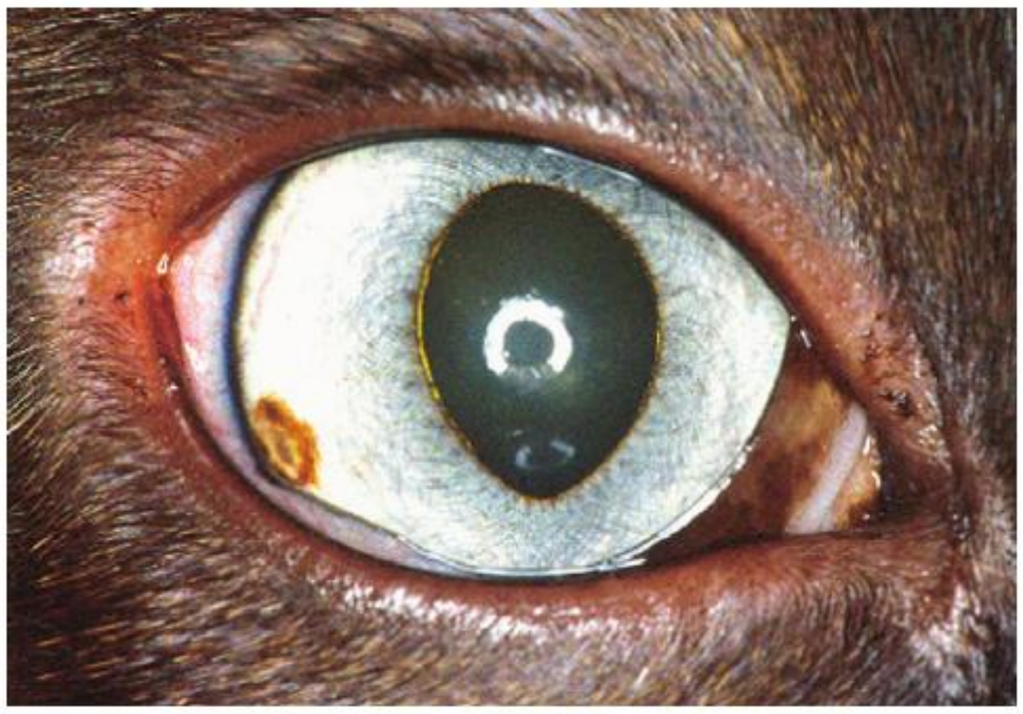

Figure 11-23 Iris nevus (freckle) in a cat. Such lesions should be regularly monitored for signs of progression.

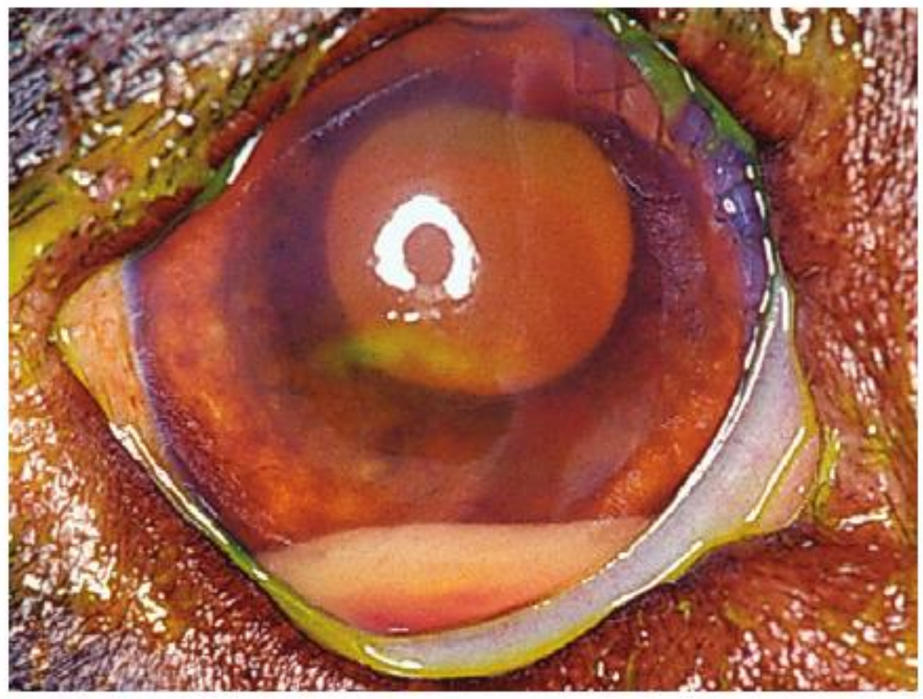

Figure 11-24 Hypopyon in the ventral anterior chamber in a dog that had suffered a penetrating ocular injury. Unless the cornea has been perforated, the anterior chamber is usually sterile in most patients with hypopyon.

Lay terms for heterochromia are as follows:

- *Wall eye:* blue and white iris or part of an iris
- *China eye:* blue iris or part of an iris
- *Watch eye:* blue and yellow-brown iris or part of an iris

In most species heterochromia is of no clinical significance.

Iris Nevus

Iris nevi (Figure 11-23) are most commonly observed in cats and dogs. They may consist of focal spots of hyperpigmentation. They must be differentiated from neoplasms that require surgical treatment. Iris nevi do not protrude above the surface of the iris and do not enlarge. Nevi have a low malignant potential and show an increase in the number of cells or greater degree of pigmentation of existing cells. They must be observed carefully for changes, especially in cats, in which they may transform into the early stages of diffuse iris melanoma, which is potentially malignant.

Waardenburg Syndrome

Waardenburg syndrome consists of deafness, heterochromia iridis, and white coat color. Although this hereditary syndrome occurs most commonly in blue-eyed white cats, it also occurs in dogs (especially the Australian cattle dog, Great Dane, and Dalmatian), mice, and humans. Not all blue-eyed white cats are affected. In the cat, the syndrome is inherited as a dominant trait with complete penetrance for the white coat and incomplete penetrance for deafness and blue irides.

UVEITIS

Clinical Signs

The detection of uveitis depends on familiarity with the clinical signs. In general the clinical signs of uveitis are similar regardless of cause or species. Signs of ocular discomfort are as follows:

- Photophobia and blepharospasm
- Pain (may manifest as anorexia or depression)
- Epiphora

Clinical signs suggesting uveitis may be present are as follows:

- Episcleral vascular injection or circumcorneal ciliary flush
- Corneal edema
- Aqueous flare
- Inflammatory cells free in the anterior chamber or adherent to the corneal endothelium (keratic precipitates [KPs])
- Hypopyon or hyphema
- Miosis
- Resistance to pupil dilation by mydriatics
- Lowered IOP
- Anterior or posterior synechiae
- Swollen or dull appearance of the iris
- Increased pigmentation of the iris
- Vitreous haze or opacity
- Retinal edema, exudate, or detachment

Aqueous flare represents increased protein in the aqueous humor and is due to breakdown of the blood-aqueous barrier. It is a hallmark of anterior uveitis.

KPs are accumulations of inflammatory cells (neutrophils, lymphocytes, or macrophages) that adhere to the corneal endothelium. In large numbers these cells not only adhere to the cornea but also form a white layer in the anterior chamber called *hypopyon* (Figure 11-24). KPs may be small and scattered (in feline infectious peritonitis) or large and yellow ("mutton-fat" KPs) in granulomatous diseases (Figure 11-25). Corneal edema frequently is present due to inflammation altering corneal endothelial cell function. Miosis may be due to iridal edema or spasm of the iridal sphincter muscle. As the inflammation subsides, synechiae may form, causing an irregularly shaped pupil or a scalloped appearance on dilation, with pigment remnants on the anterior lens capsule. If posterior uveitis is present, the vitreous may become hazy, and retinal edema, exudates, or detachments may be seen.

Sequelae of Uveitis

Posterior Synechiae

Posterior synechia are adhesions between the lens and iris typically resulting in an irregularly shaped pupil. The adhesions are

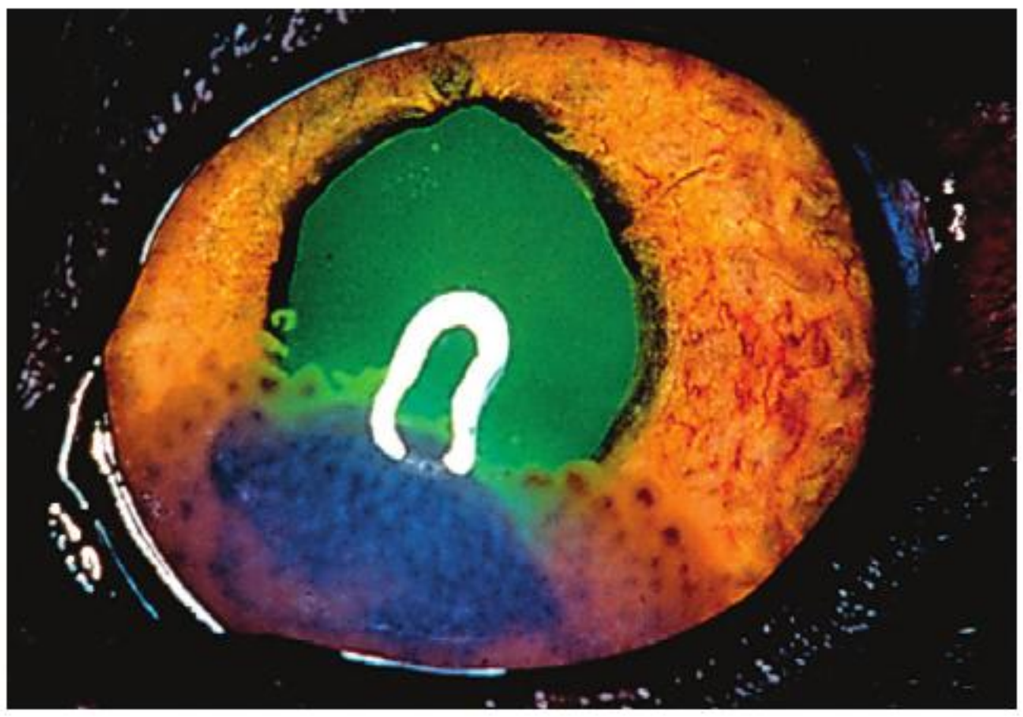

Figure 11-25 Dense "mutton fat" keratic precipitates with admixed blood in a cat with chronic anterior uveitis. The pupil margin is darker than normal and irregularly shaped as a result of eversion of the posterior surface of the iris (ectropion uveae) by a preiridal fibrovascular membrane.

initially fibrinous but later become fibrovascular and difficult to break. Formation of synechiae is more likely when aqueous protein content is high. If synechiae form around the entire circumference of the pupil, iris bombé is said to occur. This prevents the flow of aqueous humor through the pupil into the anterior chamber and secondary glaucoma almost invariably follows. If blood or exudate organizes in the anterior chamber, a connective tissue membrane may occlude or obliterate the pupil.

Peripheral Anterior Synechiae

Anterior synechia are adhesions between the iris and trabecular meshwork or between the iris and cornea. Swelling, iris bombé, and cellular infiltrates may reduce drainage of aqueous through the iridocorneal angle early in uveitis, but once peripheral anterior synechiae have formed, an alternative route for drainage must be provided, because the angle is held closed by the synechiae.

Cataract

Cataract (opacity of the lens) occurs frequently after uveitis. It is probably caused by altered composition of the aqueous that impairs lens nutrition. When an animal with a cataract and signs of uveitis is examined, determination must be made as to whether the cataract came first and caused the uveitis or the uveitis came first and caused the cataract. History usually allows this distinction to be made.

Glaucoma

IOP is usually lowered during uveitis because an inflamed ciliary body makes less aqueous humor and endogenous prostaglandins may increase uveoscleral outflow. If IOP is normal or increased in the presence of active inflammation, it is likely that aqueous humor outflow via the trabecular meshwork is impaired in one of the following ways:

- Blockage of the angle with inflammatory cells, debris, or neovascular membranes
- Peripheral anterior synechiae
- Occlusion of the pupil by posterior synechiae

Eyes with normal IOP and active uveitis may have impaired aqueous humor outflow and should be monitored carefully for glaucoma.

Intractable secondary glaucoma caused by lens-induced uveitis is a common entity, especially in dogs. This condition may be seen after penetrating injuries to the lens, in patients with long-standing cataracts undergoing lens resorption, and sometimes after cataract extraction.

Retinal Detachment

Exudation and cellular infiltration from the choroid may cause exudative retinal detachment. Inflammation-associated traction bands may also form in the vitreous and as these contract they may pull the retina away from the choroid.

Atrophy

The iris and ciliary body atrophy as the stroma is replaced by fibrous tissue. Defects may appear in the iris. Atrophy of areas of the choroid frequently results in atrophy of the overlying retina, which is visible ophthalmoscopically. Severe atrophy of the ciliary body causes hypotony (lowered IOP). In some animals the color of the iris becomes darker after uveitis. In severe cases the entire globe may shrink, a condition called *phthisis bulbi*.

Preiridal Fibrovascular Membranes

In some animals with chronic anterior uveitis, new blood vessels and fibrous membranes form on the anterior surface of the iris. These may result in eversion of the pupillary margin, called *ectropion uveae,* or glaucoma as they cover the trabecular meshwork (see Figure 11-25).

Cyclitic Membranes

A *cyclitic membrane* is a band of fibrovascular tissue extending from the ciliary body across either the pupil or the anterior face of the vitreous. It consists of fibrous tissue and blood vessels and may severely obstruct vision.

Diagnosis of Uveitis

Anterior uveitis is distinguished from conjunctivitis, superficial keratitis, and glaucoma, which also result in a red-eye (Table 11-2). The uvea is involved in numerous systemic disorders (Table 11-3). Such diseases usually affect other parts of the eye in addition to the uvea and are discussed in Chapter 18. Once uveitis is detected, every effort should be made to identify a specific cause of the inflammation so that the most effective therapy may be started. A thorough history, complete physical examination, and often additional diagnostic tests (e.g., complete blood count, serum biochemical profile, urinalysis, serologic examination, imaging, etc.) are essential for the proper diagnosis of the cause of the inflammation in a given patient.

Numerous uveitis classification schemes have been proposed, including those based on the tissues affected (anterior uveitis, posterior uveitis, panuveitis), on the presumed histologic nature of the disorder (suppurative, nonsuppurative, granulomatous, nongranulomatous), on whether the cause starts inside the eye or from its surface (endogenous versus exogenous), and on a specific cause (see Table 11-3). Although each of these schemes has its own advantages and disadvantages, classification into granulomatous or nongranulomatous and

Table 11-2 | Differential Diagnosis of Ocular Inflammations

PARAMETER	ANTERIOR UVEITIS	CONJUNCTIVITIS	SUPERFICIAL KERATITIS	GLAUCOMA
Conjunctiva	Variably thickened	Thick; folded	Variably thickened	Not thickened
Conjunctival vessels	Episcleral; not movable with conjunctiva, infrequently branch	Superficial, diffuse, extensive branching	Superficial, diffuse, extensive branching	Episcleral, not movable with conjunctiva, infrequently branch
Secretion or discharge	None to serous	Moderate to copious, serous to purulent	Moderate to copious, serous to purulent	None to serous
Pain	Moderate	None to slight	Moderate to severe	Moderate to severe
Photophobia	Moderate	None	Severe	Slight
Cornea	Clear to steamy	Clear	Clouded to opaque	Steamy
Pupil size	Small, sluggish, irregular, or fixed	Normal	Normal to small	Dilated, moderate to complete, and fixed
Pupillary light response	Variable	Normal	Normal	Absent
Intraocular pressure	Variable: may be normal, elevated, or diminished	Normal	Normal	Elevated

then by specific cause is probably the most useful method in a clinical setting, because it also helps guide specific therapy (Table 11-4). This scheme, however, is plagued by the presence of a large percentage of patients having idiopathic uveitis in which the cause remains obscure. In these patients therapy can be directed at symptoms only in terms of controlling inflammation and preventing further damage to the eye. Presumably, most of these cases are immune-mediated or involve microorganisms that are not yet recognized as pathogenic. It is hoped that over time the percentage of patients with idiopathic uveitis will decline as our understanding of the causes of this disorder improves.

Although classification as granulomatous or nongranulomatous uveitis is based on a histologic classification scheme, the criteria in Table 11-4 can also be used to make reasonable clinical inferences about the histologic nature of the inflammation and to allow for prioritization of the diagnostic tests to be performed. Most cases of granulomatous uveitis are associated with microorganism or foreign material stimulation of a chronic immune response, whereas nongranulomatous uveitis is often associated with physical, toxic, or allergic causes. After determining whether a specific animal has granulomatous or nongranulomatous uveitis, the clinician should consider specific tests to try to determine the exact cause (e.g., serum titer measurement for *Toxoplasma*). In general the following specific categories of uveitis should be considered:

- Infectious-associated—algal, bacterial, fungal, viral, protozoal, parasitic
- Immune-mediated
- Neoplastic or paraneoplastic
- Metabolic
- Traumatic
- Toxic
- Reflex
- Idiopathic

Differential diagnosis of the cause of uveitis often requires specialist assistance, notably when potential zoonotic diseases may be involved or the cause remains unclear.

A few generalizations may be made. Uveitis associated with KPs is often associated with intraocular neoplasia, feline infectious peritonitis, deep fungal agents, or intraocular foreign bodies. Severe uveitis that involves the anterior and posterior segments is often associated with a deep fungal agent, lymphosarcoma, or uveodermatologic syndrome. The last is also commonly associated with loss of pigment in the uveal tract, skin, or hair. Uveitis with hemorrhage is often associated with systemic hypertension, intraocular neoplasia, coagulopathy, or a tick-borne disorder.

General Therapeutic Principles

1. Make an Etiologic Diagnosis

The clinician must make a concerted attempt to find a cause for the uveitis. Although not all such attempts are successful, idiopathic uveitis is a diagnosis of exclusion. Often, if a specific cause is identified, more effective therapy may be instituted (e.g., removal of an abscessed tooth, treatment for deep mycosis, control corneal infection, chemotherapy for lymphosarcoma). Routine hematologic analysis and serum chemistry profiles are useful in indicating the presence of inflammatory disorders and concurrent systemic disease (see Table 11-3). In endemic areas appropriate serologic tests are indicated (e.g., for toxoplasmosis, coccidioidomycosis, blastomycosis, cryptococcosis). Blastomycosis is found most frequently in the central United States east of the Mississippi River, and coccidioidomycosis is found in Arizona, Nevada, and the central valley of California.

2. Control Inflammation

CORTICOSTEROIDS. Corticosteroids may be given via the topical, systemic, or occasionally subconjunctival route. These agents inhibit cell-mediated immune reactions, decrease antibody production, stabilize lysosomal membranes, and reduce release of intracellular proteolytic enzymes. If corticosteroids are administered via the topical or subconjunctival routes, the cornea must not retain fluorescein stain. Additionally, immunosuppressive therapy should not be instituted if active infectious diseases, such as a deep fungal agent, have not been ruled out. In general the following approach is helpful:

- For mild uveitis (mild conjunctival hyperemia, no obvious or only minimal aqueous flare, hypotony, with or without miosis):
  1. Topical corticosteroids—0.1% dexamethasone or 1% prednisolone acetate every 6 to 12 hours

Table 11-3 | Causes of Uveitis

CAUSE	MOST COMMONLY AFFECTED SPECIES
NEOPLASTIC AND PARANEOPLASTIC	
Lymphosarcoma	Any
Melanoma	Dog, cat
Histiocytic proliferative disease	Dog
Hyperviscosity syndrome	Dog
Granulomatous meningoencephalitis	Dog
Miscellaneous primary intraocular tumors	Any
Miscellaneous metastatic tumors	Any
METABOLIC	
Diabetes mellitus (lens-induced uveitis)	Dog
Systemic hypertension	Cat, dog
Hyperlipidemia	Dog
Coagulopathies	Any
IDIOPATHIC	Any
IMMUNE-MEDIATED	
Cataracts (lens-induced uveitis)	Any
Lens trauma (phacoclastic uveitis)	Any
Immune-mediated thrombocytopenia	Any
Immune-mediated vasculitis	Any
Uveodermatologic syndrome (Vogt-Koyanagi-Harada–like syndrome)	Dog
INFECTIOUS	
Algae	
Geotricha spp.	Dog
Prototheca spp.	Dog
Bacteria	
Septicemia or endotoxemia resulting from any cause	Any
Leptospira spp.	Dog, horse
Bartonella spp.	Dog, cat
Borrelia burgdorferi	Dog, horse
Brucella spp.	Dog, horse
Escherichia coli	Cattle, horse
Streptococcus spp.	Horse
Rhodococcus equi	Horse
Listeria monocytogenes	Sheep, cattle
Haemophilus spp.	Cattle
Tuberculosis	Cattle, cat
Ehrlichia canis or *Ehrlichia platys*	Dog
Rickettsia rickettsii	Dog
Protozoa	
*Toxoplasma gondii**	Any
Leishmania donovani	Dog
Yeasts and Fungi	
Aspergillus spp.	Chickens, turkeys, cat
Blastomyces spp.	Dog, cat
Coccidioides immitis	Dog
Cryptococcus spp.	Dog, cat
Histoplasma capsulatum	Dog, cat
Pseudallescheria boydii	Dog
Viruses	
Canine adenovirus types 1 and 2 (immune-mediated)	Dog
Canine distemper virus	Dog
Coronavirus (feline infectious peritonitis)	Cat
Feline leukemia virus	Cat
Feline immunodeficiency virus	Cat
Herpesvirus (Marek's disease)	Chickens, turkeys
Herpesvirus	
Feline herpesvirus 1	Cat
Canine herpesvirus 1	Dog
Equine herpesvirus 1 and 2	Horse
Ovine herpes virus 2 (MCF)	Cattle
Alcelaphine herpesvirus 1 (MCF)	Cattle
Rabies virus	Dog
Equine influenza	Horse
Equine viral arteritis	Horse
Parainfluenza type 3	Horse
MCF	Cattle
Parasitic	
Taenia multiceps	Sheep, dog
Echinococcus granulosis	Horse (rare)
Angiostrongylus vasorum	Dog
Dirofilaria immitis	Dog
Setaria spp.	Horse
Onchocerca cervicalis	Horse (equine recurrent uveitis)
Strongylus	Horse
Diptera spp. (ophthalmomyiasis interna)	Various
Toxocara spp., *Baylisascaris* spp. (ocular larval migrans)	Dog, cat, sheep and goats
Trypanosoma spp.	Cat
Elaeophora schneideri	Sheep and goats
TOXIC	
Drugs	
Pilocarpine, carbachol other parasympathomimetics	Any
Prostaglandin derivatives (latanoprost)	Any
Sulfamethazine and trimethoprim (immune-mediated)	Dogs
Endotoxemia from any systemic source	Any
Infectious keratitis with bacterial toxin production	Any
Radiation therapy	Any
TRAUMA	
Blunt or penetrating injuries	Any
Corneal foreign bodies	Any
REFLEX UVEITIS	
Ulcerative keratitis of any cause	Any
Deep necrotizing or nonnecrotizing scleritis	Dog
Episcleritis	Dog

MCF, Malignant catarrhal fever.
**Neosporum caninum* has been found responsible for some cases of previously diagnosed *T. gondii* infection in dogs. The clinical significance is undetermined.

Table 11-4 | Classification Criteria for Anterior Uveitis*

Nongranulomatous	Granulomatous
Acute onset	Gradual onset
Short course	Chronic or recurrent
No keratic precipitates	Keratic precipitates, greasy exudate on lens surface
No synechiae	Posterior synechiae
No iris nodules	Possible iris nodules
Primarily anterior uveitis	Possible posterior uveitis

*These criteria are useful but not absolute and are interpreted along with other clinical signs.

- For moderate uveitis (moderate conjunctival hyperemia, readily detected aqueous flare, normal or decreased IOP, with or without miosis):
  1. Topical corticosteroids—0.1% dexamethasone or 1% prednisolone acetate every 4 to 6 hours
  2. Systemic prednisone 0.25 mg/kg by mouth in dogs and cats; in horses a systemic nonsteroidal antiinflammatory drug (NSAID) should be used instead
- For severe uveitis (marked conjunctival hyperemia, marked aqueous flare, fibrin, or hypopyon, with or without miosis):
  1. Topical corticosteroids—0.1% dexamethasone or 1% prednisolone acetate every 1 to 4 hours
  2. Systemic prednisone 1 mg/kg by mouth (PO) in dogs and cats; in horses a systemic NSAID should be used instead
  3. Consider triamcinolone acetonide 1-2 mg per eye administered subconjunctivally.

NONSTEROIDAL ANTIINFLAMMATORY DRUGS. Significant protein leakage from uveal vessels during inflammation is mediated by prostaglandins. Inhibition of prostaglandin production decreases the amount of antibody present to engage in immunologic reactions and also decreases fibrin, which reduces synechia formation. Because endogenous prostaglandins also contribute to miosis by a mechanism that is not blocked by atropine, a NSAID may facilitate pupillary dilation with atropine. In general, topical and systemic NSAIDs are not as potent as corticosteroids in the treatment of immune-mediated uveitis but may approximate or exceed the efficacy of corticosteroids in traumatic uveitis. Topical NSAIDS include flurbiprofen, suprofen, diclofenac, ketorolac, and indomethacin. These drugs are administered every 6 to 12 hours in most species. Systemic NSAIDS are typically dosed at levels recommended for the species being treated.

IMMUNOSUPPRESSIVE AGENTS. Cyclosporine at 0. 2% to 2%, orally or as a surgically placed implant in horses, or oral azathioprine may be used in select cases of nonresponsive uveitis. Typically these agents require periodic laboratory evaluations for systemic side effects, especially those involving the bone marrow, liver, and kidney. Azathioprine has been suggested at 1 to 2 mg/kg/day for 3 to 7 days, followed by tapering to as low a dosage as possible.

3. Prevent Undesirable Sequelae

MYDRIATICS AND CYCLOPLEGICS. Pupillary dilation (mydriasis) can help reduce synechiae formation and the likelihood of iris bombé with secondary glaucoma. Relaxation of the ciliary muscle (cycloplegia) can help lessen ocular pain. In general the dose required to dilate the pupil is somewhat lower than that necessary to induce cycloplegia and provide pain relief. Atropine ophthalmic ointment or solution at 1% is a parasympatholytic agent with potent mydriatic and cycloplegic activity, whereas 0.5% to 1% tropicamide solution is a shorter-acting parasympathomimetic with relatively potent mydriatic effects but milder cycloplegic effects. Sympathomimetics, such as 10% phenylephrine given every 8 to 12 hours, can boost the mydriatic effects of atropine and tropicamide, but these drugs afford no meaningful cycloplegia. On rare occasions mydriasis can compromise the drainage angle, leading to rises in IOP, or reduce tear production, especially in animals with keratoconjunctivitis sicca. Topical atropine may also reduce gastrointestinal motility in horses. In general, atropine is used one to three times per day or to effect.

Specialists also may inject tissue plasminogen activator into the anterior chamber in an effort to dissolve fibrin clots and prevent synechia.

ANTIGLAUCOMA DRUGS. IOP is typically low in uveitis because an inflamed ciliary body makes less aqueous humor and endogenous prostaglandins increase uveoscleral outflow. If IOP is normal or elevated in the presence of inflammation, the drainage angle is probably compromised and the clinician must be concerned about impending glaucoma. It is essential that irreversible glaucomatous damage not be allowed to occur while antiinflammatory therapy works to clear the drainage angle. In general a topical or systemic carbonic anhydrase inhibitor (dorzolamide or methazolamide), a topical β-blocker (timolol), or an adrenergic agent (dipivefrin) is preferred to a parasympathomimetic (pilocarpine, demecarium bromide) or a prostaglandin derivative (latanoprost, travoprost), either of which may make the pupil miotic (and hence more prone to iris bombé) and exacerbate intraocular inflammation.

4. Relieve Pain

The cycloplegic action of atropine relaxes the ciliary muscle and helps reduce ocular pain in uveitis. The patient may also be placed in a darkened room or stall to alleviate photophobia. Topical or systemic NSAIDs can provide pain relief as well as aid in controlling inflammation. For severe pain a systemic analgesic, such as butorphanol, morphine, or oxymorphone, may be used.

Specific Forms of Uveitis

Infectious Uveitis

The infectious causes of uveitis are summarized in Table 11-3. Many of these agents are located in specific geographic regions, a feature that helps narrow the list of possible causes in a given patient. Not all patients with infectious uveitis have living organisms within the eye. Uveitis may occur as a result of intraocular infection or in response to bacterial toxins generated within or outside the eye, or may stem from an immunologic response to the organism, which may be within the eye or elsewhere in the body. It is well recognized that uveitis may be associated with infection outside the eye, including prostatitis, endometritis, gingivitis and tooth root abscess, mastitis, metritis, navel ill, and pneumonia. In these cases uveitis may result from shedding of bacteria into the circulation, the uveitis being secondary to previously sensitized lymphocytes in the uvea, or

may be due to bacterial toxins released from the primary site. Often the uveitis is recurrent in these cases, and hematologic examination or blood culture may be of value in arriving at a definitive diagnosis.

Blastomycosis, ehrlichiosis, histoplasmosis, and coccidioidomycosis are important causes of uveitis in dogs, as are cryptococcosis, toxoplasmosis, and feline infectious peritonitis in cats. If uveitis is present in association with lesions of lungs, bone, lymph nodes, skin, or testicles, or if the animal is located in an area endemic for any of these organisms, appropriate serologic, radiographic, and cytologic tests are indicated.

Immune-Mediated Uveitis

Immune-mediated uveitis may be the result of a primary reaction to a foreign antigen, an autoimmune phenomenon directed against self-antigens, or a combination of the two. It is believed that the majority of idiopathic cases of uveitis are actually immune-mediated. Often the diagnosis is made through exclusion of all known causes of uveitis. In some cases specific clinical signs (depigmentation) or historical events (a complete cataract preceding the inflammation or cat-scratch injury involving the lens) support the diagnosis of immune-mediated uveitis, and a detailed evaluation is not required.

UVEODERMATOLOGIC SYNDROME. Also known as Vogt-Koyanagi-Harada–like syndrome, uveodermatologic syndrome affects certain breeds more commonly than others—Akita, Old English sheepdog, golden retriever, Siberian husky, and Irish setter. It is a spontaneous autoimmune disease apparently directed against melanin that affects the anterior and posterior uvea, frequently resulting in blindness from retinal detachment or glaucoma. Antiretinal antibodies to previously sequestered retinal antigens may also be present. Presumably the antibodies develop after the initial insult has severely damaged the retina and may represent epitope spreading. Depigmentation of the mucocutaneous junctions, eyelids, and hair coat may precede or follow the ocular signs. Histologic examination of a biopsy specimen from the mucocutaneous junction (especially the lips), even if the tissue appears grossly normal, can be useful in the diagnosis of this disorder if results of a systemic evaluation are otherwise noncontributory and the animal has severe anterior and posterior uveitis. Neurologic signs are associated with the syndrome in humans but are rare in dogs. In some geographic regions the onset of the disease has a definite seasonal incidence (e.g., February to May in southern California).

Vigorous early antiinflammatory therapy with topical and systemic corticosteroids, NSAIDs, and azathioprine is often necessary to save vision. Recurrences of the disease can be expected, and maintenance therapy using appropriate medications between recurrences is typically required. Given the severe and relentless nature of the uveitis, the immediate assistance of a veterinary ophthalmologist should be sought in the handling of dogs affected with uveodermatologic syndrome.

LENS-INDUCED UVEITIS. The embryologic characteristic of the lens is such that the lens capsule essentially isolates the lens proteins immunologically from the immune system before birth. Therefore if the lens capsule leaks or ruptures, lens proteins may enter the aqueous and elicit an immune-mediated uveitis that may be acute or chronic. The most common causes of lens-induced uveitis are liquefaction of cataractous lens proteins that escape through an intact lens capsule, swelling of a cataractous lens with increased "porosity" of an otherwise intact lens capsule, small tears in the lens capsule from rapidly forming cataracts and lens swelling (diabetes mellitus), and traumatic disruption of the lens capsule (cat scratch, penetrating injuries).

Leakage through the Intact Lens Capsule. The most common form of lens-induced uveitis is caused by leakage through the intact lens capsule, which is most frequently seen in conjunction with the advanced stages of cataract (complete on resorbing). It should be suspected in every animal in which a complete or resorbing cataract precedes the onset of a "red eye," or in animals with a "red eye" and a cataract. It may be differentiated from uveitis-induced cataract by the fact that in the latter, the "red eye" uveitis precedes the cataract. Lens-induced uveitis should be anticipated in all eyes with cataract, although it does not always occur. In this form of the disease the lens capsule becomes permeable, allowing liquefied cortex to leak into the aqueous and creating an immune-mediated uveitis and, possibly, secondary glaucoma. Without tonometry and biomicroscopy, this inflammation may not be evident, and many such eyes exhibit a normal sized pupil—not a miotic pupil as would be expected in uveitis. Affected eyes, however, do typically exhibit at least some conjunctival hyperemia. Eyes with lens-induced uveitis before cataract surgery have a greater risk for many postoperative complications (glaucoma, retinal detachment) than eyes without it.

Therapy with topical corticosteroids or NSAIDs, often for relatively long periods, may be needed to control lens-induced uveitis. In particularly severe cases systemic antiinflammatory agents may be required. Corticosteroids, even those administered topically, should be used with caution in dogs with poorly regulated diabetes mellitus, cataract, and lens-induced uveitis so as to avoid worsening the glycemic control.

Lens-induced uveitis should be suspected in all red eyes in which cataract preceded the conjunctival hyperemia. Glaucoma should be ruled out in these cases.

Failure to recognize and treat lens-induced uveitis when cataracts are first diagnosed is a very common cause of lower success rates of cataract surgery in dogs. Medical therapy for lens-induced uveitis should be implemented as soon as the diagnosis is established.

Penetrating Lens Injuries. Penetrating injuries to the lens often quickly progress to endophthalmitis with secondary glaucoma (Figure 11-26). Bacteria are commonly inoculated during the injury, resulting in a mixed purulent inflammation with numerous neutrophils. Early lens extraction may offer the greatest chance for saving the eye, although large case studies to support this aggressive method of treatment are lacking. In many older dogs, medical treatment after lens capsule rupture cannot prevent loss of the eye through uncontrolled inflammation and secondary glaucoma. In dogs younger than 12 months much of the lens cortex may be resorbed, with less inflammation than in older animals, provided that infection is controlled. Nevertheless the long-term prognosis remains guarded in these animals.

Penetrating injury and lens capsule rupture are common causes of uveitis and endophthalmitis in dogs and cats.

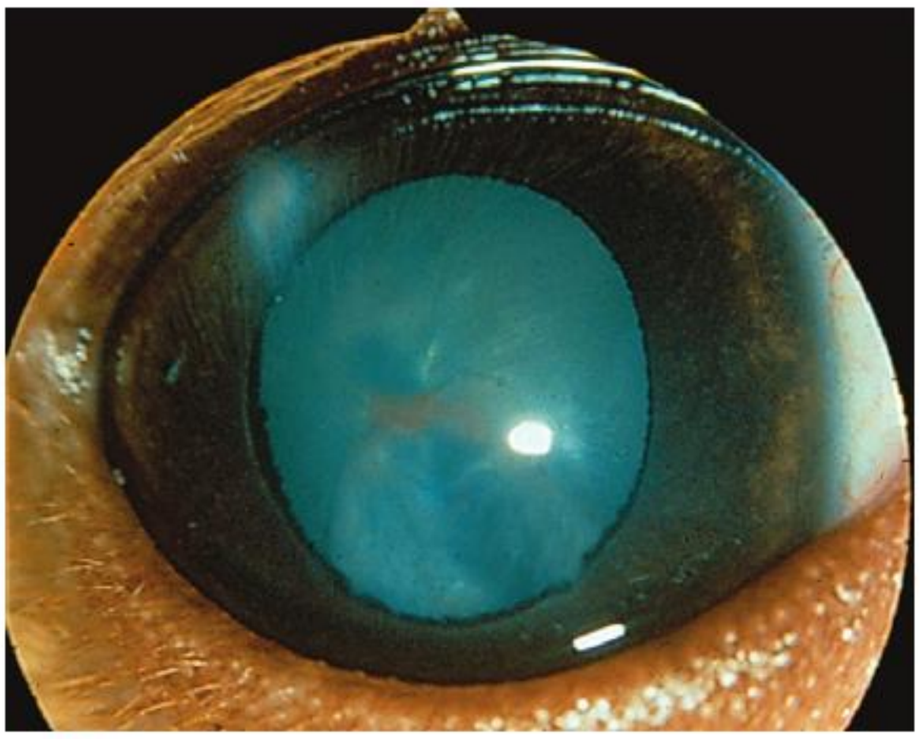

Figure 11-26 Chronic lens-induced uveitis in a basenji puppy after a cat claw injury. The lens capsule has been ruptured by the nail.

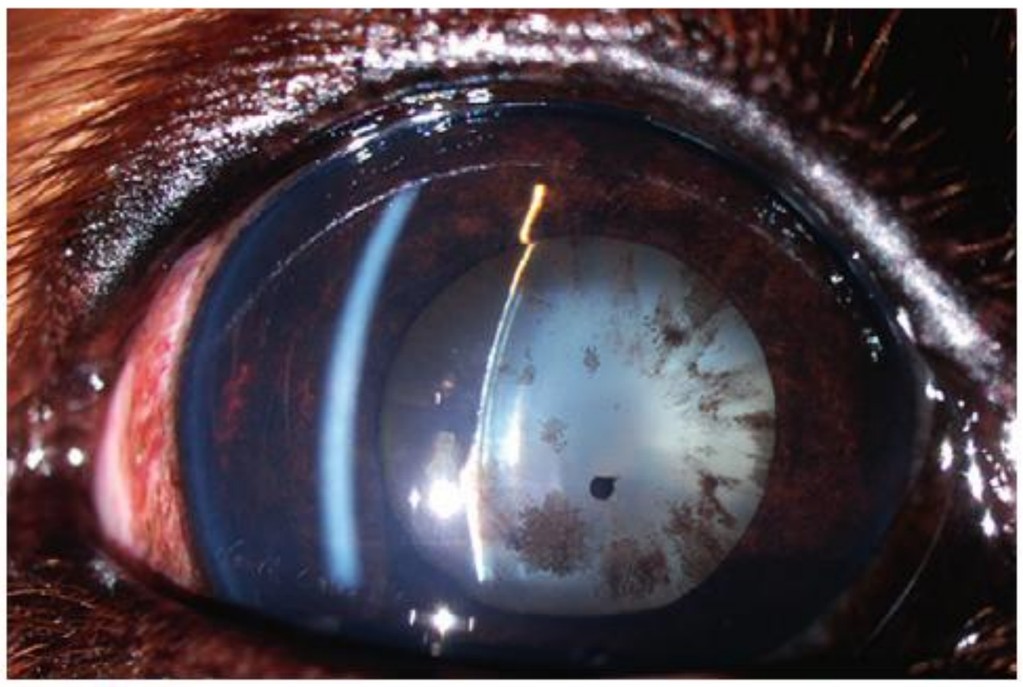

Figure 11-27 Golden retriever uveitis (pigmentary uveitis of golden retrievers) is characterized by pigmented cells in the anterior chamber, pigment deposition on the anterior lens capsule in a radial spokelike pattern, pigment deposition on the corneal endothelium, and an iris that is darker and thicker than normal. In one study all dogs had ciliary cysts, but these are not always externally visible (see Figure 11-9).

UVEITIS ASSOCIATED WITH DENTAL DISEASE. Untreated gingivitis, periodontitis, and tooth root abscesses are very common causes of severe uveitis in dogs. Treatment of dental disorders is essential before any intraocular surgery is undertaken as well as for the patient's general health.

GOLDEN RETRIEVER UVEITIS. Sometimes called "pigmentary uveitis of golden retrievers," this form of uveitis is common in golden retrievers and is characterized by the presence of pigmented cells in the anterior chamber, pigment deposition on the corneal endothelium, a darker and thickened iris, and a characteristic deposition of pigment on the anterior lens capsule in a radial pattern (Figure 11-27). Aqueous flare, fibrinlike material in the anterior chamber, posterior synechiae, cataract, and glaucoma may also occur. The cause of the disorder is undetermined, although one study found on histopathologic examination that all dogs with this disorder also had cysts on the ciliary body or posterior surface of the iris even though the cysts were not always visible clinically (see Figure 11-9). This suggests that the pigment and fibrinlike material in the anterior chamber may be liberated from the walls of the cysts as the posterior surface of the iris rubs against the cyst with changes in pupil size. Treatment is as for other forms of uveitis although the response to therapy tends to be poor and frequently vision is lost.

FELINE UVEITIS. Common causes of uveitis in cats include feline infectious peritonitis, lymphosarcoma caused by feline leukemia virus, feline immunodeficiency virus, toxoplasmosis, cryptococcosis, histoplasmosis, blastomycosis, and coccidiomycosis. The role of *Bartonella* spp. in feline uveitis is unclear. For details of the ocular manifestations of specific disorders, see Chapter 18. A specific type of nongranulomatous anterior uveitis described as *lymphocytic-plasmacytic uveitis* has been recognized as a common precursor to glaucoma if the uveitis is uncontrolled. It is also a common cause of glaucoma in cats. Idiopathic lymphocytic-plasmacytic uveitis occurs in both diffuse and nodular forms, with the nodular form being more commonly unilateral, and the diffuse form bilateral.

A minimum laboratory evaluation for cats with either unilateral or bilateral uveitis consists of the following procedures:

- Complete blood count
- Serum biochemical profile
- Urinalysis
- Thoracic radiography
- Serologic (or other fluid) tests relevant to the geographic location for *Toxoplasma* (immunoglobulin [Ig] G and IgM), feline leukemia virus, feline immunodeficiency virus, *Cryptococcus, Blastomyces* spp., *Histoplasma* spp., and *Coccidioides* spp.

Uncontrolled or chronic low-grade idiopathic lymphocytic-plasmacytic uveitis is a common cause of feline glaucoma.

In 93 cats with endogenous uveitis in Colorado in which a specific agent was identified, the following seroprevalence of infection was found: *Toxoplasma gondii,* 78.5%; feline immunodeficiency virus, 22.9%; feline leukemia virus, 4.95%; and feline coronavirus, 27%.

The treatment of feline uveitis is comparable to the approach used in other species, although systemic NSAIDS are typically avoided in cats because of the potential toxicity of the compounds in this species. The combination of topical corticosteroids and clindamycin hydrochloride (25 mg/kg, divided, twice daily) was beneficial in cats with uveitis associated with toxoplasmosis.

It is highly probable that the various causes of feline uveitis vary greatly by geographic region.

EQUINE RECURRENT UVEITIS. Equine recurrent uveitis (ERU) is also known as "moon blindness" and periodic ophthalmia. As in other species, the horse may exhibit a single episode of uveitis resulting from any one of a multitude of causes, especially those involving the cornea. In addition to this form of uveitis, however, up to 12% of horses in some geographic regions may be affected by a distinctly different type of uveitis that is immune-mediated and characterized by spontaneously recurring uveitis episodes (ERU). ERU may be initiated by a variety of different agents and in this sense it is not a single disease but a group of diseases united by a common clinical pattern of recurrent bouts of uveitis. With each subsequent uveitis attack, cumulative damage occurs to the ocular

tissues, and blindness may result. The long-term prognosis is guarded, but with therapy vision may be retained for a prolonged period in many animals.

History and Geographic Distribution. ERU has been recorded for millennia and is the most common cause of vision loss in the horse. As with many ancient disorders, the proposed causes and treatment have varied greatly over the years, and the disease has often been shrouded in folklore, ignorance, and misconceptions. For example, the term "moon blindness" has two origins: (1) the frequent recurrences were once thought coincident with the phases of the moon and (2) the cataract that often accompanies chronic ERU looked like a small moon in the eye.

The disease is worldwide in distribution, although distinct regional differences in frequency occur. It is more common in North America than in Australia, the United Kingdom (where it is uncommon), or South Africa. An incidence of up to 12% has been recorded in eastern areas of the United States, and some investigators believe it is more prevalent in low-lying areas with high rainfall. In continental Europe the prevalence is regarded to be approximately 8% to 10%. There is no age or sex predilection. The Appaloosa breed appears to be at higher risk for development of recurrent uveitis, suggesting a genetic predisposition to ERU.

Etiologic Factors. Numerous inciting causes of ERU have been described in the literature with varying levels of evidence supporting their role in the pathogenesis of this entity (see Table 11-3). The most common clinically recognized inciting cause of ERU is *Leptospira*-associated uveitis. The most commonly view held regarding the fundamental pathogenesis of ERU is that it is an autoimmune phenomenon in which IgG antibodies and autoreactive T cells specific for ocular proteins (especially retinal antigens) are present. A cell-mediated immunity to uveal antigens has also been demonstrated in horses with ERU. Additionally, the unique genetic constitution of each animal also plays a role because some breeds are at significantly greater risk than others and not all animals who are infected with *Leptospira* or *Onchocerca* develop uveitis.

Leptospira-*Associated Uveitis.* The association between ERU and previous or current infection with *Leptospira* has been studied in greater detail than any of the other known causes of ERU. *Leptospira* may trigger the majority of cases of ERU, at least in Europe. Although both experimental infections and natural outbreaks of leptospirosis have been associated with ERU, clinically apparent uveitis does not develop in most adult horses until 1 to 2 years after initial infection.

The diagnosis of *Leptospira*-associated uveitis can be challenging. Numerous serologic studies have shown widespread exposure (up to 30%) of the equine population to a variety of serotypes of *Leptospira* in North America, Britain, continental Europe, and Australia. Serotypes associated with the disease include *L. pomona, L. bratislava, L. autumnalis, L. grippotyphosa, L. canicola, L. icterohemorrhagiae, L. hardjo,* and *L. sejroe.* Serum antibody titers greater than 1 : 400 are suggestive of previous infection, although lower serologic titers may be found in many infected horses. In fact, negative serologic titers do not necessarily rule out leptospirosis as a possible cause, because the organism or its deoxyribonucleic acid (DNA) is occasionally identified in the intraocular fluids of horses with negative serologic titer results. Interpretation of serologic test results may be further confounded by the occurrence of positive serologic titer results for *Leptospira* in horses without uveitis. Vitreal titers for *Leptospira* may also be elevated, although again the value of this test remains questionable.

Several reports have described isolation of *L. interrogans* from various ocular fluids, especially the vitreous, in horses with chronic ERU. The organism is difficult to culture, however, and so polymerase chain reaction (PCR) testing for leptospiral DNA is sometimes done. It is not uncommon for an animal to be PCR positive and culture negative, suggesting that the organism may be more prevalent than once thought.

Leptospiral antigens can cross-react with a number of normal ocular proteins. Leptospira immunologically cross-reacts with the normal equine cornea and lens, and in horses with ERU, leptospiral antisera are cross-reactive with the equine iris pigment epithelium and retina. In one study certain leptospiral lipoproteins (LruA and LruB) were found to share immune-relevant epitopes (the part of an antigen that is recognized by the immune system) that can cross-react with normal ocular proteins in the lens (alpha-crystallin B and vimentin) and in the retina (beta-crystallin B_2). These types of studies suggest that an immune response initially directed against leptospiral antigens may eventually spread to involve self proteins as well.

There are at least two main theories as to the role of *Leptospira* in ERU. In the first theory, ERU after infection with *Leptospira* is primarily an immune-mediated disorder in which the organism is no longer present. In this scenario autoimmune inflammation tends to "burn out" as antiinflammatory regulatory cells get the upper hand in an active attack, leading to a clinically quiescent period. Recurrent active periods may be the result of the autoimmune response shifting from one site to another on the same autoantigen (intramolecular spreading) or to another entirely different autoantigen (intermolecular spreading). This theory is supported by the responsiveness of the disease to immunosuppressive therapy, which would be expected to ultimately result in exacerbation of the disease if a viable organism were present in the eye.

Alternatively, in Europe leptospiral strains have been isolated from the ocular fluids of horses with chronic ERU, and it is postulated that the persistence of viable leptospiral organisms within the vitreous humor may play a role in inducing and maintaining the immune-mediated uveitis. During the periods between overt episodes, the number of leptospiral organisms may decline to such a level that overt inflammation is not clinically detectable, and antibody titers decline. When the antibody titer falls below a certain threshold, bacterial numbers may increase, resulting in a resurgence of antibodies that cross-react with host antigens, leading to greater inflammation, damage to adjacent tissues, and, perhaps, recognition of new antigenic epitopes. This theory is supported by the observation that infusion of antibiotics into the vitreal cavity in conjunction with a surgical vitrectomy (especially in Europe where *Leptospira* may be frequently involved in ERU) may greatly reduce the frequency of recurrent episodes.

Given the supporting evidence for both theories regarding the role of *Leptospira* in the pathogenesis of ERU, the relative importance of the direct effects of the organism on the eye, locally produced antibodies against *Leptospira* interrogans, and autoantibodies against retinal autoantigens (retinal S-antigen and interphotoreceptor retinoid-binding protein) remains uncertain. It is quite possible that the significance of these various responses varies from animal to animal.

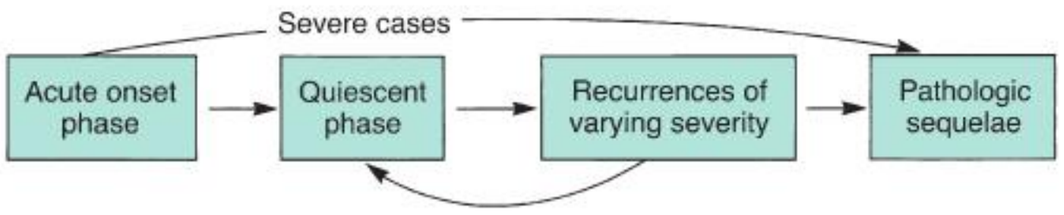

Figure 11-28 Clinical course of equine recurrent uveitis.

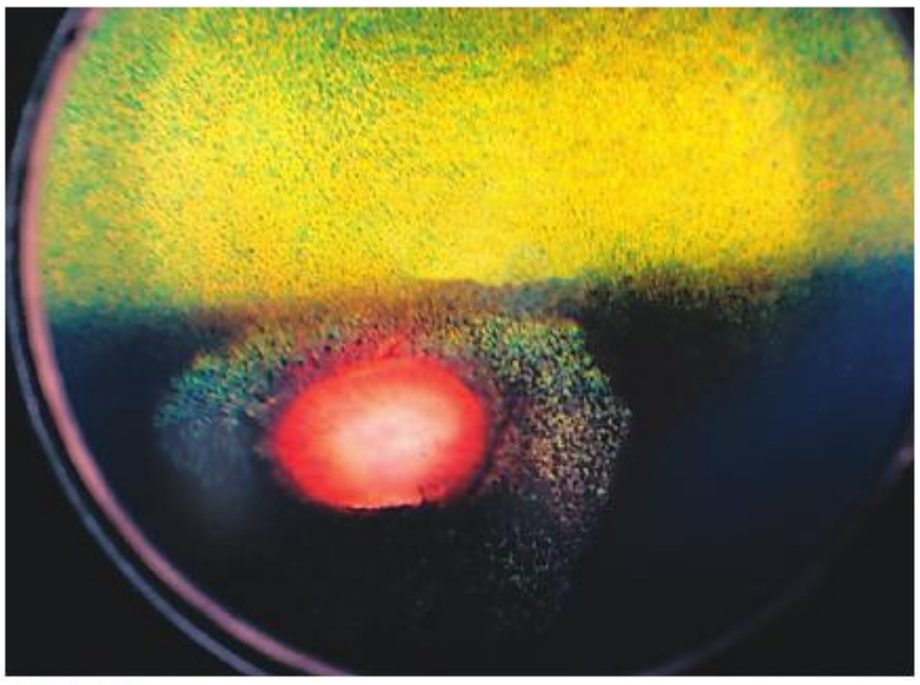

Figure 11-29 Wing-shaped hypopigmented lesions nasal and temporal to the optic disc ("butterfly lesions") are suggestive of previous uveitis. (Courtesy University of Wisconsin–Madison Veterinary Ophthalmology Service Collection.)

Clinical Signs of ERU. Clinical signs are comparable regardless of cause but vary with the phase of the disease (Figures 11-28 through 11-33).

Active Phase. Clinical signs in the active phase (see Figure 11-32) are as follows:

- Marked blepharospasm
- Photophobia
- Lacrimation
- Pain
- Protrusion of the third eyelid
- Corneal edema
- Scleral injection
- Aqueous flare (with or without hypopyon)
- Miosis
- Thickened, infiltrated iris
- Anterior and posterior synechiae
- Fibrinous clots in anterior chamber
- Decreased IOP (occasionally increased)
- Depigmented butterfly lesions near optic disc (see Figure 11-29)
- Any of the quiescent signs

In the active phase of ERU, rapid intensive treatment is mandatory to prevent severe complications (e.g., synechiae, cataract, retinal detachment). Most active periods last several days to weeks.

Quiescent Phase. Typically an active period is followed by a quiescent phase of variable duration. Although inflammation may be clinically minimal or undetectable in the quiescent phase, histologic signs of inflammation and altered vascular permeability continue. During the quiescent phase immunologically active cells and cytokines also persist, and new antigenic epitopes or autoantigens may be recognized, prompting a resurgence of inflammation (see Figures 11-30 and 11-31). It is not uncommon for horses in the quiescent phase to be offered for sale by unscrupulous individuals who represent the horse as "sound" or by those who are unaware of a horse's past history.

Although some horses may appear almost normal during the quiescent phase, most will have some residual evidence of disease. The clinical signs most likely to be seen during clinical examination of horses in the quiescent phase are as follows (see Figure 11-33):

- Corneal opacity
- Pigment on anterior lens capsule
- Anterior and posterior synechiae
- Blunted and rounded corpora nigra
- Occluded pupil
- Iris atrophy
- Cataract (poor surgical candidates)
- Vitreous bands and opacities
- Butterfly lesions or retinal detachment
- Phthisis bulbi
- Partial or complete loss of vision

The presence of inflammatory sequelae in an equine eye indicates the possibility of ERU.

Treatment. In general the number of medications and frequency of the therapy are adjusted in accordance with the severity of the clinical signs. Mild disease may be treated with topical therapy alone, whereas more severe inflammation typically demands systemic therapy as well. A subpalpebral lavage system may be required to properly treat active disease in some animals. Initial therapy usually includes the following measures:

1. Attempt to establish a definitive etiologic diagnosis, and specifically address the cause if possible.
2. Ensure good husbandry practices: Place the horse in a dark stall to relieve photophobia. Prevent ocular trauma by mowing pastures and removing sharp objects from the environment. Reduce contact with cattle and wildlife that may harbor leptospirosis, prevent access to ponds and swampy areas, and ensure good insect and rodent control. Minimize stress, ensure a good diet, and employ an optimal deworming schedule. Vaccinations should be optimized for each patient and based on the horse's use and specific needs. Multiple vaccinations should be spaced at least 1 week apart so as to avoid excessive antigenic stimulation and potential exacerbation of the disease.
3. Atropine ophthalmic ointment (1%) applied one to four times a day given to effect. The dose is adjusted until pupillary dilation is achieved and maintained. This medication reduces pain by relaxing the ciliary muscle, aids in the prevention of synechia, and may help stabilize the blood-aqueous barrier. Atropine should be discontinued or reduced in frequency if the horse shows reduced gut motility or colic. Resistance to pupillary dilation is an indicator of the severity of the uveitis, the presence of synechia, or both. Once the uveitis is controlled, the pupil may remain dilated for days to weeks, especially if the drug was used frequently during an acute attack.

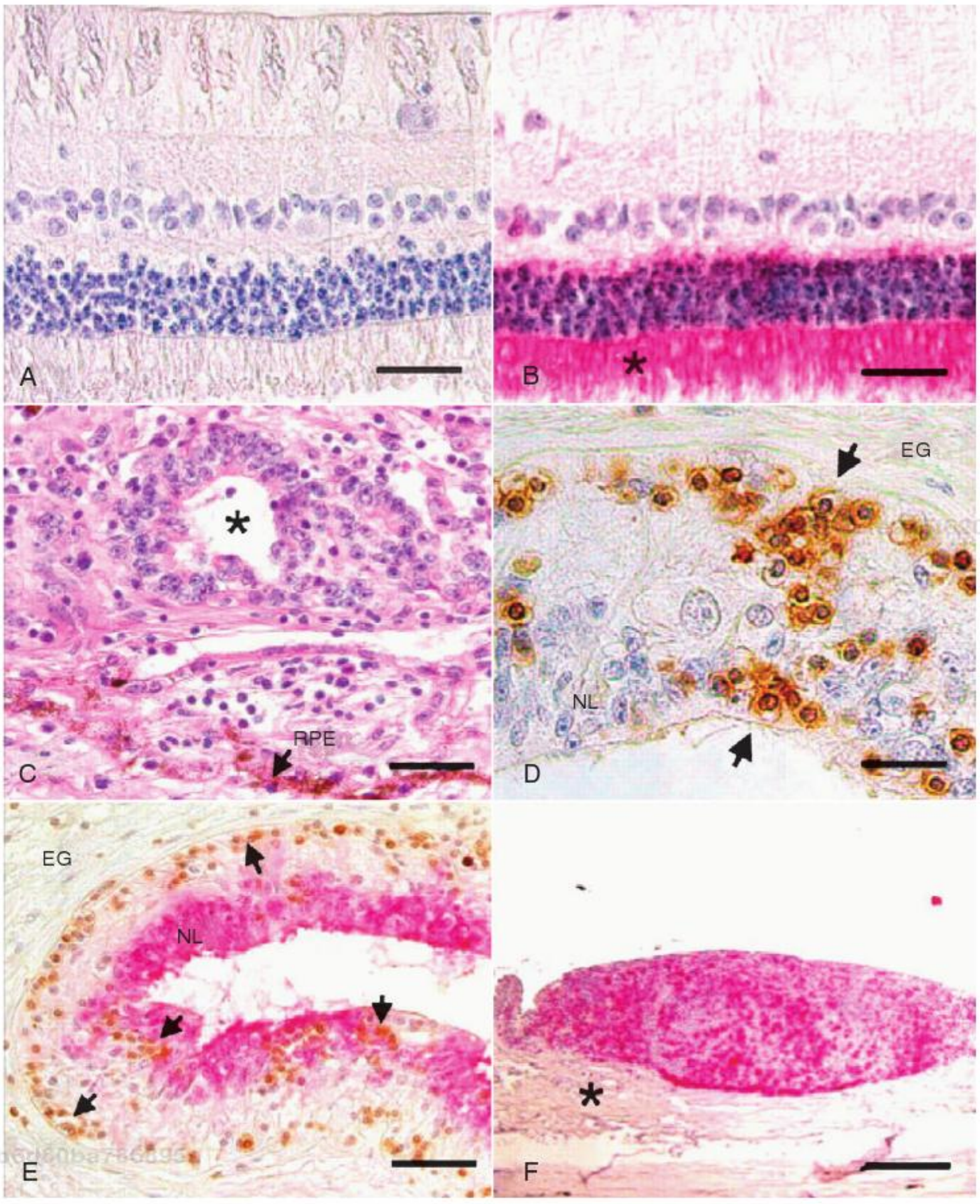

Figure 11-30 Histologic appearance of eyes from horses with experimental equine recurrent uveitis. **A,** Normal equine retina. *Bar,* 25 mm. **B,** Normal equine retina stained with antibodies to retinal S-antigen (S-Ag). Photoreceptor outer segments were clearly labeled (*red, **). *Bar,* 20 mm. **C,** Affected horse with complete destruction of retinal architecture associated with immune-mediated disease directed against retinal S-Ag. CD3+ T cells (*brown*) are infiltrated around retinal neuronal cells. Leftover retinal pigment epithelial cells and neovascularization were visible in the retina (*). *Bar,* 25 mm. **D,** Retinal infiltration by T cells (CD3+; *brown, arrows*). Destruction of photoreceptor outer segments with some remaining cells from the inner or outer nuclear layer and formation of epiretinal gliosis (EG). *Bar,* 15 mm. **E,** Severely destroyed retina in affected horse. Infiltration of CD3+ T cells (*brown, arrows*) in the nuclear layer of the remaining photoreceptor cells (visualized by red staining for S-Ag) and in the neuronal cell layer at the borderline to a severe EG. *Bar,* 40 mm. **F,** Subconjunctival lymphoid follicle (CD3+ cells stain *red*). *, Sclera; *bar,* 120 mm. (From Deeg CA et al: The uveitogenic potential of retinal S-antigen in horses. *Invest Ophthalmol Vis Sci* 45:2286, 2004.)

4. Systemic NSAIDs (in descending order of potency—use only 1 at a time):
   - Flunixin meglumine 0.25 to 1.0 mg/kg every 12 hours intravenous (IV), intramuscular (IM), or PO for 5 days; then, if required by the severity of the inflammation and if patient is appropriately monitored for gastric and renal side effects, 0.25 mg/kg PO every 12 to 24 hours on a more long-term basis. If after 5 days systemic antiinflammatory therapy is still required, many ophthalmologists switch from flunixin meglumine to phenylbutazone. Flunixin meglumine may also facilitate pupillary dilation by atropine because endogenous prostaglandins can induce miosis by directly acting on the iris sphincter muscle; this action is blocked by NSAIDS but not by atropine.
   - Phenylbutazone 1 g per adult horse (or up to 4.4 mg/kg) q12-24h IV or PO. This drug typically is used after a 5-day course of flunixin meglumine if additional systemic antiinflammatory therapy is required. On occasion, with appropriate monitoring for gastric and renal toxicity, it is

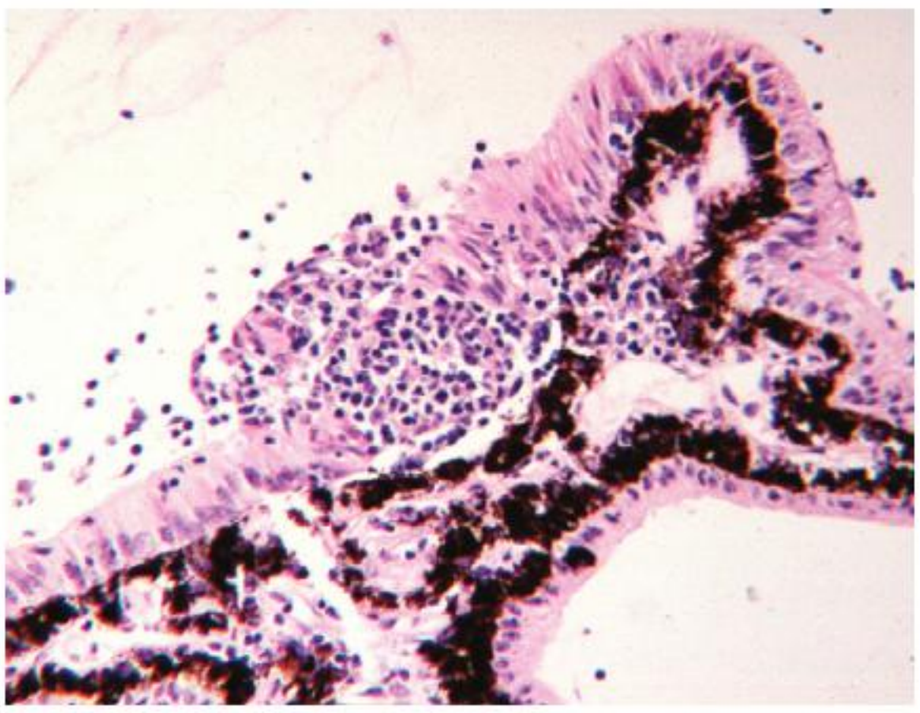

Figure 11-31 Lymphocytic inflammation of the ciliary body of a horse with chronic equine recurrent uveitis. (Courtesy Dr. Richard R Dubielzig.)

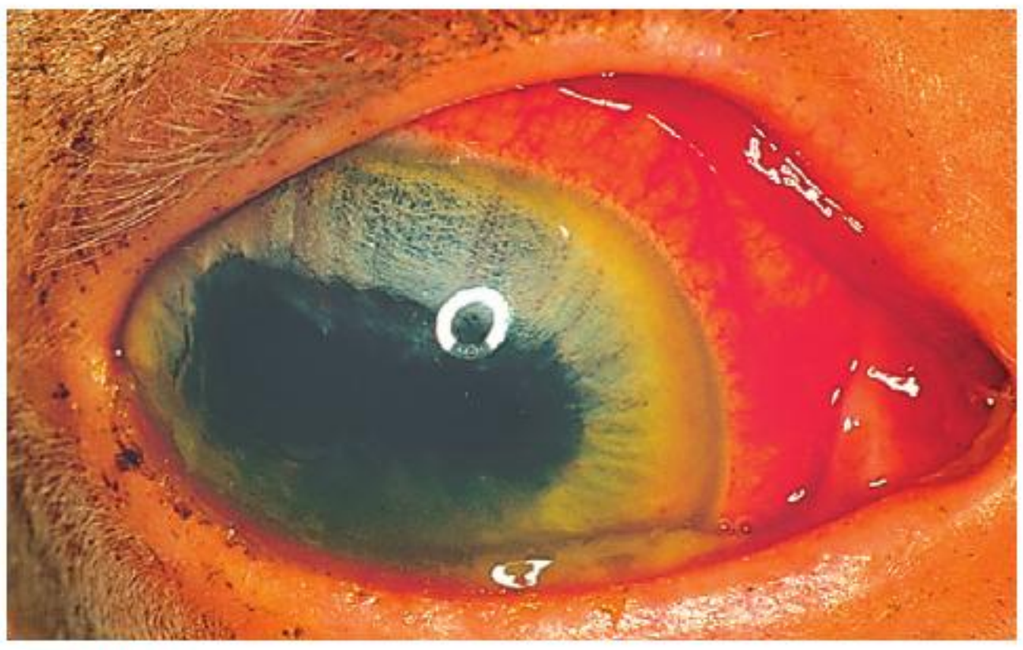

Figure 11-32 Acute equine recurrent uveitis. Note the extensive conjunctival hyperemia, miosis, and blue-green hue to the iris. The yellow serum of horses often makes a blue iris appear green.

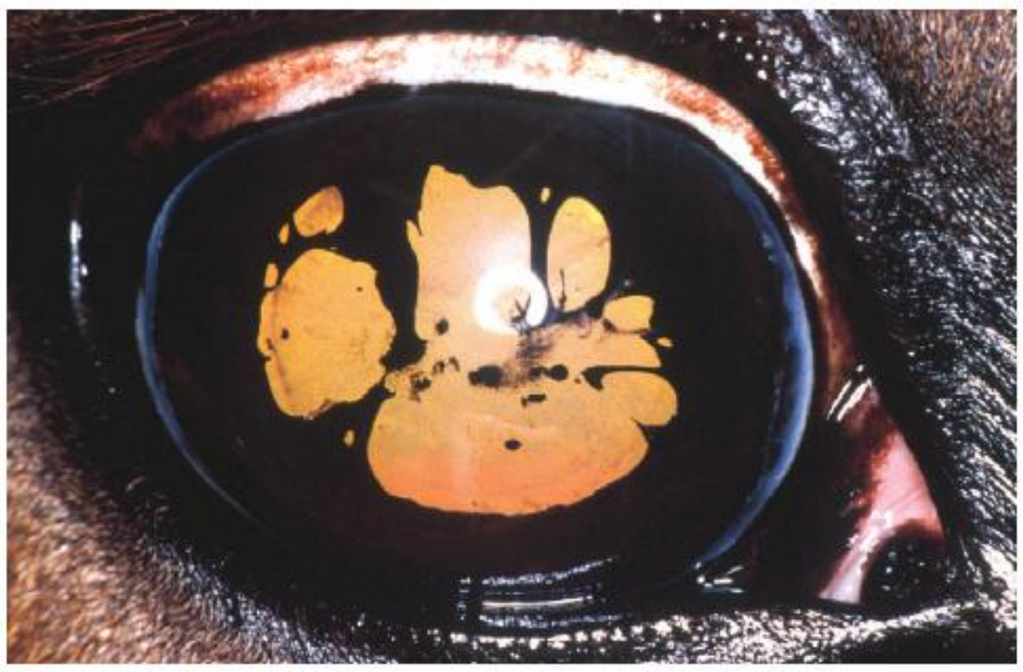

Figure 11-33 Chronic equine recurrent uveitis. The iris is hyperpigmented. Note also the numerous posterior synechiae and early cataract formation.

used as long-term therapy in an effort to reduce the frequency and severity of acute episodes, especially if aspirin is ineffective at such reductions.
- Aspirin 25 mg/kg PO every 12 to 24 hours (12.5 g/500 kg). Typically this agent is used in horses in which long-term topical antiinflammatory therapy cannot prevent recurrent outbreaks and long-term systemic NSAID therapy is required.
- Consider ranitidine (6.6 mg/kg every 8 hours) and sucralfate (20 mg/kg PO every 8 hours) or omeprazole (1 to 2 mg/kg q 24 hrs to prevent gastric ulcers or 4 mg/kg PO every 24 hours to treat gastric ulcers).

5. Topical corticosteroids (e.g., 0.1% dexamethasone ointment, 1% prednisolone) applied every 1 to 6 hours, depending on severity. Long-term therapy is often required, and it is generally advisable to treat an acute episode for at least 2 weeks after the apparent resolution of all signs of active inflammation. In many patients long-term topical corticosteroid therapy is required to reduce the frequency and severity of subsequent attacks.

Additional approaches that can be used in unusually severe cases or cases refractory to the preceding approaches are as follows:

1. Topical NSAIDs (e.g., flurbiprofen 0.03%, 0.1% diclofenac, or another topical NSAID applied every 6 hours): These agents are not as potent as topical corticosteroids in ERU therapy, but in severe cases they may be used in addition to topical corticosteroids. Alternatively, they may be used for the long term, either alone or with topical corticosteroids in an effort to prevent recurrent episodes. Topical NSAIDs can slow corneal epithelialization.
2. Cyclosporine A: This drug impairs proliferation of activated T-helper and T-cytotoxic cells, a mechanism of action that may be quite useful in preventing reactivation of disease in T cell–mediated diseases such as ERU. Topical 0.2% cyclosporine ophthalmic ointment or 2% cyclosporine in oil applied every 6 to 12 hours may be of some value in ERU patients, but intraocular penetration is poor and its efficacy via this route appears to be somewhat less than that of topical corticosteroids. However, a surgically placed suprachoroidal sustained-release implant containing cyclosporine bypasses these barriers and clinical trials have demonstrated that in select patients an implant is effective in reducing the number of episodes of uveitis (from 0.54 episodes/month to 0.05 to 0.09 episodes per month) and may be more effective at preserving vision than standard medical therapy. A new implant may need to be surgically implanted every 4 years.
3. Subconjunctival corticosteroids (triamcinolone acetonide): Reported dosages for triamcinolone acetonide vary greatly from 1 to 2 mg per eye, to 20 mg per eye, to 40 mg per eye as often as every 1 to 3 weeks. Usual duration of action is 7 to 10 days. The major concern with this drug is that it creates a strong predisposition for bacterial and fungal keratitis and that, unlike topically applied corticosteroids, it cannot be withdrawn if the disease should occur. Therefore it is typically used as an adjunct to topical corticosteroids in the acute phase in especially severe cases or when the owner has difficulty medicating the horse as often as required. *Note:* The sustained-release vehicle in methylprednisolone

acetate may result in an unsightly plaque and irritating granuloma.

4. Systemic corticosteroids (e.g., dexamethasone 5 to 10 mg/day PO or 2.5 to 5 mg daily IM or oral prednisolone 0.5 mg/kg every 24 hours): In general, because of frequent adverse effects, systemic corticosteroids are used only as a last resort in the treatment of ERU. They can be considered in unusually severe cases or when the inflammation is refractory to systemic NSAIDS and topical corticosteroids. Side effects include laminitis and gastrointestinal upset.
5. Antibiotic therapy in horses with presumed leptospiral-associated uveitis: The efficacy of this therapy remains speculative, and side effects are not uncommon. Drugs that have been suggested include streptomycin (11 mg/kg IM every 12 hours) and a 4-week course of oral doxycycline (10-20 mg/kg every 12 hours). In one study, however, doxycycline at 10 mg/kg every 12 hours orally did not result in appreciable drug concentrations in the aqueous humor or vitreous of normal eyes. It is unknown whether effective drug concentrations can be achieved in inflamed eyes with a disrupted blood-aqueous barrier. Some researchers believe that the efficacy of vitrectomy for this disorder is due to the use of gentamicin in the irrigation fluid as much as the procedure itself. This theory has prompted some ophthalmologists to give a single intravitreal injection of 4 mg of gentamicin in an effort to prevent or eliminate recurrent episodes in severely affected eyes. Gentamicin injections, however, should be made with extreme caution because the drug may cause retinal degeneration, cataract formation, intraocular inflammation, endophthalmitis, and irreversible vision loss.
6. Surgical vitrectomy via a pars plana approach has been advocated by some to reduce the frequency and severity of attacks of ERU. The rationale for its use is based on the hypothesis that persistent organisms within the vitreal cavity (and perhaps the uveal tract) are capable of perpetuating an immune-mediated uveitis. Controlled clinical trials have yet to demonstrate the superiority of this procedure over medical therapy alone, and cataracts are a common postoperative complication.
7. Vaccination is controversial. No approved vaccine is available for horses. The cross-reactivity of leptospiral antigens with normal constituents of the equine eye suggests that vaccination may actually cause the disease in some animals. Vaccination of seronegative horses with a multivalent bovine vaccine, with appropriate informed consent, may help suppress a herd outbreak. Vaccination as an adjunctive therapy in horses with ERU, however, failed to slow the progression of the disease in one study.
8. Enucleation is, on occasion, the only means of effectively treating a blind, painful globe.

Onchocerca *Uveitis*. Although commonly cited as a cause of ERU in the older literature, it is unclear whether the uveitis in horses affected with ocular onchocerciasis represents true ERU or uveal inflammation that is simply a "spill over" from adjacent corneal and conjunctival inflammation. The chronic and sometimes recurrent uveal inflammation noted in the older literature may be attributable to the persistent presence of the parasite or repeated reinfections prior to the development of highly effective dewormers. The routine use of ivermectin and other highly effective anthelmintics appears to have substantially reduced the incidence of onchocercal uveitis in the United States and the detailed immunologic investigations demonstrating autoantibodies has not been done for *Onchocerca* as has been done for *Leptospira*.

Ocular lesions are associated with the migration of the microfilariae from the ligamentum nuchae to the skin, some entering vessels of the bulbar and palpebral conjunctiva. The microfilariae are most readily found in the conjunctiva adjacent to the temporal limbus and in the corneal stroma adjacent to this area. They may infect one or both eyes. Onchocerca is discussed further in Chapter 18.

In an animal with onchocerciasis, the following may be seen in addition to the signs of uveitis:

- Focal dermatitis on the head, ventral thorax, and neck
- Vitiligo affecting the scrotum, lateral canthus, or lateral conjunctival limbus. Conjunctival vitiligo alone is insufficient to indicate the presence of microfilariae.
- Focal corneal opacities at the lateral limbus. These may appear as superficial subepithelial fluffy or feathery white opacities 0.5 to 1 mm in diameter approximately 1 to 5 mm from the limbus.
- Hyperemia and chemosis of the perilimbal temporal conjunctiva

Uveitis is said to be caused by the dead microfilariae or to be mediated by immunopathologic mechanisms involving IgE. Diethylcarbamazine, which was commonly used to treat this condition in the past, has subsequently been shown to stimulate IgE antibody responses. This feature, rather than a reaction by the host to killed microfilariae, may explain the inflammation seen after its administration.

Microfilariae are demonstrated by removing, under local anesthesia, (1) a small piece of conjunctiva from the affected area or (2) a piece of skin from the ventral thoracic midline. The tissue is minced with scissors and placed in 5 mL of saline at 37° C for 30 to 50 minutes (e.g., in a small vial in the clinician's pocket). The supernatant is centrifuged and examined for motile microfilariae. Alternatively, the tissue may be examined in saline on a slide immediately after collection. Interpretation of such slides must be made in association with other clinical findings, because many horses without uveitis have microfilariae.

Microfilaricides must not be used during acute uveitis.

Treatment. The treatment of uveitis in *Onchocerca* patients is similar to that for *Leptospira*-associated uveitis. Microfilaricide therapy is given after the inflammation has subsided as dead microfilaria may exacerbate the uveitis. Highly effective microfilaricides include ivermectin 0.2 mg/kg of 2% ivermectin equine oral paste or 0.4 mg/kg of 2% moxidectin equine oral gel. At the first sign of recurrent inflammation during treatment, corticosteroid therapy is begun.

PHACOCLASTIC UVEITIS IN RABBITS. An unusual form of uveitis associated with apparent spontaneous lens capsule rupture, phacoclastic uveitis, occurs in the rabbit and frequently results in enucleation (Figure 11-34). Organisms believed to be *Encephalitozoon cuniculi* have been identified in affected lenses. Clinical signs of infection include a white or yellowish mass in the lens, uvea, or anterior chamber that progresses to severe uveitis. Glaucoma that is usually refractory to treatment is common. Early lens removal has been suggested as a method of treatment to prevent development of uveitis.

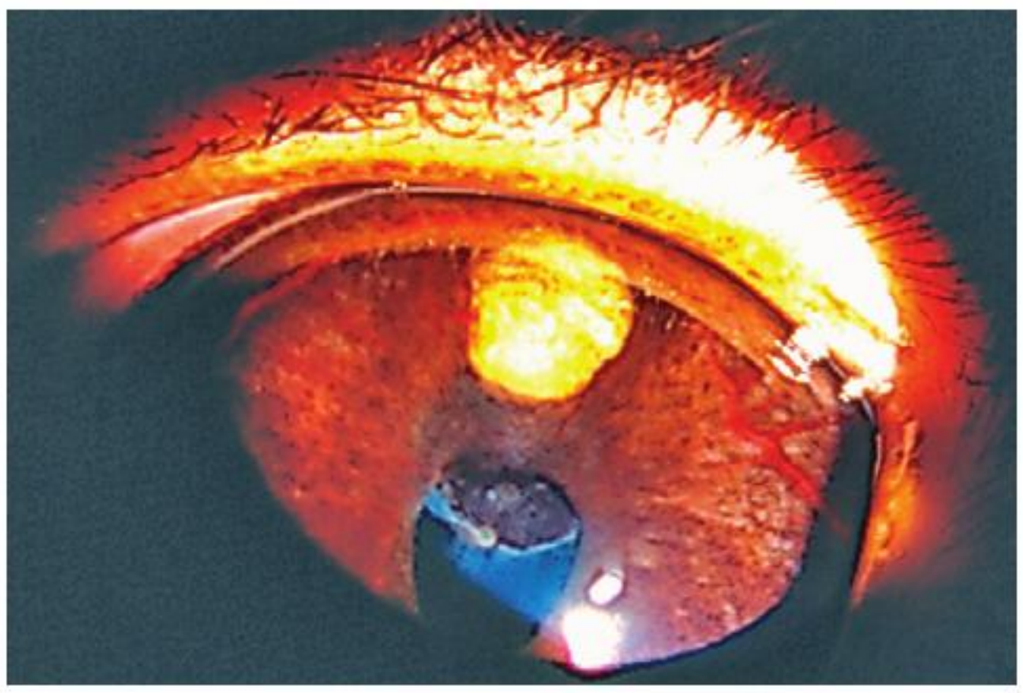

Figure 11-34 Uveitis and focal lens capsule rupture with cataract formation associated with the protozoan *Encephalitozoon cuniculi* in a rabbit.

TOXIC UVEITIS. The eye is exquisitely sensitive to bacterial endotoxins, and amounts as small as a few nanograms are capable of inducing potentially blinding uveitis. Pilocarpine and other topical parasympathomimetics as well as topical prostaglandins used in the treatment of glaucoma (e.g., latanoprost) can also result in a mild uveitis. Other compounds that can result in uveitis include ethylene glycol poisoning in dogs, sulfa-containing drugs, and compounds that cause thrombocytopenia or coagulopathies and intraocular hemorrhage.

Trauma is a common cause of uveitis in domestic animals.

TRAUMA

Traumatic Uveitis

Uveitis may result from either blunt or sharp trauma to the globe or may occur after intraocular surgical procedures. Therapy is the same as that for other forms of uveitis, although topical corticosteroids should be avoided if a corneal erosion or ulceration is present. Topical NSAIDS may be used with caution if a corneal erosion is present, although they also may impair corneal epithelialization and there is some potential for topical NSAIDS to elicit a corneal melt. Topical and systemic NSAIDs are also typically avoided if significant intraocular hemorrhage is present. If the corneal epithelium is not intact, a topical antibiotic such as neomycin-polymyxin B-bacitracin combination product applied every 6 to 8 hours should be used prophylactically. If the globe has been penetrated, the wound may require suturing and systemic antibiotics in addition to topical antibiotic and atropine therapy. Traumatic uveitis is aggressively treated in the horse because a traumatic breakdown of the blood-aqueous barrier may increase the risk of recurrent episodes of uveitis.

In severe ocular trauma, early and vigorous treatment is required to prevent permanent ocular damage and, perhaps, repeated episodes of uveitis.

In many cases the long-term prognosis of traumatic uveitis is determined more by the nature of the injury than by the therapy that was chosen.

Common uveal injuries are as follows:

- *Iris prolapse* is a protrusion of a portion of the iris through a corneal or scleral perforation.
- *Hyphema* is a hemorrhage into the anterior chamber
- *Staphyloma* is a weakened or protruding lesion in the cornea or sclera into which a portion of the uvea protrudes from the inside; the uveal tissue usually adheres to the cornea or sclera.
- *Concussion:* Energy is rapidly transmitted throughout the eye because it is fluid-filled, resulting in damage to areas distant from the point of impact.
- *Iridodialysis* is a tearing of the iris from the ciliary body at its root. This condition is uncommon in domestic animals. Iris prolapse and hyphema are discussed in greater detail later.

Iris Prolapse

Iris prolapse is a common sequela to penetrating corneal wounds or ruptured corneal ulcers. The iris is carried forward into the corneal defect by escaping aqueous. Emergency treatment of such injuries is described in Chapter 19. When iris passes through such a corneal defect, its vascular supply is usually compromised, resulting in venous congestion and edema. This changes the appearance of the protruding mass so that it commonly looks like uvea-colored fibrin or mucus adhering to the cornea. Prolapsed tissue can readily serve as a "bridge" for microorganisms to enter the eye.

Signs

Clinical signs of iris prolapse are as follows:

- The color of the prolapsed portion becomes lighter than the remaining iris.
- The protruding iris tissue forms a mound on the cornea.
- The tissue has a gelatinous mucoid appearance and frequently attracts adhering strands of conjunctival mucus.
- The pupil is eccentric as a result of traction of the protruding iris tissue.
- The corneal wound is often obscured by the edematous iris tissue. Protrusion of the ciliary body occurs most commonly in horses as a result of scleral rupture posterior to the limbus after blunt trauma.

Treatment

If the corneal wound is small, iris prolapse may be treated temporarily with a third-eyelid flap and topical and systemic antibiotic solutions until specialized assistance is available. In larger wounds requiring immediate repair, an attempt is made to replace the iris with an iris spatula before the cornea is sutured. If this is not possible, the protruding piece may be carefully excised with the use of an electrosurgical unit. The cornea is sutured, and the anterior chamber reconstituted with balanced salt solution or an air bubble. *Caution:* If the major arterial circle of the iris is transected, profuse intraocular hemorrhage can result. Enucleation or evisceration and intrascleral prosthesis are alternative therapies if the eye is blind.

Visual Outcome and Ocular Survival after Iris Prolapse in Horses

Iris prolapse is usually associated with a ruptured corneal ulcer or full-thickness corneal laceration. In one review, combined medical and surgical therapy (primary closure with or without a conjunctival graft) was successful in saving vision of 40%