakash AS: Bracken carcinogens in the human diet, Mutat Res 443:69–79, 1999.
256. Curran JM, Sutherland RJ, Peet RL: A screening test for subclinical liver disease in horses affected by pyrrolizidine alkaloid toxicosis, Aust Vet J 74:236–240, 1996.
257. Hintz HF: Molds, mycotoxins, mycotoxicosis, Vet Clin North Am Equine Pract 6:410–431, 1990.

Chapter 14

Practical Management of Blind Horses

Ann E. Dwyer

A variety of equine ophthalmic diseases may cause horses to lose their sight. In many cases, the attending veterinarians have provided proper treatment, and the caretakers have followed medication schedules, but blinding sequelae still occur. Recurrent uveitis is the most common cause of bilateral blindness, but corneal disease, cranial trauma, blunt or penetrating globe trauma, neoplasia, and infection also can cause vision loss. Data on the incidence of blindness in horses are scant, but field experience suggests that at least 1% to 2% of horses lose sight in one or both eyes during their lifetime.

Several facts are of concern if vision loss is imminent:

1. Horses have a natural history as grazing animals hunted by predators. This gives them a wary temperament. They are prone to display sudden fight-or-flight responses. When cornered, frightened, or threatened, horses may kick, strike, or run.
2. Horses are herd animals that follow a strict social hierarchy. Visual cues are paramount in establishing the dominance order of the group. Individual animals that ignore the visual cues of their herd mates are often bitten, shoved, or kicked by dominant individuals.
3. Horses are large, strong creatures, usually weighing more than 1000 pounds. Yet their lower legs have a diameter not much larger than a baseball bat. Horses trapped in fences or other hazards often panic. The result can be fractured extremity bones and other severe injuries.

Given these truths of equine social life, behavior, and anatomy, how do horses cope with the loss of their primary orienting sense? Remarkably, they may adapt well. Key elements for successful adaptation are the inherent temperament of the horse, the dedication of the owner, and a safe and predictable environment.

ADAPTATION TO BLINDNESS: GIVE THEM TIME

Although blindness can occur suddenly, onset in most horses is gradual. Caretakers of horses with failing vision usually notice progressive uncertainty, especially in low-light situations. Typically, horses may bump into walls or fences and show reluctance to walk over unfamiliar terrain. Herd behavior changes, even among horses that have been pastured together for years. Horses that are ridden may shy frequently, refuse to obey simple commands, and show reluctance to move forward as their sight dims. Balance may be altered, and horses with minimal acuity may show a head tilt or postural change.

When vision finally fails, caretakers report that blind horses go through a transition period where their behavior is unpredictable, reflecting fear and anxiety.[1,2] Rapid circling, "freezing" in place, prolonged neighing, spooking, and aggressive body motions (e.g., crashing into walls, running over a handler) may be observed. This initial adjustment period can be dangerous to both the horse and handler, but it is usually transient, lasting anywhere from a few days to several weeks. Cautious handling, patience, and common sense are needed to help the horse adjust to vision loss during this critical period. Newly blind horses should be housed in a corral or stall to allow close monitoring. Blind horses should NOT be turned out in herds. They will do best if they are initially kept by themselves or turned out with a single carefully chosen companion such as a quiet horse, goat, or donkey. It may be helpful to hang a bell on the halter or neck strap of the companion (Fig. 14-1, *A*).

Anxious blind horses appear to be settled by the voice, smell, and touch of people they knew and trusted when they had sight (see Fig. 14-1, *B*). While the transition/adaptation period is NOT a time to try to train a blind horse to do new

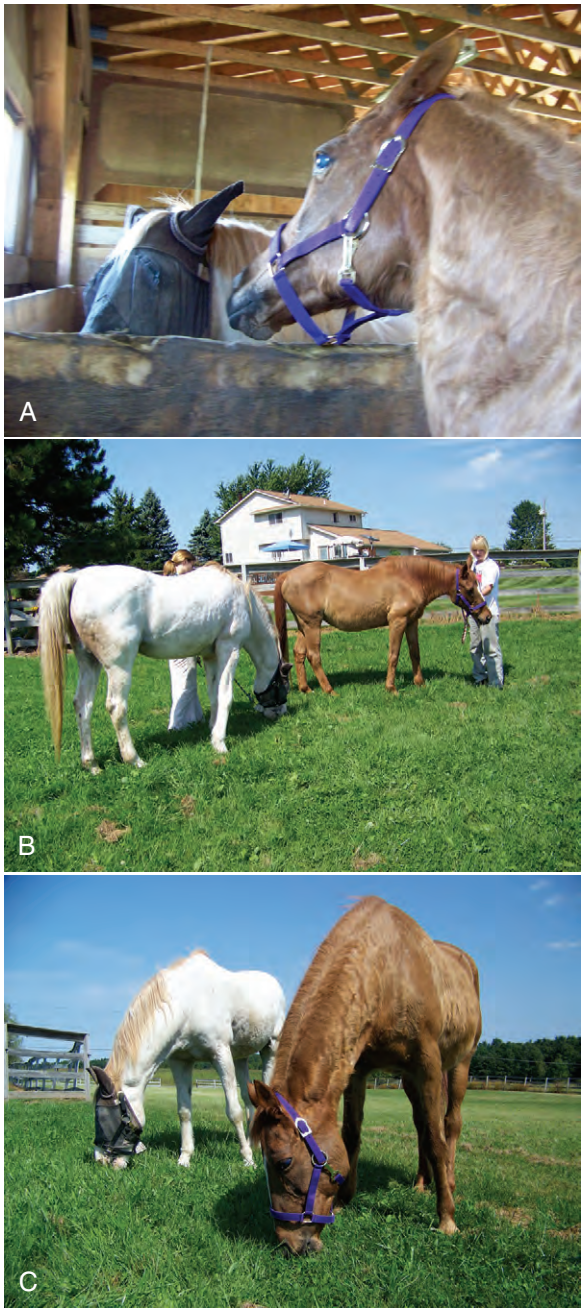


Figure 14-1. A, This photo shows Mindy, a 38-year-old mare that has just gone blind from glaucoma. Mindy is anxious but is calmed by the close boundaries of her stall and the presence of Suntan, her long-time sighted companion. **B,** Mindy shows a head tilt and an anxious posture in the early days of blindness, but she is settled by the voice, smell, and touch of her owner and the company of Suntan, who is wearing a bell on his halter. **C,** Mindy now accepts her vision loss. She is grazing contentedly with Suntan. (Photographs courtesy Deborah and Rocco Distaffen, Spencerport, NY.)

things, frequent handling and attention are appropriate. All owners report that talking is a key part of blind-horse management. The constant murmur of a handler's voice provides reassurance, lets the horse know where the handler is, and avoids surprise. Handlers also report that frequent touch is calming and comforting to blind horses. They enjoy grooming and petting and will soon learn that the tactile signals of a trusted handler indicate a safe place.

Adjustment to vision loss is helped if the horse is given a predictable daily routine. Feeding should be done at the same time and in the same place every day. Fresh water should always be available. If the horse is turned out, it should be led out along the same path each time and released at the same spot. Free-choice access to hay is a good settling aid. If the horse is being managed with a companion, the pair should not be separated during the adjustment period. Personnel visiting the farm must be aware of the status of the newly blind animal and cautioned to act with common sense and respect. Startling stimuli (farm vehicle traffic, aggressive dogs, flapping tarps, etc.) should be kept to a minimum.

Over several weeks, acceptance of vision loss and adjustment to blindness occurs in most innately calm horses, and behavior becomes settled and predictable (see Fig. 14-1, *C*) Well-adapted blind horses tend to be cautious and careful and do not have a higher rate of injury than sighted horses. Steve Smith of Rolling Dog Ranch, a sanctuary for disabled animals that houses over 20 blind horses in Montana, sums up the formula for managing blind horses as follows:

"Personality + Time + Environment = Success" [3]

COMMON SENSE SAFETY CONCERNS

A safe environment is important because blind horses can easily be traumatized. Walls and fences should be smooth and free of nails, sharp pieces of wood, or projecting pieces of wire. Stall entry and exit will be easiest if the stall has a sliding door or a door that swings out into the aisle. All hardware should be free of any sharp or hooklike projections. The J-shaped handles of water buckets should be taped over; these often become gapped with use, presenting a hazard that can trap and tear an eyelid (Fig. 14-2).

A blind horse may spook and jump sideways if something like snow sliding off a roof or a loose dog scares it. Another great stressor for blind horses is wind. The exact reason wind causes alarm is unknown, but it may be that wind interferes with the usual audible cues blind horses use for orientation. People working with blind animals should be especially careful if high winds, unusual loud noises, or loose animals are present and should always be prepared to take evasive action if the horse gets startled and makes a sudden move. Like all horses, blind horses can be dangerous to be around if they are frightened.

Signage can be posted on stalls or paddocks of blind horses to alert visitors to the animal's handicap. Regular handlers should stand near a blind horse's shoulder when working with it, because this is the safest position from which to react if the horse makes any quick moves. Veterinarians and farriers must be aware that the horse is blind and should take a little extra time to reassure the horse, using talk and touch before initiating any actions that might be painful or surprising to the horse.

The decision to turn a blind horse out into a pasture once it has adapted to vision loss is dependent on the horse and the safety of the pasture. It is a good idea to walk a horse around the perimeter of any new pasture to introduce it to the new space. The process of "mental mapping" may be aided if the

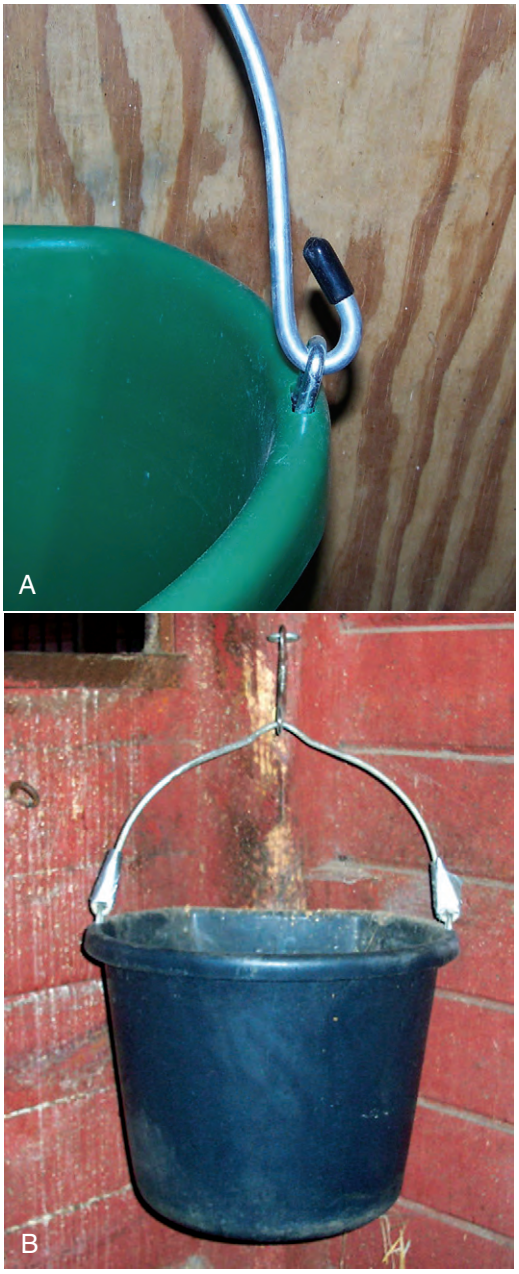


Figure 14-2. **A,** The J-shaped handles of water buckets can become gapped with time and are a common cause of eyelid tears. **B,** Tape up J-shaped bucket handles for safety.

Figure 14-3. The process of "mental mapping" is aided if the handler and blind horse circumnavigate a new pasture. Here TJ, a blind Standardbred gelding is shown the water trough. (Photograph courtesy Susan Straumann, Woodstown, NJ.)

Figure 14-4. Corral or paddock fencing should be horse safe. This photo shows detail of a practical corral boundary where pipe gate sections are secured to T posts. (Photograph courtesy Steve Smith, Rolling Dog Ranch Animal Sanctuary, Ovando, MT.)

handler taps on the fence as it is circumnavigated. Extra time should be spent at the water trough and gate (Fig. 14-3). Audible signals like swishing the water and rapping on the gate will help the horse locate the key features of the pasture.[2,4]

The footing of all enclosure(s) should be level and free of holes. Obstacles like mounting blocks, jumps, or farm equipment should be removed. Corral or paddock fencing must be horse-safe. Post and pole, split rail, plastic or wooden boards, woven wire mesh, or metal pipe panels are good choices for fence boundaries (Fig. 14-4). Barbed wire and electric wire fences are inappropriate. Wire barbs pose obvious safety hazards, and the electric shock transmitted from electrified wire can panic a blind horse, causing it to run through the fence. If smooth-wire strand fencing is the only option, strips of fabric can be tied to the wire at 6- to 8-foot intervals. The strips will flutter in the wind and the associated noise will aid the horse in respecting the fence boundary.

Tree branches, holes, ponds, ditches, insecure fencing, and farm equipment are obvious hazards that should be eliminated if possible. Immovable vertical obstacles like trees or poles can

Figure 14-5. Seasonal hazards must be taken into consideration when choosing turnout space for blind horses. This photo shows a blind horse that slipped on a large ice patch. He became exhausted trying to get up and had to be hoisted with a sling that was lifted by a tractor bucket. Hay has been spread around the horse's body to improve footing.

be made safe if they are rimmed with tires filled with sand or marked by spreading an apron of gravel or rock around their base. The water trough should be located along the fence line and should not contain any sharp corners or rough edges. Seasonal hazards must be taken into consideration. Very wet weather can create dangerous bogs or high water in pasture creeks, and very cold weather paired with freezing rain can create ice patches that are treacherous for blind horses (Fig. 14-5).

DECISION MAKING FOR OWNERS

All horses making the adjustment to sight loss require plenty of patience from their owners. Most horses adjust and accept sight loss over a period of several days to several weeks, but some may require several months for full adaptation. Owners who provide a safe environment and practice good common sense find that the majority of blind horses adapt and can eventually be managed with about the same effort and expense sighted horses require (Box 14-1). However, a minority of horses do not adjust well to blindness, even when circumstances are ideal.

Horses with high-strung, nervous dispositions are the most challenged in adapting to blindness. They appear to experience more fear and anxiety than horses of calmer disposition. Frantic behavior such as constant stall circling, compulsive calling to former herd mates, and intolerance of lead rope or cross-tie restraint may be displayed. Anxious blind horses may crash into walls or fences or run over people who try to help them. Such behavior poses obvious risk to both the horse and its handlers. Blind horses that persist in exhibiting dangerous behavior after being allowed a generous trial period for adjustment may need to be euthanized for safety reasons.

In other instances, owners may not have the resources to provide a suitable environment for a sightless horse. Some of these animals are donated to sanctuaries or placed in foster homes, and some are euthanized. Ultimately, individual circumstances will dictate the choices made in managing every horse that loses sight (Fig. 14-6).

Box 14-1 | Common-Sense Tips for Managing Blind Horses

Veterinarians can provide the following list of tips to owners of blind horses:

- Talk to the blind horse often, using a calm tone.
- Touch the blind horse often, especially when a new stimulus is pending.
- Teach the horse a few basic verbal commands: "Whoa," "Step up," "Back," etc.
- Choose a quiet companion for the blind horse, and keep them as a pair.
- Fence paddocks and pastures with horse-safe boundaries.
- Police stalls and paddocks for hazards and sharp projections.
- Tape up bucket handle hooks.
- Do not clip the muzzle whiskers or vibrissae.
- Demonstrate the boundaries of any new enclosure.
- Practice loading off and on a trailer.
- Keep food and water in a consistent location.
- Keep a consistent daily routine.
- Be aware that sudden noises or high winds may scare blind horses.
- Set limits for behavior and reinforce them. Spoiling a blind horse is NOT a good idea!

BULLIES AND BUDDIES: SOCIAL INTERACTIONS WITH OTHER HORSES

Horses in herd situations establish a social hierarchy, with dominant individuals ranking higher in the pecking order than submissive ones. In a herd situation, a blind horse usually falls to the bottom of the social order. Dominant sighted horses will take advantage of the blind one, chasing it away from feed sources. They will bully, bite, and push the handicapped horse, keeping it away from others. Blind horses are threatened and frightened by dominant individuals and will become skittish and nervous. Blind horses in herds tend to lose weight because of poor access to food, and they may not come up to the pasture gate when other horses are being brought in. For all these reasons, it is generally inadvisable to turn blind horses out in herds.

However, horses are social individuals and are usually happiest if they have a companion. Many calm horses are well suited to a "buddy" role for a blind horse. By all reports, bonding between two well-matched horses usually develops quickly. Once a compatible pair has been identified, the two equine friends can be turned out in their own enclosure and will be content to live together as a pair (Fig. 14-7). Often, buddies are housed in adjacent stalls. In some cases, they have the ability to touch noses and smell each other when stabled if the stall wall that separates them has a grating or does not go to the ceiling.

Companion horses that are visual act as "seeing eyes" and often appear to lead their unsighted companions over unfamiliar terrain. Sometimes the guidance is in the form of a nose-to-tail physical presence. Other times, the blind horse listens and scents for clues that define the location of the buddy. Vocal contact is frequent, with both individuals calling back and forth to each other. In some cases, a bell on the halter of the sighted

Figure 14-6. Individual circumstances dictate the choices made in managing blind horses. This photograph shows three blind horses. Nikki, the bay mare on the far right, is regularly used for riding. Lena, the chestnut mare in the center, is never ridden but is a steady companion horse and "pasture pet." Destiny, the young chestnut filly on the left was blind at birth. She never adapted well to blindness and had to be euthanized at the age of 3 for persistent dangerous behavior. (Photograph courtesy Steve Smith, Rolling Dog Ranch Animal Sanctuary, Ovando, MT.)

Figure 14-7. A calm sighted horse makes an excellent "buddy" for a blind horse. The two will form a very close bond when kept together as a pair. (Photograph courtesy Deborah and Rocco Distaffen, Spencerport, NY.)

horse provides guidance. Observers have seen buddy horses appear to lead the blind partner through lanes and gates.

Several sanctuaries have been developed in the past decade that house multiple blind horses.[2,5] Managers of these facilities often pair two compatible blind horses together as "pasture buddies" (Fig. 14-8). They report that the bond between the pair of blind horses is just as strong as the bond between a sighted and blind horse.[2] The horses stick close together and figure out the boundaries of their world, navigating their environment together. They groom each other's coats with their muzzles, use each other's tails as fly switches, and graze nose to nose.

Whatever the visual status of the companion pair, the attachment between them is usually strong. As such, one horse will become quite anxious if separated from the other, and this fact must be taken into consideration if the two are pulled apart. If circumstances arise where a pair must be separated permanently (e.g., if one becomes ill and dies), the remaining horse will go through a period of anxiety and distress. However, the horse will generally accept and bond with a replacement buddy quickly if their temperaments are compatible.[3]

Figure 14-8. Managers of sanctuaries that house multiple blind horses often pair two compatible blind horses together as buddies. As with sighted horses, the bond that develops is very strong. (Photograph courtesy Steve Smith, Rolling Dog Ranch Animal Sanctuary, Ovando, MT.)

BLIND BROODMARES WITH FOALS

Blind mares that deliver foals deserve special mention. They are as maternal as sighted mares and show strong protective behavior toward their offspring, especially in the first few weeks of the foal's life. They need to know that their foal is nearby and are often more relaxed if the foal wears a halter with a bell (Fig. 14-9). Like sighted mares, they show signs of panic if separated from their offspring. A blind mare that is stressed by separation and trying to reach her foal can be dangerous, because she will be heedless of people or obstacles in her path. Farm employees and veterinarians working on blind broodmares or their foals should always take care to restrain the pair in such a way that the mare is aware that the foal is near. This usually means holding the foal close to the mare's front end where she can swing her head and touch, hear, or smell the foal.

COPING IN THE DARK

There is a popular Haitian saying: *Experience is the cane of the blind*. Owners of blind horses relate remarkable stories of the navigational skills of their horses. Many say that "dark-adapted" horses travel their home terrain with such confidence that outside observers mistake them for sighted animals. Horses that have lost vision appear to have the ability to construct a mental map of their environment and are capable of knowing the perimeter of several different paddocks or large pastures, as well as their stalls. Blind horses often run and play in their fenced enclosures, halting with confidence just short of the boundary. No one knows whether horses gain this geographic knowledge by memorizing the stride distance between fences, by feeling subtle alterations in ground topography, or by some other perceptive ability. Some people have speculated that blind horses have an ability to sense echoes of

Figure 14-9. A bell on the halter of a foal helps a blind mare know the location of her offspring. Bell in photograph is larger than those normally used. (Photograph courtesy Rocking Horse Equestrian Center, Penfield, NY.)

sound off obstacles, similar to the perceptive abilities of marine mammals.

No research has been done to investigate how blind horses understand their surroundings, but it appears they rely heavily on increased use of their remaining senses, just as blind people do. In humans, the visual cortex is massive, occupying over a third of the anatomy of the cerebral cortex. Research has shown that some of the neural circuitry in the visual cortex of persons with congenital or acquired blindness is reallocated to processing other sensory inputs, especially stimuli involving hearing and touch.[6,7] It is intriguing to speculate that similar plasticity may occur in the brain function of blind horses.

Whatever the neurophysiologic mechanisms, blind horses consistently demonstrate increased use of their sense of hearing. Their ears move often, collecting sound waves like satellite dishes. They act as if their hearing is more acute than that of the average horse and orient themselves in their environment on the basis of the loudness and direction of the sounds they hear. They recognize the voices of their handlers and are calmed by learned verbal cues. Sounds from their regular pasture companions attract special attention.

The sense of smell of blind horses also appears enhanced. They often scent the ground or air, moving their noses toward perceivable smells as they search for other horses or food sources. They have no difficulty locating hay, succulent pasture, grain, or water.

Blind horses use their sense of touch, specifically their muzzles, to investigate their environment. The muzzle is one of the most richly innervated regions of the horse's body. The density of sensory nerves in the equine lip and nose region is similar to the concentration of sensory nerves in the human hand. A blind horse running its nose over a pasture fence or stall gathers information in much the same way a blind person reads Braille with the fingertips. Blind horses should be encouraged to explore their surroundings and touch new people and things with their muzzles. The long whiskers of the lower face and lips should not be clipped, because these structures help the horse "map" and understand the environment.

Blind horses with even temperaments often modify the fight-or-flight behavior that can be so hazardous to the health of a sighted horse. Many anecdotes demonstrate that these animals override their natural tendency to panic when faced with a situation in which they are stuck or trapped. Many blind horses that get tangled in fences or farm machinery escape injury because they calmly wait for assistance. A sighted horse in a similar situation would be expected to panic and sustain severe trauma.

TRAINING BLIND HORSES: TALK AND TOUCH!

Blind horses must be well adjusted to vision loss before serious training is begun. Handlers who practice constant talking and touching will help their horse adapt to blindness and set the stage for future lessons. Caretakers should speak in constant low soothing tones to calm the horse and help it become oriented. They should offer frequent hand contact and close physical presence. Blind horses will be steadied if they are led with a guiding hand on the neck or shoulder (Fig. 14-10). With time and patience, the horse will relax. Adaptation is complete when the horse navigates its environment with confidence and carries out all parts of the daily routine (eating, turnout, grazing, grooming, etc.) without undue anxiety.

After the horse has adjusted to blindness, structured training sessions can begin. The habit of constantly touching and talking to the horse should be continued, respecting the fact that these two senses are heightened in all blind animals. Trust will grow and basic commands will be learned quickly if the trainer gives consistent cues and stays relaxed and nonthreatening. Initially, commands such as "whoa," "step up," "step down," "stand," and "back" are taught. Verbal signals for the desired behavior are augmented by tactile cues that help "explain" the desired result.

"Whoa" can be taught by saying the command while restricting forward movement using pressure on the lead shank or rein and a hand on the chest (Fig. 14-11). "Step up" can be learned by guiding the horse over a known elevation like a ledge entrance into a barn or the ramp of a trailer while voicing the chosen cue (Fig. 14-12). "Stand" can be taught by speaking the command while emphasizing the halt stance with a hand on the body. The most important commands to master are the order to stop ("whoa") and a cue to let the horse know there is an obstacle ahead.[5] Good trainers use consistent pronunciation of commands and inflections that do not vary in pitch to teach blind horses the exact meaning of the chosen set of cues. They keep their tactile cues consistent and clear.

As training goes on, the horse may learn to pick up additional nonverbal cues and will start to respond to the trainer's touch, footfalls, and body position. Blind horses benefit from natural horsemanship exercises that involve positive reinforcement of desired behaviors. Most of these natural horsemanship

Figure 14-10. Blind horses will be steadied if they are led with a guiding hand on the neck. Here, Daisy, a 38-year-old blind Shetland pony is led by her owner down a lane to her barn. (Photograph courtesy Larry and Nancy Knickerbocker, Pittsford, NY.)

Figure 14-12. Commands are taught by a combination of talk and touch in the presence of a trusted handler. "Step up" and "step down" commands can be learned by guiding the horse up and down a trailer ramp. (Photograph courtesy Steve Smith, Rolling Dog Ranch Animal Sanctuary, Ovando, MT.)

Figure 14-11. TJ is being taught to halt by his owner. While walking beside him, she gives the appropriate rein aids as she says the command "Whoa." (Photograph courtesy Susan Straumann, Woodstown, NJ.)

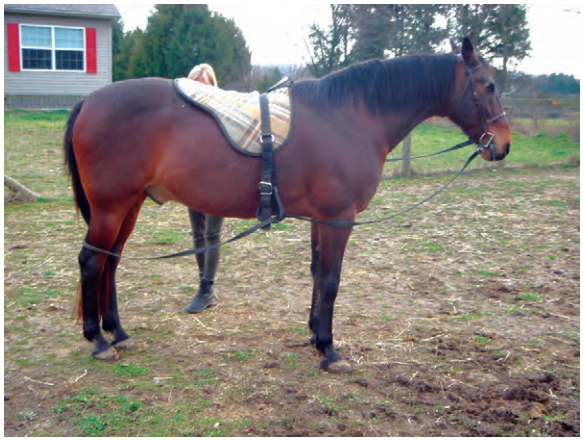


Figure 14-13. Equipment like the saddle pad, saddle, bridle, and girth should be put on and taken off repeatedly. TJ is now familiar with the sensation of being "tacked up" and accepts the pressure of all straps that hold equipment in place. (Photograph courtesy Susan Straumann, Woodstown, NJ.)

methods involve frequent auditory and tactile cues so they are easily adapted to blind horses.

Safety concerns preclude veterinarians from advising their clients to ride their blind horses. Still, many owners choose to use their blind horses for riding. Trainers of blind riding horses report that these horses benefit from long sessions of ground work before any attempt is made to put weight on their back. Equipment like the saddle pad, saddle, bridle, and girth is put on and taken off over and over until the horse is thoroughly familiar with the sensation of being "tacked up" and accepts the pressure of any straps that hold equipment in place (Fig. 14-13). Considerable time is spent teaching the horse the typical mounted aids by giving the same signals from the ground. The rein aids have been taught by using rein pressure applied to the bit by a person walking beside a bridled horse, coupled with already learned verbal commands.[4]

Figure 14-14. Long-lining sessions are a useful way to teach blind horses basic aids. Here TJ wears two long reins affixed to the bit, one on each side. His owner uses the reins to help him do slow lunge work in a circle. (Photograph courtesy Susan Straumann, Woodstown, NJ.)

Figure 14-15. Many blind horses are kept as "pasture pets." Cloud, an Appaloosa mare that has been blind for over 10 years, is regarded as a member of the family. (Photograph courtesy James and Judith Griffin, Mendon, NY.)

Many advanced riding aids have also been taught from the ground using "long-lining" sessions, where two long straps or reins are affixed to the bit, one on each side. The straps can be used to "drive" the horse from behind, or do lunge work in a circle (Fig. 14-14). The straps transmit signals that are similar to those a rider on the back would give, but the signals all originate from a handler who is actually on the ground.[4]

Trainers advise that no one should attempt to ride a blind horse alone. Initial weight-bearing sessions should be done with a competent "spotter" on the ground who can help reinforce the cues the rider gives and provide an added measure of safety. As basic training is completed, trainers then add aspects of work that match the intended use of the horse. It is important to introduce new stimuli slowly and stop the lesson or "switch gears" to a familiar task if something is frightening to the horse.

People who work with tractable, well-adapted blind horses report that these horses learn their lessons quickly. The horses seem to enjoy regular training sessions and put absolute trust in their handlers. Working with a familiar sighted person seems to give blind horses a sense of "freedom in the dark." A trained blind horse trusts that the cues the trainer gives are safe and learns to obey directions with confidence.

Communication between a blind horse and its trainer is quite refined, especially in horses used for dressage or other riding purposes. Trainers, riders, and owners cite the rewards of working with blind horses, describing heightened awareness of their own special senses and a deep and satisfying sense of partnership with these animals.

LIVES BLIND HORSES LEAD

There are thousands of bilateral blind horses alive in the world. Their owners choose to manage them in a variety of ways.

Many mares that go blind are used as broodmares. Their breeding behavior is similar to that of sighted mares. However, lacking photoreceptors, they do not respond to artificial light treatment for inducing estrus early in the year when the natural photoperiod is short. Most cycle normally by April and thus can be bred relatively early in the year. Their gestational issues are exactly the same as those of sighted horses, and they should be placed on the same schedule for nutrition, deworming, and vaccination as other mares on the farm. If a mare became blind as a result of leptospirosis-associated uveitis, serologic testing is recommended for other broodmares on the farm, because leptospiral infection is well documented as a cause of abortion. Most sighted mares foal in the middle of the night, but blind broodmares tend to foal at any time of day or night, so extra vigilance is warranted when these mares near their due dates.

A veterinary consult is advised if a blind mare or stallion is under consideration for breeding. In some instances (e.g., Appaloosas with insidious uveitis or European Warmbloods with certain equine leukocyte antigen [ELA] haplotypes), there may be a genetic predisposition to blindness.[8,9] Animals with suspected genetic issues associated with blindness should not be used for breeding.

Many blind horses are kept as simple pasture pets. They are not ridden but are treasured family members (Fig. 14-15). Their owners enjoy caring for them and are happy to provide them basic shelter, feed, and handling in return for their affection and companionship. If the horse has a calm and gentle temperament and has successfully adapted to blindness, it may provide a steadying influence in the form of company for flighty young stock or older sighted horses who do not tolerate solitude.

Other blind horses are used as trail horses (Fig. 14-16). These animals have a strong bond with their riders and are highly cued to riding aids and voice commands. Mileage on unfamiliar trails cements the trust between horse and rider because the horse depends on the rider for guidance and avoidance of hazards. Blind trail horses are taught to step over logs and small obstacles in their path in response to voice or tactile cues. Anecdotal reports indicate that many blind horses adopt a very confident attitude on the trail. Some blind horses like to take the dominant "lead" position if riding is done in a group; others prefer to follow sighted horses. Most owners who maintain blind trail horses report that these animals are very agreeable mounts. They are eager to go out on rides and willing to enter and exit trailers. Like blind people who travel with guide dogs, these horses seem to enjoy an outing using the rider as a pair of "seeing eyes."

Figure 14-16. Some blind horses are used as trail horses. This photograph shows Domino, a blind Appaloosa, and Nikki, a blind Quarter Horse going out for a ride in Montana. (Photograph courtesy Steve Smith, Rolling Dog Ranch Animal Sanctuary, Ovando, MT.)

Figure 14-18. Valiant, a Dutch Warmblood gelding, performing a dressage test in Florida. Bilaterally blind since the age of 6, this horse has been trained for upper-level dressage since he lost his sight. His rider, Jeanette Sassoon, provides performance cues or "aids" by subtle shifts in the position, pressure, and balance of her hands, legs, and body. (Photograph courtesy Dr. Dennis Brooks and Jeanette Sassoon.)

Figure 14-17. People with physical challenges want to focus on their abilities, not their disability, and find inspiration in relating to horses that have overcome similar challenges. They also experience a wide range of physical, mental, and emotional benefits. Pictured here is a blind rider performing vaulting (mounted acrobatics) during a therapeutic riding lesson, with several volunteers providing assistance on the ground. (Photograph courtesy EquiCenter Inc., Mendon, NY.)

Some blind horses have been used in therapeutic riding programs where children and adults with disabilities learn to ride and practice horsemanship. Blind horses who succeed as therapeutic lesson horses have gentle dispositions and are well trained and quiet. The riding-lesson sessions usually involve at least two assistants on the ground. One leads the horse and the other(s) provides guiding hands for rider stability and safety (Fig. 14-17).

Caring for, riding, and observing a horse that has lost the sense of vision may help people who have disabilities. The horse's ability to cope with blindness may inspire the rider to overcome his or her own special challenges. Also, enucleated or phthisical blind animals have a "different" appearance that is at first a bit startling. These horses teach children and adult family members acceptance of altered appearance relating to physical challenges.

A few blind horses have gone on to celebrated careers as high-level athletes. Dressage is an English equestrian discipline practiced by some well-adapted blind horses (Fig. 14-18). The sport involves a high level of precise communication between horse and rider. The signals used are primarily tactile because the rider uses subtle changes in the position and pressure of the hands, legs, seat, and body balance to tell the horse to change gait, speed, rhythm, and direction. Unlike other equestrian sports that involve obstacles (jumping), high speed (racing and polo), carriages (driving), or interaction with cows, poles, or barrels (many western events), dressage takes place in a level arena at fairly low speeds and thus poses fewer hazards for a blind animal. The rider tells the horse where the boundaries of the ring are by changes in his or her weight and body position and turns corners as part of the test pattern. Blind horses have been trained to advanced dressage standards by skilled and empathetic trainers and have competed against sighted animals at a variety of levels.[10]

Reining is a discipline that has attracted a small number of blind competitors in Western shows. Like dressage, reining is a sport that does not involve obstacles but is highly dependent on training and precise communication between horse and rider.

Each horse's circumstances are unique, and safety considerations must take priority in any choice of equestrian activity. Veterinarians should not make recommendations about riding a blind horse. Their job is to tend to the medical and welfare concerns of the animal and only give advice on general management. Veterinarians must always stress safety for both horses and humans and educate their clients in handling methods that are conservative and safe.

Owners who are making any decisions about working with their blind horse can be directed to several books[11,12] and websites[2-4] where they can read about choices other owners have

made. They may also find useful information in books that discuss managing blindness in small animals.[13]

HORSES WITH UNILATERAL LOSS OF SIGHT

Most of this chapter addresses the special issues of horses that are blind in both eyes. However, many horses lose vision in one eye for a variety of reasons, retaining normal vision in the fellow eye. Horses that lose vision in just one eye usually adapt well. If the blind eye has been enucleated, they may show a head tilt for a short time after surgery but generally revert quickly to a normal head carriage. Because they cannot see people or objects that approach on the blind side, they may be skittish when approached on that side. As a result, horses with unilateral vision are often led and approached on the visual side. Painful or unpleasant stimuli like injections are best administered on the sighted side. When the horse is handled on the blind half of the body, the handler should talk to the horse in a reassuring tone and keep a hand on the horse's body so the animal is aware of their position.

Veterinary ophthalmologists are not able to calibrate acuity or depth perception with certainty in either one- or two-eyed horses. Horses with unilateral blindness have only half the visual field of a fully sighted horse, so safety questions arise when athletic use of these animals is debated. For this reason, owners are usually advised to use one-eyed horses as sport horses with caution. However, a recent review of 34 horses enucleated at a referral center showed that 85% (29/34) returned to work in their previous discipline soon after eye removal. Disciplines these horses were used for prior to surgery included flat and steeplechase racing, dressage, eventing, hunter/jumper shows, trail riding, lesson work, and breeding. Most of the horses in the study had become acutely blind just prior to enucleation, and reasons for eye removal included ulcerative keratitis, perforation, uveitis, glaucoma, and neoplasia.[14]

A survey of the world of equestrian competition shows that unilaterally blind horses can be found leading just about every type of sporting life that fully sighted horses lead. Half-blind horses have run in the Kentucky Derby and other premiere stakes races, have competed in international combined training events, have won championships in western events, and have had storied careers as driving, harness, dressage, and show horses. Riders often comment that these horses approach jumps with confidence and appear to gauge distance well.

The show hunter sport sector has a rule that may restrict unilateral blind horses from their sanctioned competitions. The rules of the governing body that oversees rated hunter competition, the United States Equestrian Federation, state: "Animals with complete loss of sight in either eye may be found serviceably sound at the Judge's discretion, except in a class over fences where a Judge may ask a rider to change horses."[15] The language of this ruling is open to interpretation, but it implies that a unilaterally blind or enucleated horse may be dismissed from the hunter ring.

Polo matches governed by the rules of the United States Polo Association forbid match play by ponies that have lost the sight in one eye. However, collegiate rules allow unilateral blind ponies in their tournaments. Professional polo ponies that sustain a blinding eye injury may be "handed down" to collegiate teams and are often very successful athletes in that venue.

COMMENTS ON ENUCLEATION OF BLIND EYES

Many conditions that cause an eye to lose sight are acutely painful or rapidly progressive. Such cases must undergo prompt enucleation for humane and medical reasons. Decision making is usually clear in severe disease like intraocular neoplasia, large globe perforations, or corneal infections that progress to endophthalmitis.

Other conditions that cause blindness are not associated with any apparent pain and are static. Examples include horses that have cortical blindness from old head trauma, non-phthisical horses that have mature cataracts, and certain horses that have long-standing glaucoma that has resulted in an opaque but comfortable globe. These horses do not benefit from ocular surgery and should retain their globes.

However, other conditions that cause blindness may be associated with subtle low-grade discomfort that is debilitating for the horse. Decision making in these cases is murky; it is difficult to quantify ocular pain in a horse with a misshapen or diseased eye. Horses with phthisis bulbi, insidious uveitis, persistent corneal infections, and some kinds of glaucoma may show chronic tearing, keratitis, and blepharospasm (Fig. 14-19, *A*). These horses may be somewhat ill tempered and show aversive behavior if the periocular region is handled. When these horses have the abnormal eye(s) removed, they often show a great improvement in temperament (see Fig. 14-19, *B*). This fact suggests that some blind horses endure constant pain in their nonfunctional globes that compromises their quality of life.

Veterinarians should explain to owners that disease does not "stop" in a blind horse when vision is lost. Many structures in a nonfunctional globe can still transmit pain or be subject to ongoing complications. Blind eyes that suffer frequent corneal ulceration or show continuous blepharospasm are often candidates for removal. Many horses that develop glaucoma secondary to uveitis become painful and difficult to manage as they suffer episodes of corneal disruption, edema, and secondary infection. A point of diminishing returns is often reached where it is not rational to continue treating corneal disease in a nonfunctioning globe. If signs of chronic pain are identified, the owner should be counseled as to the potential benefits of enucleation.

Enucleation techniques are discussed in Chapter 3. Enucleation can be performed as a recumbent procedure under general anesthesia or as a standing procedure done with the horse heavily sedated. The population of blind horses with disease that requires enucleation is heavily weighted with advanced geriatric patients and horses such as Draft horses that are at high risk for major complications if they are put under general anesthesia (Fig. 14-20). Because of this, "standing enucleation" has become more common in recent years in many practices.[16,17]

In experienced hands, standing enucleation is a straightforward, humane, and relatively simple surgery. For the safety of both horse and veterinarian, standing enucleation should always be performed with the horse restrained in stocks. Patients are heavily sedated for the procedure and are maintained with an intravenous catheter in place to facilitate administration of additional tranquilization. Regional anesthesia must be exacting, involving a combination of retrobulbar block paired with local anesthesia. Head support, such as use of a table made of stacked bales, is advised.

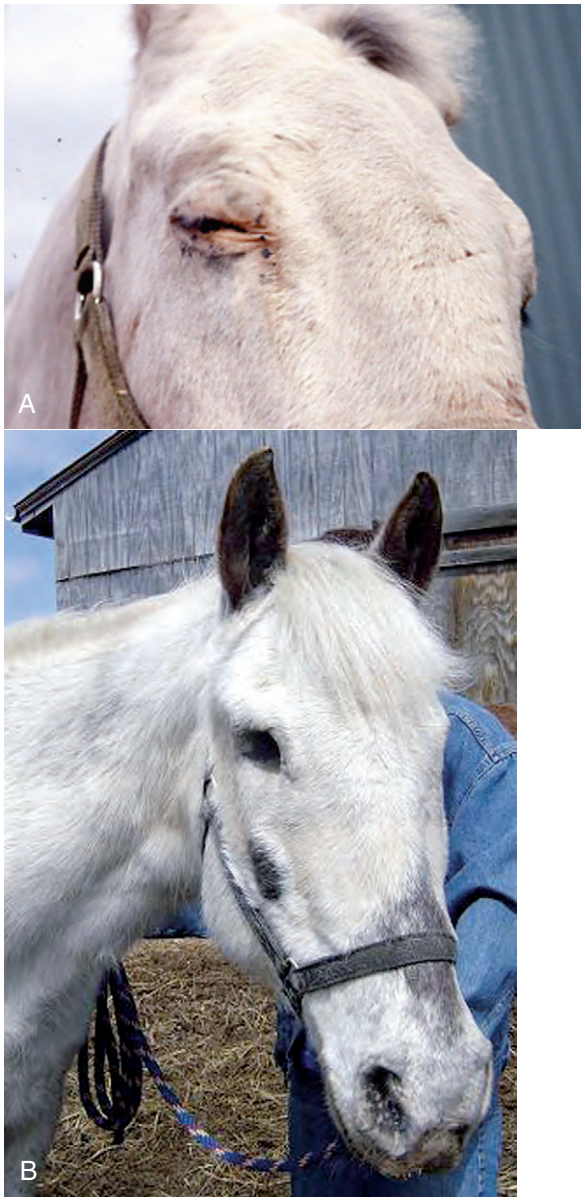


Figure 14-19. **A,** Blind horses may still experience debilitating ocular pain. This Appaloosa gelding suffers from ERU, and both globes are phthisical. Bilateral blepharospasm is a sign of persistent pain and inflammation. **B,** Enucleation is a humane option for painful blind globes. Jake is an aged Appaloosa who went blind at the age of 16 from insidious uveitis. Both globes were enucleated to resolve painful calcific keratopathy. Jake showed a notable improvement in temperament after the surgeries. (Photograph courtesy Lisa and Greg Weren, Hilton, NY.)

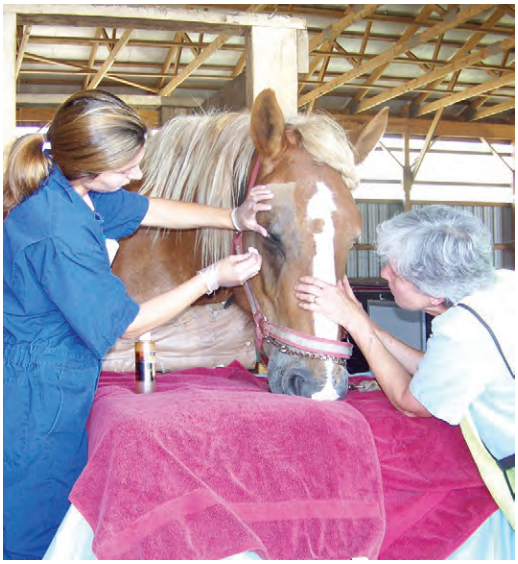


Figure 14-20. Draft horses are heavy animals at increased risk for serious complications if they undergo general anesthesia. Here a Belgian Draft horse is being prepped for enucleation that will be done as a standing procedure. (Photograph courtesy Dr. Heidi Schmitt-Weaver, Wolcott, NY.)

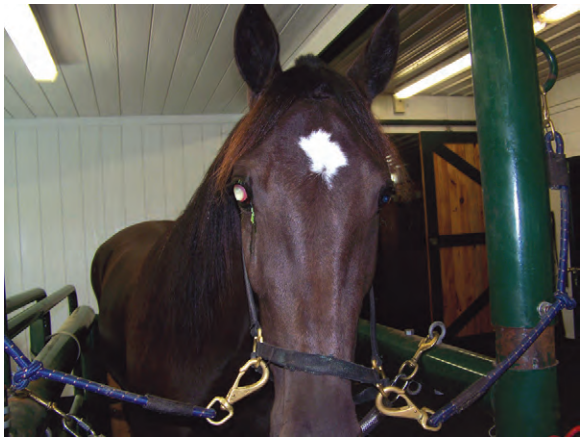


Figure 14-21. Horses recover rapidly after enucleation. Pictured here is Cocoa Bella, a Standardbred racehorse whose right eye was injured in race training. Corneal infection was complicated by perforation, and the damaged globe was enucleated the day after this photograph was taken. The mare was back in training 2 weeks after the surgery. (Photograph courtesy Chris Mazzone, Miami, FL.)

Recovery from either recumbent or standing enucleation is usually quick and uncomplicated. Horses with sight in the contralateral eye have successfully returned to riding, training, and racing as soon as a few weeks after enucleation surgery[18] (Fig. 14-21).

SPECIAL PARTNERSHIPS

Working with horses that have lost a special sense such as vision is a humbling and powerful learning experience. Observing how blind horses navigate teaches lessons of perception, adaptability, and persistence. Watching the athleticism of well-trained blind riding horses emphasizes the remarkable communication that occurs between educated horses and their riders. Anyone who helps free a blind horse trapped in a fence will be humbled by the "horse sense" that prevails when the animal needs help.

Blind horses can be an inspiration to children and adults who live with mental or physical disabilities. They can also be beloved pets that teach lessons of tolerance and acceptance of diversity. They are living proof that communication and connection between species occurs on many levels and in many ways. Few sights are more heartwarming than watching blind horses enjoy a good roll and a playful buck in a pasture on a sunny summer afternoon. These horses are telling us that life

Figure 14-22. Blind horses may enjoy life in the same way a sighted horse does. This photograph shows Scout, a blind Appaloosa who lives on Rolling Dog Ranch Animal Sanctuary in Montana, enjoying a good roll in his field. (Photograph courtesy Steve Smith.)

is sweet and full of value even when it is not perfect (Fig. 14-22).

The biggest factor that determines the success of adapting a formerly sighted horse to a life of blindness is the dedication of the owner.[1,2] Responsible owners commit to everything that is part of providing a good environment for the horse and assume the role of visual guide when the horse is in human company. The best human partners create a new, perceptive vocabulary centered on verbal and tactile signals for the horse. They may also provide a buddy horse that acts as a set of seeing eyes and provides equine companionship.

The partnership that develops between a well-adapted blind horse and its human caretaker is a very special one, based on mutual trust and respect. It is sustained by the emotional satisfaction that comes from helping a creature with special needs. Many people who care for blind horses would not trade their sightless companions for sighted horses. They report great personal rewards and satisfaction from living and working with these horses and take pride in letting them live out their natural lifespan.

References

1. Hillenbrand L: Leading the blind, Equus 229:70–80, 1996.
2. Smith S, Evans A: Web resource on blind horses, http://www.blindhorses.org/resources.html, 2009.
3. Straumann, S: Blind horse care, training and riding, http://www.blindhorsecare.org/, 2007.
4. Storch, E: Training tips: working with blind horses, http://www.flurryshope.com/, 2009.
5. Smith S: Personal communication, May 28, 2009.
6. Burton H: Visual cortex activity in early and late blind people, J Neurosci 23(10):4005–4011, 2003.
7. Liu Y, Yu C, Liang M, et al: Whole brain functional connectivity in the early blind, Brain 130:2085–2097, 2007.
8. Deeg CA, et al: Equine recurrent uveitis is strongly associated with the MHC class I haplotype ELA–A9, Equine Vet J 36:73–75, 2004.
9. Rutherford MS, Kaese H, Hendrickson JA, et al: Equine recurrent uveitis association with the major histocompatibility complex. Presented at: Plant & Animal Genomes XVI Conference, January 12–16, 2008.
10. Sassoon J: Website about "Valiant," a blind dressage horse, http://www.valianttrust.org/, 2003.
11. Stevens K: Where the blind horse sings: love and healing at an animal sanctuary, New York, 2007, Skyhorse Publishing.
12. Storch E: Horses who see with their hearts, Greensboro, 2008, Resting Place Publications.
13. Levin C: Living with blind dogs: a resource book and training guide for the owners of blind and low-vision dogs, Oregon City, 2003, Lantern Publications.
14. Utter, ME, Wotman KL, Covert KR, et al: Performance following unilateral enucleation in horses, 33 cases (2000–2008), Equine Vet J 42(2):156–160, 2010.
15. United States Equestrian Federation Rulebook: Subchapter 8F, Welfare of the horse, Section GR841, Soundness. (Accessible via www.usef.org), 2010.
16. Hewes CA, Keoughan GC, Gutierrez-Nibero S: Standing enucleation in the horse: a report of 5 cases, Can Vet J 48:512–514, 2007.
17. Pollock PJ, Russell T, Hughes TK, et al: Transpalpebral eye enucleation in 40 standing horses, Vet Surg 37:306–309, 2008.
18. Turner J: Blind ambition, Hoofbeats 77:69–71, 2009.

Glossary

This list includes commonly used terms in ophthalmology. Veterinarians should be familiar with this glossary and have a working knowledge of the terms.

Common Root Words	Meaning
blepharo-	eyelid
cor-	pupil
cycle-	ciliary body
dacryo-	tears, lacrimation
halo-	vitreous
hip-	anterior chamber
irido-	iris
kerato-	cornea
ophthalmo-	globe, eye
papilla-	optic disc
phako-	lens
tarso-	eyelid

abiotrophy tropic failure, prehensile tissue degeneration; usually used to describe retinal atrophies.

ablation removal of part of the body.

accommodation change in the degree of biconvexity of the lens to adjust the eye for seeing at different distances (poorly developed in animals).

adnexa appendages of the eye (eyelids, conjunctiva, extraocular muscles, orbital contents).

agenesis developmental absence of any body part.

amaurosis blindness, especially that occurring without apparent change in the eye itself.

aniridia absence of the iris.

anisocoria unequal pupil size.

ankyloblepharon adhesion of eyelids to each other (normal at birth in dog and cat).

anophthalmia (anophthalmos) total failure of the eye to develop (much rarer than microphthalmia).

anterior chamber space filled with aqueous, bordered anteriorly by the cornea and posteriorly by the iris and lens.

anterior chamber angle angle between the iris and corneosclera through which aqueous humor leaves the eye (also called *irido-corneal angle* or *drainage angle*).

anterior segment anterior portion of the globe (cornea, iris, lens, anterior and posterior chambers, anterior sclera).

anterior uveitis (iridocyclitis) inflammation of the iris and ciliary body.

aphakia absence of the lens.

aqueous flare visualization of a beam of light as it passes through usually transparent aqueous of the anterior chamber; seen with an increase in protein or cellular content due to uveitis (Tyndall effect).

aqueous humor clear fluid filling the anterior and posterior chambers.

asteroid hyalosis spherical and stellate opacities in the vitreous; a degenerative disease.

astigmatism spherical refractive error that prevents the light rays from coming to a single focus on the retina because of different degrees of refraction in the various meridians of the cornea or lens.

Bergmeister's papilla the remnant of the hyaloid stalk of the optic disc.

biomicroscope slit lamp, an instrument providing magnification and focused illumination for eye examination.

blepharitis inflammation of the eyelid.

blepharochalasis redundancy of the upper eyelid.

blepharophimosis inability to open eye to normal extent (similar to ptosis).

blepharospasm spasmodic blinking, spastic contraction of the orbicularis oculi muscle; often indicates pain.

blind spot small nonvisual area of the visual field, corresponding to the optic disc, since there are no photoreceptors in this area.

blood-aqueous barrier functional barrier between the vascular system and the aqueous system; consists of the tight junctions of the ciliary epithelium and endothelial cells of the iridal vessels.

bulbar pertaining to the globe of the eye as a whole.

buphthalmos (cow-eyed) enlargement of the eye due to chronic glaucoma. The appropriate term for an enlarged eye from chronic glaucoma in a horse is *hydrophthalmos*, since the equine eye is normally larger than a cow eye.

canaliculus (lacrimal) a small canal beginning at the punctum in the medial margin of each eyelid, running transversely medially to empty with its counterpart into the lacrimal sac.

canthoplasty reconstructive surgery on the canthus.

canthotomy incision of the canthus to widen the palpebral fissures.

canthus the outer or inner angle between the eyelids, where upper and lower lids join.

cataract any opacity of the lens.

chalazion a cystic dilatation or granuloma of the tarsal glands (meibomian glands) that lie in the tarsal plate.

chemosis edema of the conjunctiva.

chorioretinitis inflammation of the choroid and retina.

choristoma a mass of tissue that is normal histologically but located in an abnormal site (e.g., dermoid).

Cloquet's canal potential space passing through the middle of the vitreous from the optic disc to the lens; the hyaloid canal. Represents the remnant of the primary vitreous space.

coloboma any notch-like defects in the eye or lids; usually refers to a congenital defect.

cones retinal cells which are responsible for vision in bright light.

conjunctiva the mucous membrane lining the back of the eyelids (palpebral) and the front of the eye (bulbar) except for the cornea.

conjunctivitis inflammation of the conjunctiva.

corectopia abnormal position of the pupil.

corneal dystrophy corneal degeneration; used more broadly in veterinary medicine than in human ophthalmology.

corpora nigra cystic prominences of the posterior pigment epithelial layers of the iris that have extended around the pupillary edge of the iris. More common in herbivores and more prominent on the dorsal pupil margin. Now known as *granula iridica*.

cul-de-sac the fold between the conjunctival layers covering the lower eyelid and the eyeball.

cyclitic membrane membrane formed along the plane of the anterior vitreous face, anchored on each side at the pars plana. It originates from cells in the adjacent ciliary body and retina; common following cataract surgery.

cyclitis inflammation of the ciliary body.

cyclocryotherapy freezing of the ciliary body and processes; used for treatment of glaucoma.

cyclodialysis antiglaucoma operation which separates ciliary body from sclera to establish an alternative drainage pathway for aqueous.

cycloplegia paralysis of the ciliary muscle, resulting in loss of accommodation.

cycloplegic drug producing cycloplegia. (All cycloplegics are mydriatics; not all mydriatics are cycloplegics.)

dacryoadenitis inflammation of the lacrimal gland.

dacryocystitis inflammation of the lacrimal sac.

dacryocystorhinography radio contrast study of the nasolacrimal apparatus.

dark adaptation the ability of the retina and pupil (iris) to adjust to decreased illumination.

dermoid skinlike tumor of the cornea and conjunctiva; a type of choristoma.

descemetocele a stromal ulcer deep enough to expose Descemet's membrane.

deturgescence normal state of corneal hydration; loss of deturgescence results in edema.

diopter the unit in which the refracting strength of a lens is measured.

diplopia seeing one object as two; double vision.

disc (disk) optic nerve head (papilla); the intraocular portion of the optic nerve.

distichiasis an abnormal row of eyelashes arising from the meibomian gland orifices; individual lashes are termed *distichia*.

dystrophy (corneal) opacities of the cornea related to an inherited defect in metabolism.

ectasia dilatation, distention; usually pertaining to cornea or sclera and resulting from acquired weakness or congenital malformation.

ectropion eversion of the eyelids; drooping away from normal contact with the cornea.

electroretinography (ERG) recording of the retinal electrical potentials generated by flashes of light.

emmetropia refractive condition of the normal eye such that images focus on the retina.

endophthalmitis inflammation of the interior of the eye.

enophthalmos recession of the eyeball into the orbit.

entropion inversion of the free eyelid margin.

enucleation removal of the entire globe, leaving the eye muscles and other orbital tissue in place.

epiphora overflow of tears.

equine recurrent uveitis (ERU) recurrent iridocyclitis of horses (also called moon blindness).

esotropia inward (medial) deviation of the eye.

evisceration removal of the internal contents of the eye, with retention of the cornea and sclera.

exenteration removal of all soft tissue within the bony orbit.

exophthalmos forward displacement of the eyeball.

exotropia lateral deviation of the eyeball; divergent strabismus.

flare increased protein content of aqueous, resulting in the Tyndall effect. Flare indicates breakdown of the blood-aqueous barrier (uveitis).

floaters particles in the vitreous that cast shadows onto the retina.

fluorescein water-soluble dye which fluoresces green, particularly with blue illumination. Useful to detect corneal epithelial defects and intravenously to evaluate chorioretinal circulation or integrity of blood-aqueous or blood-retinal barriers.

fornix the reflection of the conjunctiva from the eyelid or nictitating membrane to the globe.

fovea the small depression in the macula (of the retina) adapted for the most acute vision in many primates and birds.

fundus the inside of the eye, particularly the retina, optic disc, and retinal vessels that can be seen with an ophthalmoscope.

glaucoma intraocular pressure exceeding physiologic limits.

gonioscopy examination of the iridocorneal angle with the aid of a special lens that counteracts the refractive curvature of the cornea.

hamartoma abnormal growth or malformation of tissue normally found in that location.

haw lay term for the nictitating membrane.

hemeralopia day blindness.

hemianopia loss of half the visual field.

heterochromia different colored irides (anisochromia).

hippus spasmodic, rhythmic movements of the pupil, independent of illumination.

hordeolum a sty or inflammation of the sebaceous gland or the eyelash (cilia) follicle.

Horner's syndrome sympathetic nerve paralysis characterized by miosis, ptosis, enophthalmos, and protrusion of the nictitating membrane.

hyalitis inflammation of the vitreous.

hyalosis degeneration of the vitreous.

hydrophthalmos the appropriate term for an enlarged eye from chronic glaucoma in a horse, since the equine eye is normally larger than a cow eye ("buphthalmos")

hyperopia refractive error in which the focal point of light rays is behind the retina (farsightedness).

hypertropia upward deviation of the eye.

hyphema (hyp + heme) blood in the anterior chamber.

hypopyon (hyp + pyo) pus in the anterior chamber.

hypotony (hypo + tonus) reduced intraocular pressure.

intumescent lens swollen lens due to imbibition of water.

iridectomy surgical excision of iris tissue.

iridocyclitis inflammation of the iris and ciliary body.

iridodonesis trembling of the iris with eye movements, indicating loss of the support of the lens/zonule diaphragm.

iridotomy incision of the iris.

iris bombé synechiae of the posterior surface of the iris to the anterior lens capsule so that the aqueous is trapped in the posterior chamber, causing the iris to balloon forward, often blocking the draining angle.

keratectomy excision of part or all of the cornea.

keratic precipitate (KP) aggregate of inflammatory cells on corneal endothelium, indicating uveitis.

keratitis inflammation of the cornea.
keratoconjunctivitis sicca dry eye, usually due to lacrimal gland dysfunction or inadequate distribution of tear film.
keratoconus conical protrusion of the cornea.
keratomalacia severe corneal necrosis resulting from collagenase, protease, and hydrolase enzymatic activity. Common with *Pseudomonas*, *Streptococcus*, and mycotic infections and with alkali burns.
keratomycosis fungal infection of the cornea.
keratoplasty corneal grafting.
lacrimation tear production.
lagophthalmus inadequate eyelid closure.
lenticonus conical projection of the anterior or posterior surface of the lens.
lenticular pertaining to the lens.
lenticular sclerosis (nuclear sclerosis) aging change within the lens, resulting from continual growth and compaction of the lens nuclei.
leukoma a dense, white opaque scar (*adherent leukoma* denotes a scar of the cornea, incorporating the iris).
limbus junction of the cornea and sclera.
macula a small spot; (1) a moderate corneal opacity, (2) central area in some primate and avian retinas.
megalocornea congenitally large cornea that may be confused with congenital glaucoma.
meibomian glands modified sebaceous glands of the upper and lower tarsal margin. Excretory ducts form the "grayline" of the eyelid margin.
microcornea small or hypoplastic cornea.
microphthalmia congenitally small eyeball.
miosis constriction of the pupil.
miotic *n.* drug that causes constriction of the pupil; *adj.* a small pupil.
Mittendorf's dot the remnant of the anterior hyaloid in the region of the posterior pole of the lens capsule.
morgagnian cataract a hypermature, partially liquefied cataract.
mydriasis dilation of the pupil.
mydriatic *n.* drug that causes the pupil to dilate; *adj.* term to describe a dilated pupil.
myopia refractive error in which the point of focus of the eye is in front of the retina (nearsightedness).
nebula minor corneal opacity.
nevus focal pigmented area in the iris, choroid, others.
nyctalopia night blindness.
nystagmus involuntary oscillation of the eyeballs; implies vestibular deficit or vision deficit.
O.D. (oculus dexter) right eye.
O.S. (oculus sinister) left eye.
O.U. (oculi uterque) both eyes.
palpebral pertaining to the eyelid.
pannus subepithelial proliferation, pigmentation, and vascularization of the cornea.
panophthalmitis inflammation involving all tunics of the eye.
papilla optic disc.
papilledema edema of the optic disc (papilla).
papillitis inflammation of the optic disc.
penetrating a wound going completely through an ocular structure.
photophobia abnormal sensitivity to or discomfort from light.
photoreceptors rods and cones; retinal cells which convert photic energy into electrical impulses.
phthisis bulbi shrinking of the eyeball; small, shrunken eyeball following inflammation.
plasmoid aqueous fibrin in the anterior chamber.
posterior chamber space between the posterior surface of the iris and the anterior surface of the lens; filled with aqueous.
posterior segment portion of the eye posterior to the lens.
presbyopia loss of accommodation due to compaction of the lens material in advancing age.
proptosis anterior displacement of the globe, with entrapment by the eyelids; usually traumatic.
ptosis drooping of the eyelid; usually refers to the upper eyelid.
pupil opening in the axial iris.
pupil occlusion obstruction of the pupil to obstruct aqueous flow.
pupil seclusion complete posterior synechiae restricting movement of the pupil; may lead to iris bombé.
refraction (1) deviation in the course of rays of light in passing from one transparent medium into another of different density; (2) determination of refractive errors of the eye and correction by various lenses.
refractive error deviation from emmetropia.
refractive media the transparent parts of the eye having refractive power either by their density or their curvature.
retinoscope instrument for the objective determination of refractive error.
retroillumination illuminating from behind by reflecting light from a deeper structure. Useful in evaluating the transparent media of the eye.
rods retinal cells which are responsible for vision in dim light.
rubeosis irides neovascularization of the iris stroma; may be seen with anterior uveitis, especially if chronic.
sclerotomy incision of the sclera.
scotoma a blind or partially blind area in the visual field.
sicca dry; usually used to describe keratitis.
staphyloma a bulging defect of cornea or sclera lined with uveal tissue.
stars of Winslow end-on view of small choroidal vessels perforating the tapetum to connect deeper choroid vessels to the choriocapillaris, seen as a mosaic or regularly spaced minute dark foci. Most prominent in herbivores.
stereopsis binocular vision, seeing three dimensions, giving depth perception.
strabismus deviation of the eye(s); may be lateral, medial, ventral, or dorsal; unilateral or bilateral; converging or diverging.
striate keratopathy irregular linear opacities in the cornea, usually associated with changes in Descemet's membrane. Seen in glaucoma (breaking) and phthisis bulbus (folding).
symblepharon abnormal adhesions of the conjunctiva, often affecting eyelid structure.
synechia an inflammatory adhesion of the iris to the lens or cornea.
syneresis the process of liquefaction of the vitreous with separation of fluid and contraction of the gel component.
tapetum a reflective structure within the choroid; cellular in carnivores and fibrous in ungulates.
tarsorrhaphy (temporary or permanent) an operation to decrease the size of the palpebral fissure; may be complete or partial.
tarsus the margin of the eyelid; portion containing glandular structures and hair follicles.

Tenon's capsule a connective tissue sheath encompassing the eyeball posterior to the limbus and incorporating the muscles of the orbit.

tonography continuous measurement of intraocular pressure to evaluate aqueous humor outflow potential.

tonometry measurement of intraocular pressure (usually in mm Hg).

transillumination passing a light beam through a structure; usually reflective transillumination in ophthalmology.

trichiasis eyelashes that turn against the cornea.

uvea the vascular tunic, composed of the iris, ciliary body, and choroid.

uveitis inflammation of the uveal tract.

vibrissae tactile hairs growing about the eye, nose, and/or muzzle.

visual field the area which can be seen without shifting the gaze; can apply to each eye separately or both eyes combined.

xerophthalmia keratinization of the cornea and conjunctiva secondary to lack of tears.

Index

Note: Page numbers followed by "f" refer to illustrations; page numbers followed by "t" refer to tables; page numbers followed by "b" refer to boxes.

B

C

D

E

F

G

L

M

N

O

Q

R

S

T

U

V

W

X

Y

Z