

Ophthalmology

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OUTLINE

Ophthalmic Examination and Diagnostic Techniques, 807

Orbital Disease, 812

Eyelid and Adnexal Disease, 813

Corneal and Conjunctival Disease, 817

Diseases of the Uveal Tract, 827

Diseases of the Lens, 834

Glaucoma, 836

Chorioretinal Disease, 837

Feline ophthalmology is a vast and important field in which feline practitioners need to be reasonably adept, given the frequency with which clients note ocular disease in their cats and the importance they place on good vision from a pain-free globe. In this chapter we have attempted to highlight conditions that are unique to cats and emphasize feline-specific considerations for more common ocular diseases. Less attention has been paid to those conditions for which management strategies differ little from those employed in dogs, insofar as these topics have been amply covered in standard veterinary ophthalmology texts.

OPHTHALMIC EXAMINATION AND DIAGNOSTIC TECHNIQUES

History

A great deal of information can be gleaned from a complete history and thorough ophthalmic examination. A detailed history does much to narrow the list of differential considerations. Important background information includes the chief complaint, duration of clinical signs, concurrent ocular or systemic medical conditions, previous therapies, and current ophthalmic or systemically administered medications.

Examination Techniques and Order

Basic necessities for a complete ophthalmic examination include a consistent, systematic approach to the

examination; a bright, focal light source; magnification; and a darkened room. Diagnostic tests such as the Schirmer tear test (STT), tonometry (assessment of intraocular pressure), fluorescein staining, and funduscopic examination are important components of the examination and need to be done at prescribed times. The following is a recommended order for the ophthalmic examination.

Whereas assessment of dogs begins by observing while the patient navigates into the examination room, most cats are carried in and refuse to participate in any obstacle courses set up by the examiner. Cats also seem to mask vision loss much more effectively than dogs; therefore clinical assessment of vision tends to be much more difficult in the cat than in the dog. For this the examiner may need to rely more heavily on historical information and other examination findings.

The examiner should begin at eye level with the cat. The cat's head should first be observed from a distance, avoiding excessive manipulation of the face by the restrainer. This allows for detection of nonocular abnormalities that may be related to the ocular disease, such as facial asymmetry, oral or nasal discharge, and the presence of a head tilt. The examiner should then perform the neuro-ophthalmic examination (Table 29-1). The neuro-ophthalmic assessment for cats can yield very different results than that for the dog. For example, the menace response (Figure 29-1) tends to be inconsistently elicited in cats, with many normal cats failing to blink in response to a menacing gesture. Likewise, stressed cats with higher sympathetic tone often have resting mydriasis and diminished pupillary light reflexes (PLRs).



FIGURE 29-1 Proper technique for eliciting the menace response. The contralateral eye must be covered with one hand to prevent it from viewing the menacing gesture. Care should be taken to keep from generating wind currents or directly touching the highly sensitive vibrissae when performing the menacing gesture.

TABLE 29-1 Components of the Neuro-Ophthalmic Examination

Test	Tested Structures
Menace response	CN II and VII, visual cortex, and cerebellum
Palpebral reflex	CN V and VII
Oculocephalic reflex	CN III, IV, and VI
Direct and consensual pupillary light reflexes	CN II and III and central visual pathways excluding the visual cortex
Dazzle reflex	CN II and VII and subcortical visual pathways

If a STT is to be performed, it must be done before any eye drops are applied to the eye. It is performed in the same manner as in the dog (Figure 29-2); however, normal STT measurements vary widely in cats.¹⁹⁴ For example, the authors have recorded STT values less than 5 mm/min in cats without detectable ocular disease. Conversely, cats with significant keratoconjunctival disease may have STT results within the normal reference range.¹⁰⁶ Such discrepancies emphasize the importance of interpreting the STT in context with the overall clinical examination and comparing them between the affected and unaffected eyes in cats with unilateral or asymmetric ocular disease. After the STT, intraocular pressure (IOP) should be assessed. Although there is some variability, normal feline IOP tends to be between 10 and 25 mm Hg.¹⁴⁰ Both the Schiotz and TonoPen tonometers require application of a topical anesthetic agent before obtaining an IOP measurement, whereas the TonoVet does not (Figure 29-3). Although



FIGURE 29-2 The Schirmer tear test in a cat. The test strip should be folded at the notch and placed in the ventrolateral conjunctival fornix and left in place for 60 seconds. Care should be taken not to touch the lower part of the strip with the hands because oil on the skin can affect the capillary action of the strip and test result. (From Maggs D: Slatter's fundamentals of veterinary ophthalmology, ed 4, St Louis, 2007, Saunders.)

retropulsion can be useful in detecting space-occupying lesions of the orbit, it is not considered an acceptable technique for measurement of IOP. If the IOP is within normal limits, a single drop of 0.5% or 1% tropicamide should then be applied to each eye to achieve pupillary dilation, which is essential for examination of the lens, vitreous, and ocular fundus. In cats tropicamide induces mydriasis within 15 minutes, for 8 to 9 hours.⁸⁷ Pharmacologic mydriasis is not recommended if the IOP is elevated because dilation may further increase the IOP.

The remainder of the ophthalmic examination may be performed during and after pupillary dilation, and the techniques used in cats differ little from those used in other species. Sequential examination of all structures moving from peripheral to axial and from superficial to deep ensures a complete and orderly examination. The examiner should begin with retroillumination of the tapetal reflection from arm's length (Figure 29-4) to identify opacities in the visual axis. Magnification, in the form of head loupes (Figure 29-5), should then be employed throughout the entire ophthalmic examination, except for the fundic examination. The examiner should employ focal illumination and transillumination (Figure 29-6) from various angles when assessing the ocular surface. Depth and spatial relationships are best assessed using the slit beam of the direct ophthalmoscope. The detection of aqueous flare (plasma protein in the anterior chamber) is a pathognomonic change in anterior uveitis, and therefore its detection forms a critical part of the ophthalmic examination in all cats. Aqueous flare is best detected when the room has been darkened completely and the smallest, most focal white light beam on the direct ophthalmoscope head is used



FIGURE 29-3 The TonoVet (A) and TonoPen (B) being used to measure intraocular pressure in cats. The tips of both instruments should be directed toward the central cornea according to the manufacturer's directions. The operator should take care to ensure that excessive pressure is not placed directly on the globe when holding the eyelids open or on the jugular veins as the animal is restrained because both can elevate intraocular pressure readings.



FIGURE 29-4 Correct technique for performing retroillumination. The light source is held next to the examiner's eye and the patient examined at arm's length in a darkened room. The examiner should alter his or her viewing angle until the fundic reflection is elicited. This can be used to assess pupil symmetry and any opacities within the tear film, cornea, anterior chamber, lens, and vitreous.



FIGURE 29-5 Magnification is an essential component of the entire ophthalmic examination, with the exception of the fundic examination. It is especially important for assessment of aqueous flare and after application of fluorescein stain. The Optivisor is inexpensive and extremely useful for the ophthalmic examination, as well as surgery and suture removal in general practice.



FIGURE 29-6 Technique for transillumination. The light source and examiner should move around the animal such that multiple highly variable combinations of viewing and illumination angles are achieved throughout the ophthalmic examination. This will greatly increase the chance that lesions will be found. In particular, this technique improves or facilitates depth perception within the eye, assessment of topography, and evaluation of reflections from transparent surfaces. (From Maggs D: Slatter's fundamentals of veterinary ophthalmology, ed 4, St Louis, 2007, Saunders.)

very close to the cat's eye to examine the clarity of the anterior chamber. Any "smokiness" detected as the beam traverses the anterior chamber between the cornea and the lens should prompt consideration of and further investigation for anterior uveitis. The iris face is a frequent site of pathology in cats and must be evaluated before dilation. By contrast, thorough assessment of the lens, vitreous, and fundus can be performed only after full dilation has been achieved. Also, aqueous flare may be more easily detected after full mydriasis has been

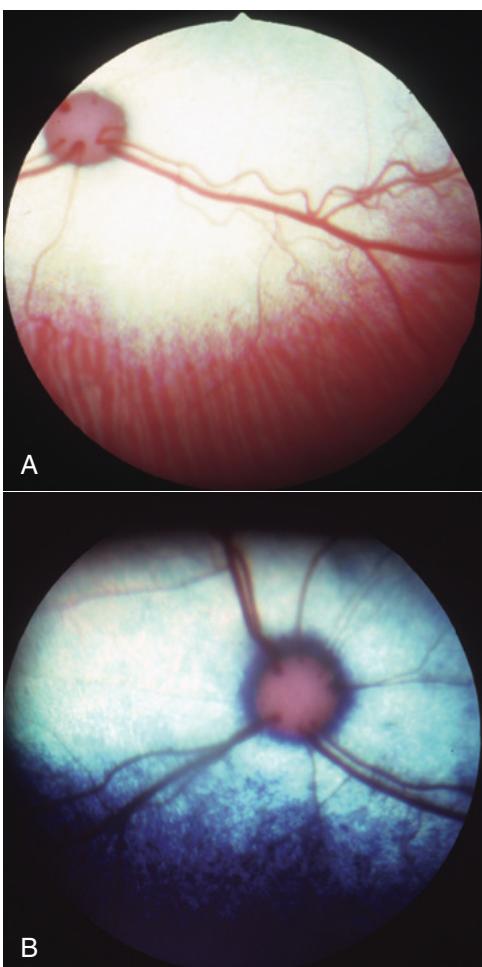


FIGURE 29-7 Two variations of the normal feline fundus. **A**, A subalbinotic fundus is a normal variation typically seen in pigment-dilute individuals. The relative lack of melanin in the retina and choroid allows visualization of the choroidal vessels in the nontapetal fundus. In some subalbinotic fundi, the tapetum is absent. **B**, Normal feline fundus. Melanin in the retina and choroid prevents visualization of the choroidal vessels seen in image A. The optic disc appears circular and gray because of the lack of myelin and is located immediately dorsal to the tapetal–nontapetal junction. Three or four larger retinal venules extend from the edges of the optic disc to the periphery of the retina. The tapetum is usually green or yellow.

achieved, insofar as the black background of the pupil provides contrast with which to view the gray beam of light traversing the anterior chamber. Direct and indirect ophthalmoscopy are the two traditional methods for examining the fundus (Figure 29-7). Direct ophthalmoscopy is relatively easy to learn and provides the examiner with an upright image of the retina but is not a good method for examination of the fundus. The main disadvantage of direct ophthalmoscopy is the limited field of view, a result of extreme magnification. This makes complete retinal examination difficult, and peripheral regions and smaller lesions are often missed. Indirect ophthalmoscopy is considered to be the best method for viewing the fundus, despite the steeper learning curve. The image produced is an inverted representation of the



FIGURE 29-8 The binocular headset improves depth perception and frees one hand for manipulation of the patient's eyelids and head.

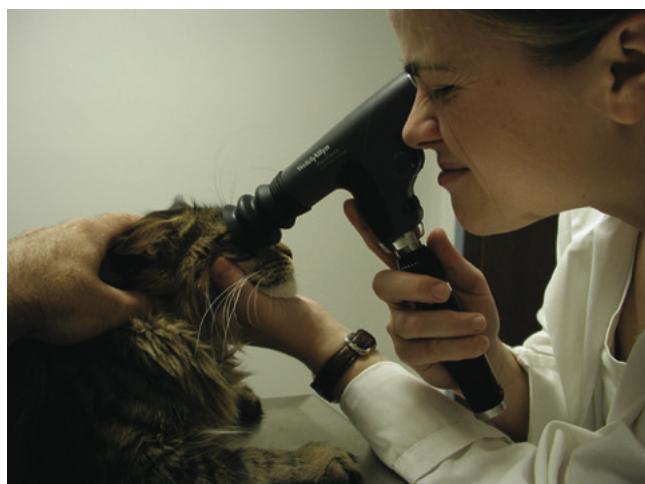


FIGURE 29-9 Technique for fundic examination using the Panoptic. After the instrument is focused for the examiner's eye, the fundic reflection is identified while looking through the Panoptic from approximately 10 to 15 centimeters away from the patient. The examiner then moves toward the patient until the eyecup of the ophthalmoscope contacts the patient's face. If this causes eyelid closure, the eyecup can be removed.

fundus. When the binocular headset (Figure 29-8) is used, indirect ophthalmoscopy provides superior depth perception. The larger field of view obtained by indirect ophthalmoscopy makes complete fundic examination easier and allows the practitioner to view a larger portion of the fundus in less time, which is extremely valuable for uncooperative patients. The direct ophthalmoscope can then be used for more detailed examination of any focal lesions identified. A newer ophthalmoscope, the Panoptic offers a field of view and level of magnification intermediate to the traditional ophthalmoscopes (Figure 29-9). Although it is unable to provide much depth perception, its ease of use and moderate field of view make the Panoptic a reasonable compromise between direct and indirect ophthalmoscopy.



FIGURE 29-10 The Jones test. Appearance of fluorescein dye at the nares or in the mouth within a few minutes after application to the ocular surface indicates patency of the nasolacrimal ducts, or a positive Jones test. In many cats, especially those with brachycephalic conformation, the nasolacrimal duct opens sufficiently caudally within the nose that fluorescein is noted on the tongue rather than at the nares. This highlights the importance of testing the side of interest first, because laterality cannot be determined when fluorescein is detected in the mouth. (Image courtesy UC Davis Veterinary Ophthalmology Service.)

Application of fluorescein dye may be used to detect corneal ulceration and corneal perforation and may be used to assess tear film stability and patency of the nasolacrimal drainage system. It should be performed only after all other parts of the examination are complete because it will affect results of microbial testing, the STT, and the appearance of many ocular structures.

The Jones test is an assessment of nasolacrimal duct patency (Figure 29-10). A minimum of 2 minutes after placing fluorescein dye into the conjunctival sacs, the nares and mouth are examined for evidence of fluorescein. Presence of fluorescein (positive Jones test) confirms patency of the nasolacrimal duct, whereas absence of fluorescein (negative Jones test) is suggestive of obstruction and should be followed with nasolacrimal flushing.

The tear film break-up time (TFBUT) evaluates stability of the precorneal tear film. It is the time between eyelid opening and the first spot of evaporation within the precorneal tear film. The examiner first places fluorescein dye into the conjunctival sac, then closes the eyelids. Timing begins when the eyelids are opened. Using magnification, the examiner observes one area of the cornea, usually the dorsolateral aspect. Timing ends when the first black spot, signifying evaporation, appears within the green tear film. The normal TFBUT in a cat is $16.7+/-4.5$ seconds,³⁶ whereas more rapid TFBUTs suggest tear film instability.

Ancillary Tests

Techniques for ancillary diagnostic tests such as corneal scrapings (Figure 29-11), conjunctival swabs, and



FIGURE 29-11 Technique for collection of corneal or conjunctival samples for diagnostic testing. After application of topical anesthetic, the blunt end of a scalpel blade is used to carefully scrape surface cells from the cornea or conjunctiva. These can then be gently blotted onto a microscope slides for cytologic or immunologic assessment or can be inoculated onto a swab or directly into agar plates for microbiologic assessment.



FIGURE 29-12 A biopsy of the conjunctiva can be easily obtained in almost all cats without sedation or general anesthesia. After application of topical anesthetic, forceps are used to tent the conjunctiva, which is then incised with small scissors. The conjunctival defect will heal by second intention. (From Maggs D: Slatter's fundamentals of veterinary ophthalmology, ed 4, St Louis, 2007, Saunders.)

conjunctival biopsies (Figure 29-12) are identical to those for the dog. However, the effect of topical anesthetics required to obtain these samples is shorter in cats than it is in dogs. Whereas a single drop of 0.5% proparacaine provides up to 45 minutes of corneal anesthesia in the dog, the same dose achieves only 25 minutes of corneal anesthesia for the cat, with maximal effect 5 minutes after application.^{16,88} This time difference should be taken into account if the practitioner is unable to obtain samples shortly after administering topical anesthesia. Cannulation of the nasolacrimal puncta is more challenging in cats than dogs because of the tight fit of the eyelids to the globe. Also, in cats more often than in dogs, the nasal opening of the nasolacrimal duct is located more



FIGURE 29-13 Ultrasonographic appearance of the normal feline globe. This technique is particularly useful for assessing intraocular structures, especially retinal detachment, in globes with anterior segment pathology that prevent direct visualization. Normal features include the highly echoic convex anterior lens capsule and concave posterior lens capsule; the anechoic anterior chamber, lens, and vitreous cavity; and the echoic concave monolayer of the posterior globe representing sclera, choroid, and retina in close apposition with one another. Orbital structures such as the optic nerve and extraocular muscle cone are sometimes seen. Because of the close proximity of the ultrasound probe to the anterior structures, the anteriormost ocular structures are less well defined than those posterior to them. In the example shown, the anterior chamber and anterior lens appear artificially hyperechoic. (Image courtesy UC Davis Veterinary Ophthalmology Service.)

caudally, such that fluid will be flushed into the oral cavity rather than out the nares (as with fluorescein in Figure 29-10).

Advanced imaging is required when opaque ocular media prevent complete examination of the globe or when orbital or neurologic disease is suspected. Ocular ultrasound is very useful for characterizing lesions within the globe but may not allow full evaluation of orbital lesions¹⁵⁶ (Figure 29-13). Skull radiography and computed tomography (CT) also may not clearly show borders of a lesion, but they will detect bony changes.¹⁵⁶ Magnetic resonance imaging (MRI) is of limited value for bony lesions but offers excellent resolution of soft tissues, including the globe, orbit, and optic nerves.⁷³

ORBITAL DISEASE

In cats the most common clinical sign accompanying orbital disease is exophthalmos.⁶⁶ Epiphora, enophthalmos, strabismus, elevation of the third eyelid, and decreased retropulsion are other possible examination findings (Figure 29-14). If eyelid movement has been compromised, exposure keratitis or corneal ulceration may also be found (Figure 29-15). Inflammatory and neoplastic conditions make up the bulk of feline orbital disease; orbital vascular anomalies and cystic lesions



FIGURE 29-14 Left-sided orbital disease in a cat. Comparison of the palpebral fissures shows distortion of the left palpebral fissure, as well as dorsal and lateral displacement of the left globe and elevation of the left nictitans, all of which are highly supportive of orbital, rather than ocular, disease. (Image courtesy WCVM Veterinary Ophthalmology Service.)



FIGURE 29-15 Right-sided orbital disease caused by squamous cell carcinoma. The globe is enophthalmic. In this patient tumor-induced facial nerve paralysis resulted in exposure keratitis and ulceration of the central cornea. (Image courtesy UC Davis Veterinary Ophthalmology Service.)

have not been reported in cats. Identification of the underlying disease process is important because of significant differences in treatment and prognosis. At minimum, a complete blood count (CBC), serum biochemical profile, urinalysis, and fine-needle aspirate or biopsy of the orbital lesion are recommended. Based on the results of these tests, CT or MRI may be warranted to determine the extent of the lesion.

Infectious and Neoplastic Orbital Disease

Orbital cellulitis and abscess formation in the cat are diagnosed and treated in a similar manner as in dogs. As in dogs, orbital extension of dental disease is responsible for many of these cases, but foreign body migration, fungal infections, and iatrogenic trauma (mainly during dental procedures) are also documented causes.^{110,157} However, these conditions occur much less frequently in cats than in dogs, and neoplasia should always be considered when a cat presents with orbital disease.¹⁵⁷ In cats the majority of orbital neoplasia is secondary, with direct extension from adjacent structures accounting for 71% of cases.⁶⁶ Squamous cell carcinoma (SCC) is the most common orbital neoplastic process in cats,⁶⁶ but many other neoplasms may occur.* Regardless of type, 90% of orbital neoplasms are malignant, with mean postdiagnosis survival times less than 2 months.^{8,66}

Ocular Proptosis

Ocular proptosis is seen less commonly in cats than in dogs, likely because of cats' deep orbits and relatively tightly fitting adnexa. For this reason the amount of force required to displace the globe from the feline orbit is large, and cats with ocular proptosis usually present with severe intraocular trauma, as well as concurrent cranial or systemic injuries that require more immediate attention. Ocular proptosis in cats often occurs in conjunction with skull fractures and trauma to the globe.⁶⁵ As with dogs, enucleation or emergency replacement of the globe followed by temporary tarsorrhaphy is required. However, the prognosis after traumatic ocular proptosis in cats is worse than in dogs. In one retrospective review, all proptosed feline eyes were permanently blind, and 12 of 18 required enucleation.⁶⁵

Feline Orbital Pseudotumor

Feline orbital pseudotumor (FOP) is currently described as a progressive inflammatory disease with similarities to idiopathic orbital inflammation in humans. However, only eight feline cases have been described, and the definition is still evolving.^{15,127} All affected cats were middle-aged to older.^{15,127} The majority of cats presented with

unilateral disease that later became bilateral. In all cases onset of clinical signs was insidious, ultimately characterized by exophthalmos, lagophthalmos, exposure keratitis, and restriction of ocular movements.^{15,127} Resistance to retropulsion was also found in the majority of cases.^{15,127}

No specific changes are seen on blood work, and fine-needle aspirates tend to be nondiagnostic. Orbital ultrasound may show increased echogenicity of orbital tissues.¹⁵ CT appears to be the most useful imaging modality, often revealing physical compression of the globe. Biopsy of orbital tissues (often obtained during enucleation or exenteration) is essential, with histopathology being characterized by proliferating fibrous tissue with lymphocytic–plasmacytic inflammation.¹⁵

As for its human counterpart,²⁰ prognosis for FOP is poor and specific therapeutic guidelines do not exist. Immunosuppressive doses of systemic corticosteroids, oral antibiotics, and radiation therapy have all been attempted with little success.^{15,127,192} One author reports having managed FOP for a period of 1.5 years with immunosuppressive corticosteroid therapy before clinical disease returned.¹⁹² This author also reports clinical improvement in one cat after radiation therapy, but this case has not been described nor followed up in the literature.¹⁹² Enucleation or exenteration followed medical therapy in all published cases,^{15,127} and in one case series, all seven cats were eventually euthanized because of either recurrence of disease or appearance of the disease in the contralateral orbit.¹⁵

A viral etiology has been suggested for FOP, perhaps in part because of the suggestion that herpes simplex virus (HSV-1) is a proposed cause of human idiopathic orbital inflammation.¹⁸⁹ In the case series of seven cats, three exhibited signs suggestive of feline herpesvirus (FHV-1) infection, including upper respiratory disease before or after development of clinical signs of orbital disease, followed by development of gingival hyperplasia.¹⁵ However, the authors were unable to establish FHV-1 infection in these cats. More recently, FOP has been suggested to be a neoplastic disease, with spindle cell sarcoma identified in the orbital tissue of one cat and the suggestion that FOP be renamed *feline restrictive orbital sarcoma*.⁴⁸

EYELID AND ADNEXAL DISEASE

Eyelid Agenesis

Eyelid agenesis, or eyelid coloboma, is the most common congenital eyelid disease of cats.¹³³ It has been documented to occur in the Persian, Burmese, and domestic shorthair, as well as snow leopards and a Texas cougar.^{11,40,100,124,205} Affected cats have bilateral, incomplete development of the upper lateral eyelids (Figures

*References 8, 44, 66, 73, 94, 161, 197, 206.



FIGURE 29-16 Right eye of a cat with agenesis of approximately 30% of the upper lateral eyelid margin. The result is trichiasis, incomplete eyelid closure (lagophthalmos), and exposure keratitis. (Image courtesy WCVM Ophthalmology Service.)

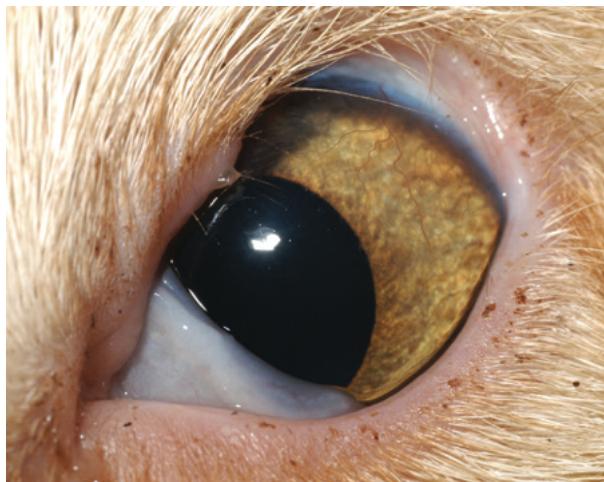


FIGURE 29-17 Agenesis of almost 50% of the left upper eyelid. Although the eyelid defect in this patient is larger than the defect in Figure 29-16, the degree of keratitis is less. (Image courtesy UC Davis Veterinary Ophthalmology Service.)

29-16 and 29-17). The extent of the defect ranges widely, from a barely perceptible absence of the eyelid margin at the lateral extent of the eyelid to complete absence of the upper eyelid margin. The cause is unknown; viral etiologies, intrauterine events, and genetic mutations are proposed mechanisms, although there is no clear evidence supporting any of these theories.¹²⁴

Most owners do not notice abnormalities until kittens are a few months of age, probably because of the small eye size of young kittens. On occasion, eyelid agenesis has been mistaken for upper eyelid entropion; however, close inspection reveals absence of the eyelid margin rather than an inward roll. Varying degrees of chronic keratitis resulting from trichiasis and lagophthalmos almost always accompany the eyelid defect (see Figure



FIGURE 29-18 Patient in Figure 29-17 after completion of a rotating skin flap and subsequent cryoepilation of resulting trichiasis. Although the eyelids are not completely normal, there is improved coverage of the globe during normal blinking and the trichiasis is decreased from before surgery. (Image courtesy UC Davis Veterinary Ophthalmology Service.)

29-16). The conjunctival fornix at the site of the malformed eyelid also tends to be shallow or replaced by a thin band of conjunctiva directly connecting the globe to the eyelid. Other ocular abnormalities may accompany eyelid agenesis—most commonly, persistent pupillary membranes, which are remnants of dysplastic uveal tissue visible as thin sheets of pigmented tissue usually extending from the iris to the cornea. Colobomas of the iris, choroid, or optic nerve; retinal dysplasia; and keratoconjunctivitis sicca may also accompany eyelid agenesis.^{71,124} Like the eyelid defect itself, the associated developmental abnormalities range in severity, sometimes even among kittens from the same litter.¹²⁴

Treatment varies with the extent of the eyelid malformation. Very small defects may require cryoepilation or primary closure for resolution of trichiasis; however, most defects of clinical significance require more extensive blepharoplasty. Surgical reconstruction usually involves two separate surgeries, the first to correct the defect and the second to correct residual trichiasis. The most common procedure is rotation of a flap of skin from the lower eyelid with a functional outcome (Figure 29-18). Subsequent cryoepilation or a Holtz–Celsius procedure can be employed to address trichiasis from the skin flap.

Entropion

In the authors' experience, feline breed-related entropion differs greatly from the same condition in dogs. In cats the majority of breed-related entropion is mild and located at the medial aspect of the lower eyelid in brachycephalic cats (Figure 29-19). The clinical significance is often minimal but may be associated with



FIGURE 29-19 Ventromedial entropion is present in all brachycephalic cats and usually does not require treatment. Surgical correction is required when entropion causes excessive frictional irritation with corneal ulcer or sequestrum formation or epiphora with moist dermatitis and tear staining. (*Image courtesy Dr. Kathleen Doyle.*)

epiphora and tear staining caused by wicking of the tears by trichiasis, kinking of the nasolacrimal canaliculi, and frictional irritation of the cornea. However, these cats frequently have other abnormalities, such as exophthalmos, poor corneal sensitivity, unstable tear film, low blink rates, and lagophthalmos, that predispose them to chronic keratitis, including sequestrum formation. In these patients medial canthoplasty may be necessary to correct the entropion, lagophthalmos, and macropalpebral fissure. Breed-related entropion is believed to be more clinically significant in intact male Maine Coon cats, where it may be related to excessive skin around the face.²⁰²

Unlike breed-related entropion, acquired entropion in cats is often associated with clinically significant keratitis. Acquired entropion occurs in response to a primary pathologic process, typically as a result of blepharospasm or symblepharon formation caused by keratoconjunctivitis, or because of changes in globe position or size owing to enophthalmos or phthisis-microphthalmos, respectively. Enophthalmos may be seen in older cats or cachexic cats because of the loss of orbital fat. Surgical correction of feline entropion uses similar techniques as for the dog, which are published elsewhere. However, treatment (and preferably resolution) of any underlying cause before surgery is essential, and some authors have suggested that although the surgical technique is the same, cats require excision of a larger amount of tissue than do dogs.²⁰²

Herpetic Dermatitis

Periodically, FHV-1 has been identified as a cause of dermatologic lesions, particularly those surrounding the



FIGURE 29-20 Herpetic dermatitis causing a chronic ulcerative dermatitis of the periocular skin, nasal planum, and muzzle. Histology revealed extensive eosinophilic infiltration and viral inclusion bodies and polymerase chain reaction confirmed presence of feline herpesvirus-1 DNA. This patient responded very well to famciclovir administration. (*Image courtesy UC Davis Veterinary Ophthalmology Service.*)



FIGURE 29-21 In contrast to Figure 29-20, in this cat the herpetic dermatitis manifests as dry, proliferative crusts over the nasal planum. (*Image courtesy UC Davis Veterinary Dermatology Service.*)

eyes and involving nasal skin of domestic and wild felidae* (Figures 29-20 and 29-21). This is not surprising given the marked epithelial tropism of this virus and the reliability with which HSV-1 causes dermal lesions.¹¹⁵ Herpetic dermatitis typically presents with raised, thickened plaques and chronic, nonhealing cutaneous ulcers. Most commonly, the periocular skin, nasal planum, and the skin around the muzzle are affected; however, lesions may also occur on forelimbs and other sites in contact with oral and ocular secretions.^{80,97} Oral ulcers and rhinitis may accompany dermal lesions.^{80,132,184} Most published cases had concurrent immune compromise, in the form of recent glucocorticoid administration or systemic

*References 79, 80, 93, 97, 132, 184.

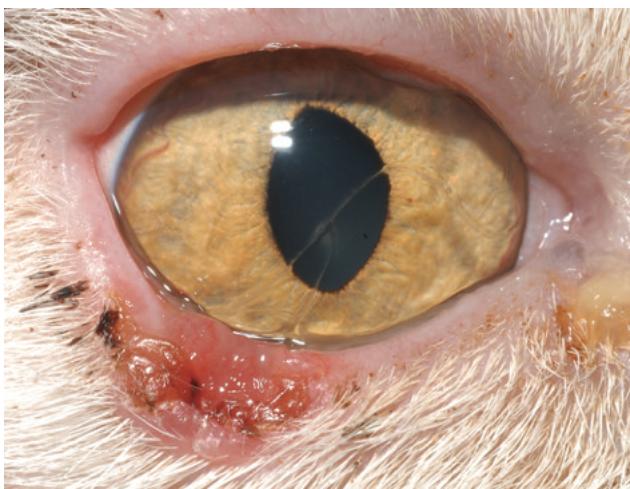


FIGURE 29-22 An alopecic, hyperemic ulcerative lesion is characteristic of eyelid squamous cell carcinoma in cats. Usually, the adjacent skin and conjunctiva are inflamed to some degree. Cats with lightly pigmented skin are more often affected. These tumors tend to be locally invasive and can require extensive blepharoplasty procedures. (Image courtesy UC Davis Veterinary Ophthalmology Service.)

disease.^{80,184} Histologic changes are often diagnostic; however, because of the eosinophilic infiltration, misinterpretation of lesions as eosinophilic granuloma may occur.⁸⁰ Unlike herpetic corneal or conjunctival disease, which is not reliably diagnosed using the polymerase chain reaction (PCR), this assay seems diagnostically useful for herpetic dermatitis. When results of histologic examination were used as the gold standard in one study of cats with dermatitis, sensitivity and specificity of the PCR assay were 100% and 95%, respectively.⁹³ Although prospective controlled studies are lacking, this disease seems responsive to systemic administration of famciclovir (see the section on corneoconjunctival disease later in this chapter).

Eyelid Neoplasia

In contrast to dogs, most feline eyelid neoplasms are malignant, and many tumors are locally invasive.^{125,138,204} SCC is the most common feline eyelid tumor, although a variety of neoplasms have been reported (Figure 29-22).^{*} Eyelid neoplasia tends to occur in cats older than 10 years of age.^{125,138} However, one study found SCC affected slightly older cats (12.4 years), whereas mast cell tumors were more common in younger cats (6.5 years).¹³⁸ This same study also underscored the systemic significance of eyelid tumors. Cats with eyelid or third eyelid lymphoma, adenocarcinoma, SCC, and peripheral nerve sheath tumors frequently experienced tumor recurrence or died as a result of tumor-related causes.¹³⁸ Conversely, the literature suggests that recurrence is unlikely after excision of hemangiosarcoma or mast cell tumor.^{83,138,149}



FIGURE 29-23 Immediate postoperative photograph of the cat in Figure 29-22. An advancement flap was performed to close the large defect created by excision of the eyelid tumor with adequate surgical margins. (Image courtesy UC Davis Veterinary Ophthalmology Service.)

Regardless, presurgical diagnosis through incisional biopsy or aspirate, diagnostic assessment for systemic metastases, and tumor resection with wide surgical margins are recommended for all eyelid tumors of cats. Given the essential role that eyelids play in ocular, especially corneoconjunctival, health, extensive blepharoplasty procedures are often required to guarantee postoperative eyelid function when surgical margins result in loss of more than 25% of the eyelid length (Figure 29-23). In some cases sufficiently wide margins cannot be achieved without enucleation or exenteration of a normal globe, and even then these procedures are often accompanied by extensive axial pattern flaps to cover the defect created (Figure 29-24).

Apocrine hidrocystoma is an unusual and relatively uncommon neoplasm affecting feline eyelids and, as one of the few benign neoplasms affecting the eyelid of cats, warrants separate discussion. It represents a proliferative lesion of the apocrine glands within the eyelid. Although histologic confirmation is necessary for definitive diagnosis, the typical appearance of the lesion is a smooth-surfaced, hairless, often pigmented, slightly translucent eyelid mass (Figure 29-25). Apocrine hidrocystomas may occur singly, or there may be multiple lesions on the same eyelid.⁶⁹ Persian cats are predisposed.^{25,69,208} Isolated masses may be removed with simple excision, although recurrence is common and cryosurgery is recommended as an adjunctive therapy.^{25,28} There is one report of ablation using trichloroacetic acid (TCA).²⁰⁸ In this case the hidrocystomas were eliminated without adverse effects, and no recurrence was noted 1 year after treatment.²⁰⁸ This treatment should be used with caution because TCA has the ability to cause painful blisters and burns to normal skin.²⁰⁸

*References 83, 92, 125, 138, 204, 206.



FIGURE 29-24 Immediate postoperative photograph after exenteration of the globe and orbital contents for removal of a large, infiltrative eyelid squamous cell carcinoma. Previous surgeries in this patient failed to completely remove the eyelid tumor, and exenteration was necessary to obtain adequate surgical margins. An advancement flap was required to close the surgical defect. (Image courtesy UC Davis Veterinary Ophthalmology Service.)



FIGURE 29-26 Haw's syndrome is characterized by bilateral elevation of the nictitans. This condition is idiopathic and self-limiting, usually within days. (Image courtesy UC Davis Veterinary Ophthalmology Service.)



FIGURE 29-25 The typical appearance of an apocrine hidrocystoma is a smooth, hairless, darkly pigmented round mass on the eyelid of a cat. (Image courtesy UC Davis Veterinary Ophthalmology Service.)

Third Eyelid Disease

Disease affecting only the third eyelid in cats appears to be uncommon; however, the third eyelid is occasionally the site of primary neoplasia.^{138,149} Prolapse of the gland of the third eyelid ("cherry eye") has been reported in the cat, and it has been suggested that the Burmese may be predisposed.¹⁰⁰ As in the dog, surgical replacement of the gland is required, with specific techniques being published elsewhere.⁷ Elevation of the third eyelid, without gland prolapse, may be a sign of Horner's syndrome if accompanied by signs such as miosis and ptosis. Pharmacologic testing and other diagnostic

investigations are similar to those used for dogs. Cats also occasionally have bilateral elevation of the third eyelids without other ocular abnormalities (Haw's syndrome) (Figure 29-26). Infectious etiologies have been proposed for this syndrome when it occurs in conjunction with diarrhea,^{123,131} but the condition is thought to be self-limiting when no other abnormalities are found.

Nasolacrimal System Disease

Primary disease of the nasolacrimal duct occurs infrequently in the cat. However, its physical characteristics make it prone to involvement when adjacent structures are diseased. For example, the lack of osseous protection of the distal lacrimal sac leaves it susceptible to inflammation from adjacent respiratory mucosa.¹³⁹ In addition, a portion of the nasolacrimal duct lies in very close proximity to the root of the canine tooth, which is a common site of dental disease in cats.^{122,139} Because of ventromedial entropion, the puncta are often in poor apposition with the globes of brachycephalic cats. This, combined with the fact that the nasolacrimal ducts of brachycephalic cats undergo sharper turns, increases the chances of impaired tear drainage and epiphora²¹ (Figure 29-27).

CORNEAL AND CONJUNCTIVAL DISEASE

Surface ocular disease is common in cats and, in contrast to dogs, is almost always infectious in origin. The most commonly implicated agents are FHV-1—a primary conjunctival and, to a lesser extent, corneal pathogen—and *Chlamydophila felis* (previously *Chlamydia psittaci*)—a pathogen of the conjunctiva but not the cornea.

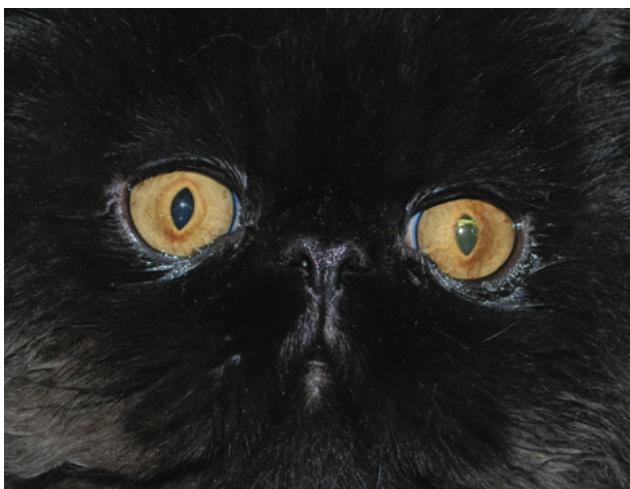


FIGURE 29-27 Brachycephalic cats often exhibit chronic epiphora as a result of ventromedial entropion and sharper turns in the course of the path of the nasolacrimal ducts. (Image courtesy Dr. Kathleen Doyle.)

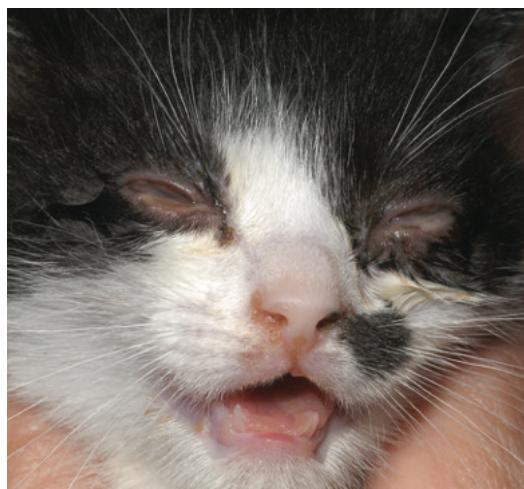


FIGURE 29-28 Primary infection with feline herpesvirus-1 is characterized by upper respiratory disease in addition to bilateral ocular disease. The mucopurulent and serosanguineous ocular and nasal discharge seen in this photo is typical. (Image courtesy UC Davis Veterinary Ophthalmology Service.)

Mycoplasma species and *Bordetella bronchiseptica* are also conjunctival, but not corneal, pathogens. Although feline calicivirus is often included in lists of differential considerations for feline conjunctivitis, patients infected with calicivirus are presented to veterinarians with severe upper respiratory disease and glossitis, although close examination can sometimes reveal mild conjunctivitis. This knowledge leads to a basic philosophical approach to feline surface ocular disease that can be helpful: Corneal disease should be presumed infectious and likely caused by FHV-1, and conjunctivitis should be assumed to be caused by *C. felis* or FHV-1 until proven otherwise. Because therapy for these two organisms differs so markedly, the obvious question is how to make a definitive etiologic diagnosis. Because both FHV-1 and *C. felis* can be detected in normal cats, diagnostic tests are unable to differentiate vaccine from wild-type organism, and false-positive and false-negative test results are common, laboratory testing is usually unhelpful. For these reasons the mainstay of diagnosis in cats with surface ocular disease is critical observation of clinical signs and judgment of response to therapy. This requires understanding of the biologic behavior of both organisms and the mode of action and expected effect of common antichlamydial and antiviral therapies. This will be the major focus of the subsequent sections.

Feline Herpesvirus

As a typical alphaherpesvirus, FHV-1 is highly host-specific; replicates rapidly in epithelial cells, where it causes cytolysis; establishes lifelong latency within ganglia; periodically reactivates from latency, especially during periods of stress; and during reactivation can either cause cell lysis again or activate immune-mediated

pathology. Although the virus typically persists for life in the ganglia of latently infected cats, it is extremely labile in the environment and is susceptible to most disinfectants and to desiccation. For example, FHV-1 is relatively rapidly killed in fluorescein stain and proparacaine; however, it can survive in eyewash for 5 days.¹⁸¹ Assuming that adequate hygiene is practiced in veterinary clinics, this short environmental survival time means that cats, rather than fomites, are the major source of viral persistence. Infection results from direct mucosal (oral, nasal, conjunctival) transfer of viral-laden macro-droplets, generated during sneezing but not normal respiratory movements. Up to 97% of cats are seropositive, and the virus is considered to be responsible for 45% of all upper respiratory infections.^{58,118,182} All studies to date suggest little variation in pathogenicity between viral strains, found worldwide.^{95,111-112,166}

After initial infection of a naïve cat, the incubation period is 2 to 10 days; however, this and disease severity are likely dose dependent. Viral shedding in ocular, oropharyngeal, and nasal secretions begins as early as 24 hours after inoculation and can persist for 1 to 3 weeks. Subsequent intermittent shedding is characteristic of the lifelong carrier state. The virus causes disease through a number of theorized mechanisms, each of which requires a different therapeutic approach. The initial period of rapid intraepithelial replication and associated cytolysis manifests clinically as erosion and ulceration of the ocular, oropharyngeal, and nasal mucosa, often with a serosanguineous discharge (Figure 29-28). The pathognomonic dendritic ulcerative pattern is sometimes seen in the cornea (Figure 29-29); however, their absence should not be used to rule out FHV-1 as a causative agent.

Primary disease is usually self-limiting within 10 to 20 days. Viremia occurs during this phase of infection,

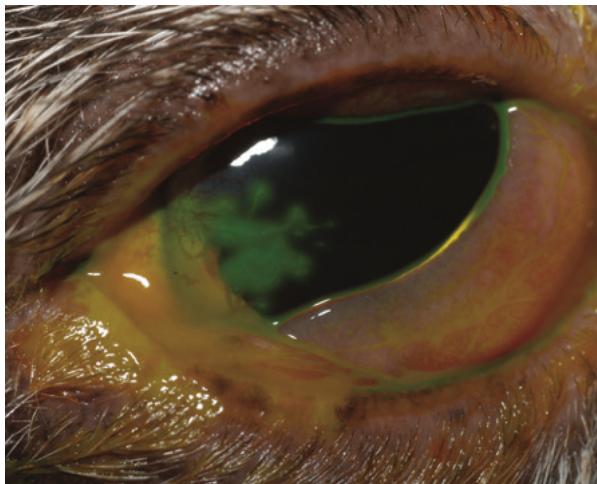


FIGURE 29-29 Dendritic corneal ulcers are considered pathognomonic for disease resulting from feline herpesvirus-1 infection. These can be very small and reinforce the need for examination with a cobalt blue light and a source of magnification after application of fluorescein dye. (Image courtesy UC Davis Veterinary Ophthalmology Service.)

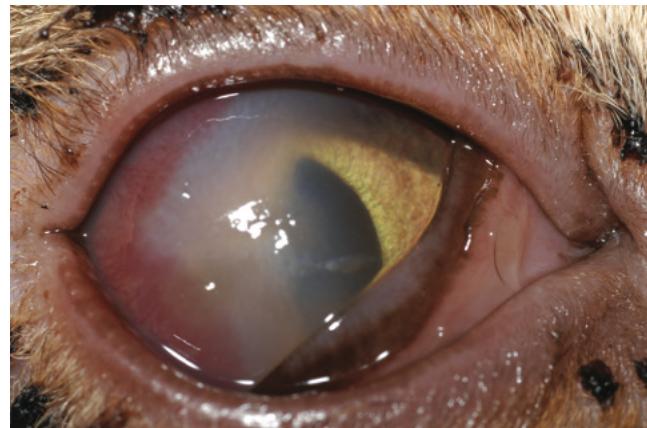


FIGURE 29-30 Stromal keratitis is characterized by vascularization, fibrosis, edema, and white blood cell infiltration of a nonulcerated cornea. It is believed to be due to persistence of feline herpesvirus-1 antigen within the corneal stroma. (Image courtesy UC Davis Veterinary Ophthalmology Service.)

but because systemic FHV-1-related syndromes are poorly defined, its significance is unknown. Also during this period, viral latency is established in the majority of cats, often as early as 4 days after infection, presumably by way of the ascent of the sensory axons of the trigeminal nerve. Latency is a period of viral quiescence during which there is no clinical evidence of disease, no histologically detectable inflammation within nerves or ganglia, no detectable virus using standard culture techniques, and limited viral transcriptional activity. In some animals intermittent episodes of viral reactivation from the latent state may be followed by centrifugal spread of virus along the sensory axons to peripheral epithelia. Viral recrudescence occurs when this results in clinically evident disease at peripheral epithelial sites. Recrudescent disease may be of the same ulcerative character as primary disease or may cause disease through recruitment of host immunologic mechanisms. It is often unilateral and typically not associated with generalized malaise or severe respiratory signs. The severity and extent of recrudescent disease range widely among individuals and even between episodes, making diagnosis more challenging. However, as a rule, conjunctivitis is milder and less ulcerative than seen in the primary infection, sometimes instead with substantial conjunctival thickening and hyperemia secondary to inflammatory cell infiltration. Corneal recrudescence may involve only the epithelial tissues, in which case dendritic and later geographic corneal ulceration may be seen; however, stromal keratitis is also common. This is characterized by vascularization, fibrosis, edema, and white blood cell infiltration of a nonulcerated cornea (Figure 29-30) and is believed to be due to FHV-1 antigen persistence within these tissues. Predicting which animals within a

population are going to suffer recrudescent disease is currently not possible. The important concept is that although the majority of cats appear to become latently infected, only a minor percentage of them experience chronic or recurrent herpetic disease (Box 29-1). The pathogenesis of FHV-1 is summarized in Figure 29-31.

Chlamydophila felis

Although *C. felis* has some unique biological features, it shares a number of them with FHV-1: It is an obligate intracellular organism spread by macrodroplets and direct contact, it replicates within epithelial cells, it persists within the host but poorly in the environment, and it is highly host adapted. The recent reclassification of the feline chlamydial organism from *Chlamydia psittaci* var. *felis* to its own distinct species reflects this host specificity and low zoonotic potential.¹⁰⁸ Although there is little evidence of zoonotic transmission,⁸⁴ owners, especially the immunosuppressed, should be advised to practice adequate hygiene when handling cats with suspect chlamydial conjunctivitis. Like FHV-1, *C. felis* prefers to replicate in epithelial cells; however, it appears to do so in a more diverse range of tissues than does FHV-1, including rectal and vaginal epithelia, as well as lung, spleen, liver, peritoneum, and kidneys.¹⁸⁵ This knowledge helps explain why systemic therapy is now recommended for cats with chlamydial conjunctivitis, even if no extraocular signs are noted.

After an incubation period of approximately 3 to 5 days, cats develop conjunctivitis, mild fever, and sometimes submandibular lymphadenopathy. In contrast to FHV-1, respiratory signs are mild to absent, and the clinical disease course tends to be more insidious and persistent but not lifelong. The typical clinical

BOX 29-1**Important Virologic Considerations for Cats Infected with Feline Herpesvirus-1**

1. Feline populations themselves, not the environment, act as the major reservoir of feline herpesvirus-1 (FHV-1).
2. FHV-1 infection (but not necessarily disease) is common in individual cats.
3. FHV-1 establishes lifelong latency within neural tissues in approximately 80% of infected individuals.
4. FHV-1 reactivates from latency commonly with or without obvious cause and with or without clinical evidence of reactivation.
5. FHV-1 reactivation is associated with recrudescent disease in only a small percentage of cats.
6. FHV-1 induces disease by way of (at least) two distinct mechanisms, with important therapeutic implications:
 - Cytolysis (cell-rupturing) due to viral replication. An antiviral agent may be needed; immunomodulation is contraindicated.
 - Immunopathology (immune-mediated injury); however, the antigen is not proven, and the immune-mediated disease may involve no or low-grade viral replication. Antiviral agents may not be effective as sole therapeutic agents. In these cases, antiinflammatory therapy may be indicated, usually in addition to antiviral agents.

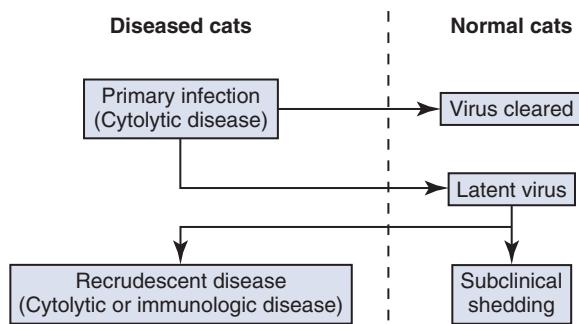


FIGURE 29-31 Summary of the pathogenesis of feline herpesvirus-1. Although most cats are exposed to the virus, become infected, and may even shed virus later in life, only a minority of these cats are expected to experience recrudescent disease. This figure also highlights why diagnostic tests can produce false-positive results.

presentation is periods of chronic mild conjunctivitis alternating with quiescent phases. Many cats shed chlamydial organisms for at least 60 days. Although the organisms may be spontaneously cleared, many cats require appropriate therapy for complete elimination. This helps explain why treatment of in-contact cats is often recommended for individual cats with chlamydial conjunctivitis. Co-infection with FHV-1 and *C. felis* appears to be very uncommon.^{24,109,155,195,196}

TABLE 29-2 Comparison of the Biological Behavior of *Chlamydophila felis* and Feline Herpesvirus-1

	Feline herpesvirus-1	<i>Chlamydophila felis</i>
Organism	Obligate intracellular alphaherpesvirus	Obligate intracellular gram-negative bacterium
Strains	Few; biologically similar	Multiple; variable virulence
Environmental stability	12-18 hours	A few days
Preferred replication site	Conjunctival epithelium	Conjunctival epithelium
Infection	Macrodroplets	Macrodroplets
Carrier state	Lifelong latency within trigeminal ganglia	Persistent (6-9 months) ocular and nonocular infections
Reinfection	Unlikely	Common
Subclinical shedding	More likely	Less likely

Diagnosis

A major paradox exists with respect to the diagnosis of FHV-1.¹¹⁸ Cats experiencing primary FHV-1 infection shed virus in sufficient quantities that viral detection is relatively easy. However, clinical signs during this phase of infection tend to be characteristic and self-limiting, making definitive diagnosis less necessary. By contrast, the diversity and ambiguity of clinical signs in more chronic FHV-1-associated syndromes makes viral identification more desirable, but the elusive nature of the virus in these syndromes makes this difficult. Indeed, the diagnosis of FHV-1 in individual cats represents one of the greatest challenges in the management of chronic FHV-1-related diseases. The situation is equally challenging for *C. felis*. Culture is the gold-standard method of diagnosis; however, this requires special transport media and conditions and rigorous culture techniques and is expensive. The increased sensitivity and ease of organism detection using PCR have made it a preferred technique; however, it appears that many chlamydial organisms may not be detected by standard PCR assay.¹⁹⁶ For these reasons clinical judgment using assessment of a number of helpful, but not pathognomonic, characteristics (Table 29-2) followed by response to appropriate therapeutic trials may be preferred.

Antiviral Treatment

Several antiviral drugs have been studied for their efficacy against FHV-1 and their safety in cats. However, it is critical to realize that because they were developed for use against human herpesviruses, they are not approved for use in cats, many are toxic to cats, some have

BOX 29-2**General Principles Regarding Antiviral Drugs**

Virostatic

- Apply frequently
- Do not taper

Not antibacterial or antifungal

- Use an adjunctive antimicrobial when indicated

Generally more toxic than antibacterial drugs

- Use only when necessary

Monitor for systemic or topical toxicity

dramatically reduced efficacy against FHV-1, and the pharmacokinetics and metabolism are often notably different in cats compared with humans. Provided that these limitations are understood and antiviral drugs are chosen in an evidence-based manner, response to therapy is an excellent way to support or refute the clinical diagnosis of FHV-1. Naturally, this must be tempered by an appreciation that both chlamydial and herpetic disease can wax and wane without therapy. The more commonly used and available antiviral drugs will be individually discussed in subsequent sections; however, some general comments regarding antiherpetic drugs are possible (Box 29-2).

First and perhaps most important is the fact that all antiviral drugs are virostatic and therefore merely reduce viral replication, permitting host immune response to overcome the virus. An appreciation that inappropriate immune response is likely what allows viral reactivation and disease recrudescence helps moderate clinical expectations for antiviral drugs in FHV-1-infected cats. It also reinforces the critical importance of administering these drugs at an appropriately high frequency. Next, the fact that no antiviral drugs have antibacterial or antifungal properties necessitates that the clinician consider adjunctive antimicrobial therapy for primary or secondary nonviral organisms. This is most relevant when treating a herpetic corneal ulcer, when a topical antibiotic is also required. Finally, these drugs typically target enzymes or replicative mechanisms that are shared between viruses and their eukaryotic hosts, creating a much narrower margin of safety than for most antibacterial agents. This is most important when antiviral agents are administered systemically but may also be evident after topical use, especially if therapy is protracted. Signs of topical toxicity include conjunctivitis and punctate corneal erosions, which closely mimic the signs of viral infection; it is therefore particularly important that the clinician remain alert to this potential and discontinue or change topical antiviral agents if there is worsening of disease during therapy or after prolonged therapy. One reasonable approach is to discontinue topical antiviral therapy after 4 to 6 weeks of therapy, even if clinical signs have

not resolved, and to wait 1 to 2 weeks before restarting or changing the topical antiviral. Corneal toxicity can also be avoided through use of systemic, rather than topical, antiviral medication.

In vitro efficacy data permit us to concentrate in vivo attention on the more efficacious agents and to ignore, for example, foscarnet. Clinical application requires at a minimum that consideration be given to cost, frequency of application, adverse effects, toxicity, pharmacokinetics, and route of therapy. This often means that some of the more potent drugs are not widely used clinically. Idoxuridine is a nonspecific inhibitor of DNA synthesis. Therefore host cells are affected, systemic therapy is not possible, and corneal toxicity can occur. It was commercially available in Canada and the United States as a 0.1% ophthalmic solution or 0.5% ointment but now must be compounded. It should be applied to the affected eye a minimum of 5 to 6 times daily. This drug is reasonably tolerated by most cats and seems efficacious in many. Vidarabine is believed to reduce viral DNA synthesis by interfering with DNA polymerase. Like idoxuridine, vidarabine is well tolerated when applied topically but because it is nonselective in its effect, it is associated with notable host toxicity if administered systemically. Vidarabine may be effective in patients whose disease seems resistant to idoxuridine because it affects a viral replication step different from that targeted by idoxuridine. Vidarabine is also commercially unavailable in Canada and the United States but can be compounded as a 3% ophthalmic ointment, which should be applied at least 5 to 6 times daily. Trifluridine is a nucleoside analog of thymidine that is too toxic to be administered systemically and often produces unacceptable signs of toxicity (keratoconjunctivitis and apparent stinging on application), even when applied topically. This is unfortunate because it is the most potent drug against FHV-1 in vitro and it has excellent corneal epithelial penetration. It is commercially available in both Canada and the United States as a 1% ophthalmic solution that should be applied to the affected eye at least 5 to 6 times daily.

Acyclovir has relatively low potency, poor bioavailability, and potential bone marrow toxicity when systemically administered to cats.¹⁴² In the authors' opinion, the availability of safer and more effective drugs makes systemic administration of acyclovir difficult to justify. However, in countries where acyclovir is available as an ophthalmic ointment and can be applied very frequently, this may be effective and should circumvent systemic toxicity.²⁰³ In vitro data suggest that interferon exerts a synergistic effect with acyclovir that could permit an approximately eightfold reduction in acyclovir dose,¹⁹⁸ but in vivo validation of these data is needed. Valacyclovir is a prodrug of acyclovir that is more efficiently absorbed from the feline gastrointestinal tract and is converted to acyclovir within the liver. Unfortunately,

valacyclovir administration is associated with plasma acyclovir concentrations that are elevated to a point of causing fatal myelosuppression and renal and hepatic necrosis,¹³⁵ and valacyclovir should never be used in cats. Penciclovir has a similar mechanism of action as acyclovir but with much more potent antiviral activity against FHV-1. Like acyclovir, its relatively poor bioavailability can probably be overcome by oral administration of the prodrug famciclovir. Pharmacokinetic, safety, and efficacy studies in cats reveal that famciclovir is remarkably effective and apparently safe in cats when administered at 90 mg/kg orally, thrice daily.^{121,187,188} Although clinical efficacy at lower doses has been reported,¹²¹ because of the nonlinear pharmacokinetics of famciclovir in the cat, further research is needed to establish the appropriate dose.

Cidofovir is a relatively new antiviral with good efficacy against FHV-1. When compounded with methylcarboxycellulose into a 0.5% ophthalmic solution and administered twice daily to experimentally infected cats, cidofovir was associated with reduced viral shedding and clinical disease.⁶² Although twice-daily dosing offers a clear advantage over all other topical antiherpetic drugs, cidofovir is not yet commercially available in Canada or the United States, and there are reports of its topical use in humans being associated with stenosis or cicatrization of the nasolacrimal drainage system components. As cidofovir becomes used more widely in cats, this potential side-effect should be monitored.

Lysine is an adjunctive therapy for FHV-1, but there are contradictory research data regarding its efficacy. In vitro data suggest that lysine exerts its antiviral effect by antagonism of arginine.¹¹⁶ In vivo studies demonstrated that administration of 500 mg lysine orally, twice daily, was associated with less severe conjunctivitis during primary infection¹⁷⁹ and that 400 mg lysine orally, once daily, reduced viral shedding during latent infections.¹¹⁹ However, other clinical studies failed to show a positive effect or even demonstrated worsening of disease and increased viral shedding^{47,120,158} in two studies in which lysine was administered as a dietary supplement rather than in bolus form.^{47,120} For that reason cat owners should be advised to administer lysine as a twice-daily 500-mg bolus rather than by sprinkling it on food. Because lysine appears to be most effective when initiated before clinical disease, it may be most useful when administered indefinitely to cats experiencing repeated recrudescent disease,¹⁷⁹ rather than being administered only during periods of active disease.

The interferons are a group of cytokines that have diverse immunologic and antiviral functions largely through limiting cell-to-cell viral spread. Although interferons may play important physiologic roles in the control of viral infections, data regarding potential therapeutic applications are conflicting. In vitro, interferon significantly reduced FHV-1 titer or cytopathic effect (or

both) without detectable cytotoxic changes in the host cell lines^{162,170} and was associated with a nearly eightfold reduction in the required dose of acyclovir, especially when introduced to the viral culture before infection.¹⁹⁸ However, there are relatively few peer-reviewed, placebo-controlled, prospective clinical trials of interferon administration in cats. Those that exist show minimal or no beneficial effects.⁷⁶ Further research is necessary to determine dosage, timing, and efficacy (if any) of this group of compounds, especially in the more chronic or recrudescent infections.

Antichlamydial Treatment

Traditionally, feline chlamydial conjunctivitis has been treated with topical tetracycline ointment. However, because cats harbor and shed *C. felis* from nonocular sites and apparently normal cats can shed organisms, systemic drugs should also be used and consideration should be given to treating all cats in contact with the affected cat.^{141,172,185} The preferred systemic drug is doxycycline at 5 to 10 mg/kg orally once to twice daily for at least 3 to 4 weeks. Azithromycin has good efficacy against chlamydial (and mycoplasmal) organisms and shows reasonably rapid absorption, adequate bioavailability, and useful concentrations in ocular tissues for at least 3 days after a single oral dose of 5 mg/kg. However, doxycycline has superior capacity to reduce organism shedding. A topical tetracycline or erythromycin ointment should be considered in addition to systemic doxycycline if conjunctivitis is severe so as to guarantee high drug concentrations at the ocular surface and provide some surface ocular lubrication.

Contraindicated Therapies

Because triple antibiotic is ineffective against *C. felis* and FHV-1, it should not be used to treat primary conjunctivitis in cats. It is useful for prevention of infection of a superficial corneal ulcer. Topically or systemically administered corticosteroids may sometimes produce symptomatic improvement in infectious corneoconjunctival disease but do not reduce, and may actually increase, organism load. This is presumably why they are often associated with rebound worsening of disease once they are discontinued. Ironically, this can falsely lead the clinician to reinstitute the steroid therapy, further exacerbating the underlying disease. Topically administered corticosteroids induce deeper and more persistent corneal disease and protracted viral shedding.¹³⁷ Systemic administration of corticosteroids is contraindicated and is a well-established, reliable means of inducing viral reactivation.⁹¹ Although steroids may be used in select cases that are suspected to be due to immunopathologic mechanisms, the potential for dramatic clinical decompensation warrants extreme caution, close monitoring, and concurrent use of antiviral medication. The potential complications from using

corticosteroids have prompted interest in the use of nonsteroidal antiinflammatory drugs (NSAIDs) for managing the inflammatory effects of ocular FHV-1 infection. Although there are no studies of their effects in cats infected with FHV-1, they have similar negative effects to corticosteroids in humans infected with HSV-1. Use of cyclosporine in chronic feline herpetic disease has been inadequately studied. Cyclosporine is capable of suppressing inflammatory events operative in viral stromal and eosinophilic keratitis but also impairs viral clearance from the eye and suppresses some beneficial immune responses. The authors are unaware of any studies examining the effects of tacrolimus on ocular herpetic infections in any species. This suggests that use of these agents should, as a minimum, be restricted by the same principles that govern the use of corticosteroids in humans with HSV-1.

Conjunctivitis

Conjunctivitis is an extremely common finding in the cat. However, when reaching this clinical diagnosis, clinicians must always first determine if the cat is affected by conjunctivitis only and then must determine the cause of the conjunctivitis. The first consideration is crucial because many diseases, including blepharitis, keratitis, uveitis, glaucoma, orbital disease, and scleritis all produce conjunctival hyperemia (Figure 29-32). However, these diverse diseases often have completely different causes, require completely different diagnostic investigations, have different ramifications for vision or even patient survival, and necessitate completely

different treatments. This emphasizes why a complete ophthalmic examination should always be performed, even if the clinical presentation looks like simple conjunctivitis. If ocular examination fails to reveal further pathology, then it is justifiable to diagnose conjunctivitis and begin searching for the cause. Fortunately, in contrast to dogs, there are few likely causes of feline conjunctivitis. As discussed previously, FHV-1 and *C. felis* are the top two etiologic diagnoses with *Mycoplasma* spp., *Bordetella*, and possibly *Bartonella* lower on the list. Once clinical judgment has identified the most likely cause (see Table 29-2), specific and evidence-based treatment should be initiated because response to therapy is the next "diagnostic test." These therapies are described earlier in this chapter and should include systemic doxycycline with or without topical tetracycline or erythromycin ointment if *C. felis* is suspected, or a topical or systemic antiviral with or without lysine if FHV-1 is suspected. Antichlamydial treatment is required for 3 to 4 weeks, whereas antiviral drugs should be continued for approximately 1 week after clinical resolution is noted.

Mucinomimetic therapy is a safe and important component of the treatment of conjunctivitis. Chronic conjunctivitis is associated with conjunctival goblet cell atrophy and an associated mucin-deficient qualitative tear film abnormality characterized by premature evaporation of the tear film and corneal drying. This, in turn, worsens conjunctivitis, leading to a perpetually exacerbating cycle unless remedied with topical mucin replacement.³⁸ Although this is likely true for many causes of conjunctivitis, FHV-1 has specifically been proved to induce a drastic decline of conjunctival goblet cell density to normalize for at least 1 month after FHV-1 infection.¹⁰⁶ Mucinomimetic tear replacement agents break this cycle by increasing stability of the precorneal tear film. Numerous formulations exist; however, sodium hyaluronate demonstrates superior corneal retention time compared with other tear substitutes.¹⁷¹ Unlike most medications, artificial tear substitutes have the added advantage of being available in single-dose packaging, bypassing corneal cytotoxicity that is a feature of preservatives in ophthalmic medications^{23,30} (Figure 29-33).



FIGURE 29-32 Conjunctival and episcleral vascular congestion and mild corneal edema in a cat with uveitis. Although the conjunctival hyperemia suggests "simple" conjunctivitis, the larger episcleral vascular engorgement along with the corneal edema make this diagnosis untenable and instead make glaucoma or uveitis most likely. This underscores the importance of always performing a complete ophthalmic examination, including assessment of aqueous flare and intraocular pressure. (Image courtesy UC Davis Veterinary Ophthalmology Service.)

Symblepharon

Symblepharon is a term that describes adhesions between conjunctiva and adjacent conjunctiva or cornea, and is expected after marked or chronic ulceration and exposure of subepithelial connective tissue. Its clinical appearance is characteristic, but significance varies greatly depending on the extent and location of adhesions (Figure 29-34). Corneal involvement is associated with reduced vision, and conjunctival adhesions may obstruct lacrimal drainage, prohibit normal globe or



FIGURE 29-33 Artificial tear formulations are often available in single-dose containers. Single-dose medications are advantageous because they are free of preservatives, which are toxic to the corneal epithelium. This is especially important when medications are administered 4 or more times daily, multiple medications are being administered, or there is known hypersensitivity.

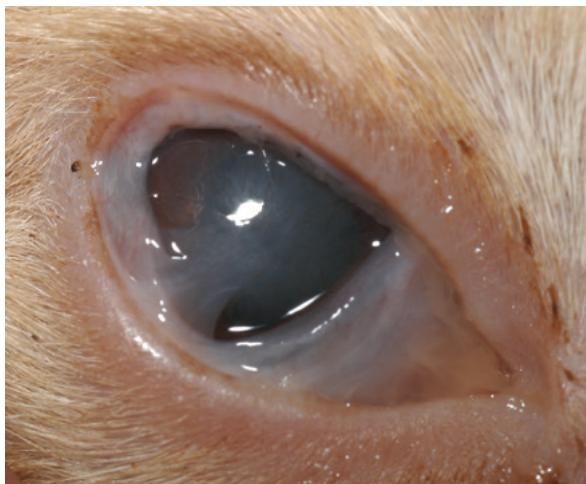


FIGURE 29-34 Symblepharon between the conjunctiva and the cornea following primary infection with feline herpesvirus-1. Because of the central location of the adhesions in this cat, reduced vision is probable. (Image courtesy UC Davis Veterinary Ophthalmology Service.)

eyelid movements and position, or cause nictitans protrusion (Figure 29-35). Feline herpesvirus is most frequently blamed, presumably because it is so common in cats. Because medications cannot break down adhesions, surgical resection is the only possible therapy. However, recurrence is common because surgery involves a combination of conjunctivectomy and superficial lamellar keratectomy, which re-expose subepithelial connective tissue. Minor adhesions are therefore best left untreated. When surgical management is elected, preoperative and postoperative control of active herpetic recrudescence is essential. In addition, various mechanical devices to separate the exposed surfaces during healing, often

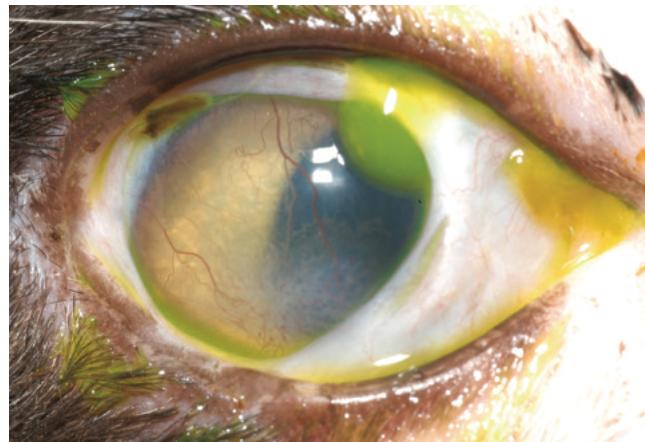


FIGURE 29-35 Symblepharon involving the bulbar and palpebral conjunctiva, nictitans, and cornea. The adhesions in this cat prevent normal movement of the third eyelid. Epiphora is caused by adhesions over the nasolacrimal puncta. (Image courtesy UC Davis Veterinary Ophthalmology Service.)

accompanied by a staged approach, have been used. Referral for these procedures is recommended.

Corneal Ulceration

As in dogs, there are three main principles for treating corneal ulceration in cats:

1. Find and treat the primary cause.
2. Prevent secondary infection.
3. Provide specific supportive care if stromal involvement or chronicity are present.

The major difference between feline and canine ulcers is that infectious causes of ulcers are rare in dogs, whereas feline ulcers are considered to be due to FHV-1 until proved otherwise. If thorough clinical examination fails to reveal evidence of a foreign body, ectropion, entropion, distichia, ectopic cilia, trichiasis, lagophthalmos, blepharitis with an abrasive eyelid margin (all of which are very uncommon in cats), or periocular or intraocular trauma, then the ulcer should be assumed to be herpetic in origin. Herpetic ulcers have either a pathognomonic dendritic pattern or a highly suggestive appearance—superficial, epithelial loss, sometimes with a nonadherent lip. Herpetic ulcers do not involve stromal loss unless there is secondary bacterial infection. If FHV-1 is believed to be the originating cause, then a decision must be made regarding antiviral therapy. If the ulcer is acute, unilateral, and in an otherwise healthy cat without previous recrudescent herpetic disease, then allowing the patient's own immunity the chance to overcome the herpetic reactivation is justifiable. Otherwise, the clinician must initiate topical or systemic antiviral medication. Antiviral therapy should be continued until ulcer resolution and should not be tapered.

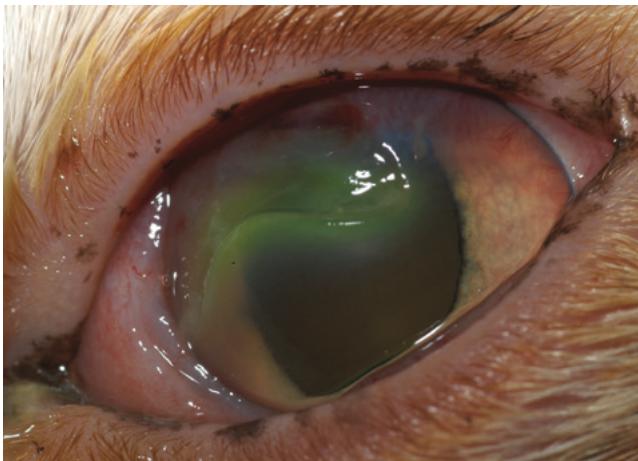


FIGURE 29-36 Deep corneal ulcer secondary to feline herpesvirus-1. Note the loss of corneal stroma; the thickened, hyperemic conjunctiva; mild corneal edema; and deep corneal vessels. (Image courtesy UC Davis Veterinary Ophthalmology Service.)

All ulcers require topical antibiotics because the epithelial barrier is lost and because secondary infection is one of the more devastating complications that can occur. This is true even if an antiviral drug is instituted, because antivirals do not have antibacterial properties. A broad-spectrum bactericidal antibiotic such as triple antibiotic is an excellent choice. In ulcers that are not bacterially infected, twice- or thrice-daily application until the cornea no longer retains fluorescein stain is adequate.

Additional supportive treatment is required for any ulcer with stromal involvement (stromal loss, malacia, or white blood cell infiltration) (Figure 29-36). These changes typically indicate secondary bacterial infection, and as in other species, cytology and culture and sensitivity are recommended. Unlike in dogs, *Mycoplasma* spp. can cause rapidly progressive stromal ulcers in cats; this should be considered when requesting culture at the laboratory. A broad-spectrum bactericidal ophthalmic antibiotic solution such as fluoroquinolone should be administered as often as 6 times daily until culture results are available. If *Mycoplasma* is suspected, then tetracycline ointment should be considered. In all deep ulcers, adjunctive therapy with serum should be considered to provide anticollagenases, which reduce stromal melting, and growth factors, which speed healing. Typically, serum is administered at the same frequency as the topical antibiotic. If there is danger of rupture or healing is delayed, referral for placement of a conjunctival graft is recommended. Third eyelid flaps are not recommended because they prohibit the two things the ulcer needs most: medication and observation.

Ulcers are also classified as complicated when they persist beyond 7 days, even if they remain superficial. A particular type of chronic nonhealing superficial ulcer occurs in cats and shares some features with the



FIGURE 29-37 Corneal sequestrum with chronic, superficial keratitis. Superficial corneal vessels span the entire visible cornea, and a lip of granulation tissue is seen at the ventral edge of the sequestrum. (Image courtesy UC Davis Veterinary Ophthalmology Service.)

indolent ulcer of dogs; it involves epithelium only (no stromal loss) and has a lip of nonadherent epithelium that is easily débrided with a cotton-tipped applicator. However, indolent ulcers of dogs are caused by an anatomical defect preventing adhesion between the corneal epithelium and stroma and are treated by grid keratotomy. No such syndrome has been proved to occur in cats. In fact, if nonhealing ulcers in cats are treated by grid keratotomy, they are particularly likely to form corneal sequestra (discussed later in this chapter). These chronic, superficial ulcers, which débride easily in cats, may be due to FHV-1. One treatment protocol involves use of a topical antiviral and antibacterial agent following corneal débridement. If this is unsuccessful, referral is wise.

Corneal Sequestration

Corneal sequestration is an entity unique to the cat. It is an area of ulcerated, necrotic cornea characterized clinically by gradual progression of a dark (amber, brown, or black) discoloration usually involving the central cornea (Figure 29-37). Prior, and usually chronic, corneal ulceration is common but not always reported. Blood vessels often extend to the lesion and are deep or superficial, depending on depth of the sequestrum. The necrotic corneal stroma may be surrounded by zones of variably intense corneal stromal edema, inflammatory cell infiltration, or both. Sequestra are usually unilateral but may occur bilaterally. Frequently, the eye appears to be causing the cat pain, but some cats display only minor signs of discomfort. Histologically, the plaque consists of a sequestered, desiccated region of necrotic corneal stroma surrounded by a variable “foreign body-type” inflammatory cell response with extensive granulation tissue development. The characteristic



FIGURE 29-38 Postoperative photo after excision of a corneal sequestrum. In this case excision of the sequestrum resulted in a deep corneal defect that required grafting. A corneoconjunctival transposition was performed to maintain a relatively clear visual axis in the central cornea. (Image courtesy UC Davis Veterinary Ophthalmology Service.)

clinical appearance is considered diagnostic; however, differential diagnoses should include corneal foreign body; dermoid, anterior synechia–staphyloma; or limbal melanoma. Feline herpesvirus may be involved in approximately 50% of cases.¹³⁶ Other causes of chronic corneal irritation such as entropion, distichiasis, tear film deficiencies, and lagophthalmos appear also to predispose to sequestrum formation. This may explain the predilection for Persian, Himalayan, and Siamese cats to develop corneal sequestra. Identification and correction of any underlying causes are important whenever possible. Lamellar keratectomy with a sliding corneal or conjunctival graft is the treatment of choice, especially if the cat appears to be in pain or the lesion is deep or chronic (Figure 29-38). Unfortunately, approximately 33% of cases experience recurrence. Medical management is generally not recommended because of the potential for corneal perforation and the degree of discomfort usually present. However, if the cat appears comfortable, it may be attempted because sequestra can spontaneously slough over a period of weeks to months. Medical management includes prophylactic topical antibiotics, as for corneal ulceration and treatment of reflex uveitis, if evident. Many recommend using antiviral medications and mucinomimetic tear-replacement formulations because altered tear film quality or evaporation or both have been blamed for these lesions. Surgical procedures to reduce corneal exposure and irritation such as temporary or permanent partial tarsorrhaphy and correction of entropion should be considered to reduce recurrences.

Eosinophilic Keratoconjunctivitis

Feline eosinophilic keratitis (FEK) is an enigmatic disease of cats. Clinically, FEK appears as a focal, raised, yellow

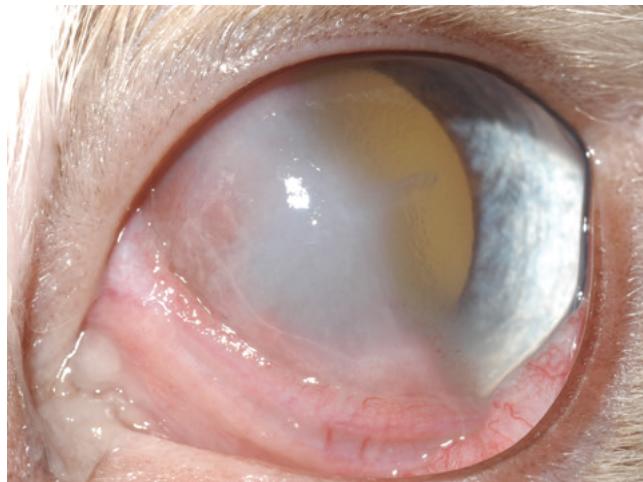


FIGURE 29-39 The characteristic appearance of feline eosinophilic keratitis includes thickened and hyperemic conjunctiva, corneal vascularization, and white corneal plaques. Cytologic assessment of the corneal plaques revealed eosinophils and mast cells. (Image courtesy UC Davis Veterinary Ophthalmology Service.)

to pink corneal plaque resembling granulation tissue (Figure 29-39). Typically, only the lateral cornea is affected initially, but in advanced cases the entire cornea may be involved. Adjacent areas of corneal ulceration are often present. Eyelid or conjunctival involvement (including third eyelids) is seen relatively commonly with keratitis but occasionally occurs alone. Cytologic evaluation of scrapings from affected cornea or conjunctiva reveals neutrophils, eosinophils, and mast cells, along with hyperplastic or dysplastic epithelial cells. Histology may reveal lymphocytes and plasma cells. Diagnosis is suggested by clinical appearance and confirmed using cytology. The cause is undetermined; however, the condition appears to be due to an aberrant immune response. In many cases the antigenic stimulus is unrecognized; however, FHV-1 DNA can be detected in corneal samples from approximately 75% of cats with FEK.¹³⁶ Given the inability to identify the inciting antigen, this disease has traditionally been treated with topical corticosteroids. Potential involvement of FHV-1 presents clinicians with a dilemma, because use of immunomodulatory drugs, especially topical corticosteroids, for treatment of an eye that is potentially infected with FHV-1 warrants caution. Given the likely involvement of FHV-1, it is prudent to simultaneously administer an antiviral agent and recheck frequently. If there is improvement and the owners are compliant, continuation of this regimen may be all that is necessary. The use of 1.5% cyclosporine has recently been described, with promising results.¹⁷³ Antiviral treatment should be continued for as long as there is evidence of active viral replication and certainly while ulceration is present, and corticosteroids are tapered judiciously as clinical signs improve. Early diagnosis and treatment of recurrences will limit the need for protracted therapy.

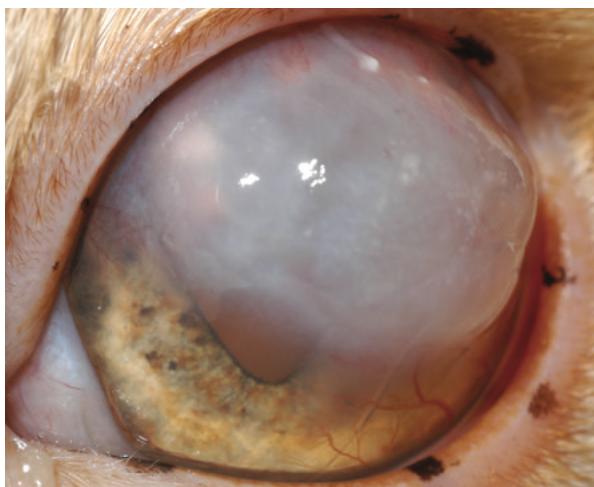


FIGURE 29-40 Acute bullous keratopathy is characterized by rapid onset of massive corneal edema, with bulla formation and keratoconus. Superficial corneal vessels are also visible in this cat, suggesting a previous keratitis. This is not a necessary feature. Urgent surgical intervention is required to stabilize the cornea. (Image courtesy UC Davis Veterinary Ophthalmology Service.)

Acute Bullous Keratopathy

Although acute bullous keratopathy (ABK) is a rare condition, feline clinicians should be aware of it because it is seen only in cats, has a characteristic clinical appearance, and requires emergency management to avoid globe rupture.

As its name suggests, ABK involves the cornea only and is extremely rapid in onset, occurring within minutes to hours. Profound edema and bullae formation within the corneal stroma are the predominant features⁷² (Figure 29-40). There is usually marked epiphora and blepharospasm, as well as some conjunctival hyperemia and chemosis, as is expected with all cases of keratitis. With this clinical appearance, the major differential considerations are a peracute progressive stromal ulcer or a corneal laceration; however, the bullous nature of the corneal distention and the typical lack of stromal inflammatory cells are characteristic of ABK. The condition can present in one or both eyes. Cats of any age may be affected, but the few cases reported in the literature suggest that the syndrome is more common in younger cats. To date, no predisposing cause or history is recognized, although an association with systemic antiinflammatory and immunosuppressive medication has been suggested.^{147a} Unlike other causes of corneal edema, which result from defects in the corneal epithelium or endothelium, the defect in ABK is proposed to involve the corneal stroma itself. Bacterial, viral, protozoal, and fungal organisms have not been detected when tested for by cytology, culture, or serology.

Some cases have been reported to improve without treatment; however, most require referral for emergency conjunctival grafting and sometimes

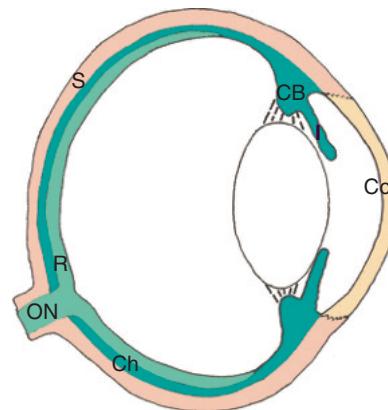


FIGURE 29-41 Basic anatomy of the globe. The anterior uvea is composed of the iris and ciliary body, and the posterior uvea is composed of the choroid. Co, Cornea; I, iris; CB, ciliary body; R, retina; Ch, choroid; S, sclera; ON, optic nerve. (From Maggs D: Slatter's fundamentals of veterinary ophthalmology, ed 4, St Louis, 2007, Saunders.)

thermokeratoplasty. In the latter technique, the cornea is treated with multiple, very carefully applied, highly focal applications of heat. A scar forms in the treated area, and associated tissue contraction expels fluid from the corneal stroma, limiting further corneal distention. Application of a bandage in the form of a temporary tarsorrhaphy has also been reported to reduce edema. Although third-eyelid flaps may provide some support to the cornea, they are not recommended because they prevent medication and observation of the cornea, which are critical to proper management. If aggressive treatment is initiated promptly, the prognosis for vision and for the globe is good; however, extensive bullous keratopathy, especially with globe perforation, carries a poorer prognosis.

DISEASES OF THE UVEAL TRACT

Uveitis

The uvea or vascular layer of the eye is composed of the iris and ciliary body (anterior uvea), and choroid (posterior uvea) (Figure 29-41). Uveal inflammation may involve the iris and ciliary body alone (anterior uveitis), the choroid and adjacent retina (posterior uveitis or chorioretinitis), or the entire uveal tract (panuveitis). Recognition of this common, painful condition is vital, as the consequences of untreated uveitis can be blinding and underlying causes of uveitis can be fatal.

Unlike dogs, cats with uveitis less commonly present with sudden, overt clinical signs. Instead, feline uveitis is insidious, with subtle changes that may easily be dismissed, often as "conjunctivitis," unless a thorough ophthalmic examination is performed. Therefore all reddened eyes in cats should be assessed for signs considered pathognomonic or at least highly suggestive of



FIGURE 29-42 Examination findings typical of uveitis include corneal edema, rubeosis iridis, a thickened or “muddy” iris, and keratic precipitates on the ventral corneal endothelium. (Image courtesy of the WCVM Ophthalmology Service.)

anterior uveitis (or at the very least incompatible with a diagnosis of conjunctivitis), such as aqueous flare; hypopyon; hyphema; anterior chamber fibrin; keratic precipitates; episcleral congestion; corneal edema; rubeosis iridis; a thickened, swollen, or “muddy”-looking iris; miosis (or a delayed response to mydriatic agents); anterior or posterior synechiae; and altered IOP (Figure 29-42). The IOP in eyes with anterior uveitis is generally low; however, with secondary glaucoma, it may also be normal or elevated. Posterior uveitis is not always accompanied by outward clinical signs or anterior segment changes, which emphasizes the importance of performing a fundic examination with each ophthalmic examination. Clinical findings indicative of posterior uveitis include vitreous debris, hyporeflective areas within the tapetum, chorioretinal infiltration with white blood cells, retinal vascular tortuosity, retinal or vitreous hemorrhage (or both), or retinal detachment (Figure 29-43).

Once uveitis has been diagnosed, the next important step is to search for an underlying cause, even if this is expected to be unrewarding (Table 29-3). Causes of uveitis are generally referred to as *exogenous* or *endogenous*. Exogenous causes are usually easily diagnosed by clinical examination, tend to result from trauma or surgery, and include corneal ulceration and blunt or penetrating ocular trauma. Endogenous causes require further testing to achieve a diagnosis, and include infectious, neoplastic, and immune-mediated factors. Although examination findings are nonspecific with regard to etiology, some clinical findings are more suggestive of certain etiologies. For example, large, cellular keratic precipitates (often described as resembling mutton fat) usually reflect diseases causing granulomatous inflammation, such as systemic mycoses or feline

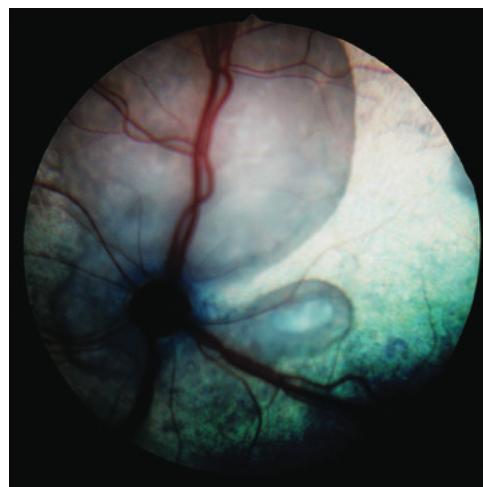


FIGURE 29-43 Multiple focal bullous retinal detachments around the optic nerve of a cat that also demonstrated neurologic abnormalities. A diagnostic workup failed to reveal an underlying cause; however, the owner reported that the cat regained normal mentation, neurologic status, and vision. This case reinforces the importance of a fundic examination in patients demonstrating neurologic signs. (Image courtesy UC Davis Veterinary Ophthalmology Service.)



FIGURE 29-44 Mild corneal edema and granulomatous keratic precipitates in a cat with uveitis caused by feline infectious peritonitis. (Image courtesy UC Davis Veterinary Ophthalmology Service.)

infectious peritonitis (FIP) (Figure 29-44). Presence of a mature or hypermature cataract may be suggestive of lens-induced uveitis; however, unlike dogs, cats tend to develop cataracts secondary to uveitis, and the cataract should not be assumed to be the original cause of intraocular inflammation. Idiopathic uveitis occurs more often in male cats older than 9 years and is more likely to be unilateral, whereas uveitis secondary to systemic disease is more often bilateral.⁴³

Because many systemic diseases have been implicated as being able to cause uveitis in cats, the list of differential considerations is long (Box 29-3). Feline immunodeficiency virus (FIV) and FIP directly cause

TABLE 29-3 Suggestive Clinical Examination Findings for Several Common Causes of Uveitis in the Cat

Cause	Clinical Course	Typical Location	Suggestive Signs*
Trauma	Acute	Anterior uveitis	Hyphema; AC fibrin; miosis; aqueous flare; hypotony
Reflex uveitis (due to ulcerative keratitis)	Acute	Anterior uveitis	Miosis; aqueous flare; hypopyon (if ulcer is infected); hypotony
FIP	Subacute	Panuveitis (anterior uveitis may dominate)	KPs; aqueous flare; AC fibrin; hypopyon; retinal vascular engorgement and increased tortuosity; perivasculär chorioretinal granulomas; retinal detachment
Lymphoma	Subacute	Anterior uveitis	Hypopyon; hyphema; AC fibrin; aqueous flare; iridal thickening; iridal nodules; rubeosis iridis; iris bombé; secondary glaucoma
Systemic mycoses	Subacute	Panuveitis (posterior uveitis dominates)	Hypopyon; hyphema; AC fibrin; aqueous flare; iridal thickening; rubeosis iridis; iris bombé; vitreal debris/infiltrates; secondary glaucoma; chorioretinal granulomas; retinal detachment
Lens-induced uveitis	Phacoclastic (acute)	Anterior uveitis	Hypopyon; hyphema; AC fibrin; aqueous flare; iridal thickening; posterior synechiae; ocular hypertension; miosis
	Phacolytic (chronic)		Aqueous flare; iridal thinning/atrophy; rubeosis iridis; posterior synechiae; mature/hypermature cataract; secondary glaucoma
Idiopathic	Chronic or recurrent	Anterior or intermediate uveitis	Iridal thinning/atrophy; iridal nodules; rubeosis iridis; aqueous flare; KPs; snow banking; vitreous debris/infiltrates; posterior synechiae; cortical cataract; secondary glaucoma
Primary uveal neoplasia	Chronic	Anterior uveitis or chorioretinitis depending on site of tumor	Anteriorly located Hypopyon; hyphema; AC fibrin; aqueous flare; anterior iridal displacement; rubeosis iridis; vitreous debris/infiltrates; secondary glaucoma Posteriorly located Retinal detachment; subretinal neoplasm; vitreous debris/infiltrates
FIV	Chronic	Intermediate uveitis	Vitreous debris/infiltrates; snow banking; iridal thinning/atrophy; rubeosis iridis; aqueous flare; posterior synechiae; cortical cataract; secondary glaucoma

AC, Anterior chamber; FIP, feline infectious peritonitis; KPs, keratic precipitates; FIV, feline immunodeficiency virus.

*Note the considerable overlap of signs. No sign is pathognomonic for a given cause, and absence of one or more of the signs listed does not allow a cause to be eliminated. Rather, these features can be used to rank the likelihood of potential causes for further diagnostic testing.

From Maggs DJ: Feline uveitis: an "intraocular lymphadenopathy," *J Feline Med Surg* 11:167-182, 2009.

BOX 29-3

Infectious Causes of Uveitis in Cats

Viral	Bacterial	Fungal/algal	Parasitic	Protozoal
FIP	<i>Bartonella</i> species	<i>Cryptococcus neoformans</i> [†]	<i>Cuterebra</i>	<i>Toxoplasma gondii</i>
FeLV*	<i>Mycobacterium</i> species	<i>Histoplasma capsulatum</i> [†]		<i>Leishmania</i> species
FIV*	<i>Ehrlichia</i> species [‡]	<i>Blastomyces dermatitidis</i> [†]		
FHV	<i>Borrelia burgdorferi</i> [‡]	<i>Candida albicans</i> <i>Coccidioides immitis</i> [†] <i>Aspergillus</i> species		

FIP, Feline infectious peritonitis; FeLV, feline leukemia virus; FIV, feline immunodeficiency virus; FHV, feline herpesvirus.

*Via immunosuppression or oncogenesis.

[†]Chorioretinitis predominates.

[‡]Seroprevalence data only (no clinical evidence).

From Maggs DJ: Feline uveitis: an "intraocular lymphadenopathy," *J Feline Med Surg* 11:167-182, 2009.



FIGURE 29-45 Multiple focal bullous retinal detachments and chorioretinal hemorrhage in a cat with systemic cryptococcosis. (Image courtesy UC Davis Veterinary Ophthalmology Service.)

uveitis in cats.^{59,114} Lymphoma or superinfection resulting from immunosuppression and anemia induced by feline leukemia virus (FeLV) also cause uveitis; however, FeLV itself does not seem to directly result in ocular disease.²² There is also evidence suggesting that intraocular presence of FHV-1 may be associated with feline uveitis.¹¹⁷ Bacteremia or septicemia may also manifest as uveitis. Although *Bartonella* species have been implicated by some authors,¹⁰³ other controlled studies have revealed that many normal animals are seropositive⁶¹ and can even have organism DNA demonstrated in their aqueous humor.¹⁰³ These facts confound diagnosis of these and many other organisms. By contrast, *Toxoplasma gondii* and *Leishmania* species are well established as a cause of feline uveitis.* Intraocular migration of nematodes such as *Cuterebra* species may cause uveitis.^{82,177,207} Dematiaceous fungi, as well as systemic infections of *Cryptococcus* species, *Histoplasma capsulatum*, *Blastomycetes dermatitidis*, and *Coccidioides immitis*, may also cause uveitis in cats[†] (Figure 29-45). Primary and metastatic neoplasia also causes uveitis. In cats, iris melanoma is the most common primary ocular tumor, whereas lymphoma is the most common metastatic tumor associated with feline uveitis.^{43,147}

Although a large number of systemic diseases are capable of causing uveitis, uveitis remains idiopathic in approximately 70% of cats undergoing a thorough diagnostic investigation.^{43,147} Regardless, thorough diagnostic investigation is indicated because many causes are treatable, have human health implications, or affect management of cats. In particular, failure to identify a

cause means that corticosteroids may be used at sufficiently high doses to be effective without concern regarding their safety in systemically infected animals or animals with neoplasia in which a more complete chemotherapeutic protocol might be chosen. Therefore a diagnosis of uveitis without obvious exogenous cause should always be followed by a complete physical examination, CBC, serum biochemical profile, urinalysis, and testing for FIV and FeLV. Further diagnostics, such as chest or abdominal radiography and ultrasonography or fine-needle aspirates of lymph nodes, may be indicated depending on clinical suspicion.

Serology for infectious disease is variably useful for obtaining a diagnosis. Serology is unable to differentiate between vaccine-associated virus and wild-type virus, and titers against some infectious diseases may remain elevated long after infection has occurred. For example, immunoglobulin G titers to *T. gondii* remain elevated for years after initial exposure in healthy cats.¹⁰⁴ With *Bartonella* there appears to be no correlation between titers and uveitis.⁶¹ It may be of more value to use negative titers to rule out disease than to use positive titers to rule in infectious disease; however, care must be taken not to falsely interpret negative titers in acutely affected animals. Aqueous humor may also be submitted for infectious disease titers. However, similar pitfalls exist for interpretation of aqueous titers as for serum titers. In addition, intraocular antibody production can persist or recur in response to nonspecific antigenic stimuli and may occur in the absence of uveitis. Cytology of aqueous humor also tends to be of low-yield except for lymphoma. Culture is of benefit only with endophthalmitis, typically after a penetrating injury. However, evaluation of aqueous may be of some value when uveitis is unresponsive to treatment and other diagnostics have been unrewarding. When an eye has become blind and painful despite treatment, enucleation is indicated and histopathologic evaluation of the globe is essential.

Treatment for uveitis should be aggressive and prompt given the high potential for blinding sequelae. The main goals of treatment are to address any underlying etiology, control intraocular inflammation, provide analgesia, and minimize secondary complications. Anterior uveitis may be treated with topical medications alone; however, the presence of posterior uveitis requires systemic administration of medications because of the inability of eye drops to achieve therapeutic drug concentrations posterior to the lens. Treatment of an identified underlying etiology is essential. Failure to address an underlying cause will almost certainly lead to failure to control uveitis. In addition, specific treatment often does more to reduce inflammation than nonspecific anti-inflammatory medications and can result in lower doses of and shorter treatment periods with antiinflammatory medications.

*References 42, 89, 90, 105, 151, 152.

†References 6, 13, 19, 67, 75, 144, 147.

Corticosteroids or NSAIDs are used to control intraocular inflammation. In the absence of corneal ulceration, topical 1% prednisolone or 0.1% dexamethasone ophthalmic suspensions may be used up to 4 times daily to treat anterior uveitis. Hydrocortisone, found in combination antibiotic–corticosteroid preparations, is a weak steroid that does not penetrate an intact corneal epithelium and should not be used to treat uveitis. Because systemic absorption from topically applied medications is generally minimal, especially acutely, and because control of inflammation is essential (irrespective of cause), topical steroids are usually safe for use when infectious systemic disease is present. However, when treating posterior uveitis, the clinician should refrain from using systemic steroids until infectious etiologies have been ruled out or when results of diagnostic tests may be affected by the use of corticosteroids. Topical 0.1% diclofenac, 0.03% flurbiprofen, and 0.1% nepafenac are NSAIDs that may all be used up to 4 times daily to control uveitis. Because they tend to be more expensive and less potent than steroids, they are usually reserved for situations in which corticosteroids are contraindicated. Because of the potential for platelet inhibition, these medications should be avoided if hyphema is present. Likewise, systemic NSAID therapy is used when systemic corticosteroids are contraindicated or while awaiting results of diagnostic testing but should be avoided if a bleeding disorder is suspected.

The pain associated with anterior uveitis results from spasm of the ciliary body muscle. Although this cannot be assessed directly, it can be assumed to be present if the pupil is miotic. Administration of cycloplegic medication such as 1% atropine will provide analgesia by preventing ciliary muscle spasm. Clinicians should use the presence of a dilated pupil to infer that paralysis of the ciliary muscle has also occurred. Initially, atropine may be required up to 3 times daily to achieve mydriasis. After the pupil has dilated, atropine is administered only as often as is required to maintain dilation, which may be as infrequently as every other day or every few days. The bitter taste of atropine may result in profuse salivation after administration in cats; use of the ointment form rather than the solution may minimize this side effect. In addition to its analgesic effects, atropine also stabilizes the blood–ocular barrier, and the resulting mydriasis decreases the chance of posterior synechia formation. The IOP should be checked frequently in patients receiving atropine treatment because the dilated pupil may potentiate peripheral anterior synechia, which obstruct the iridocorneal angle, and cycloplegia can also reduce aqueous outflow, thereby increasing IOP.

Initial uveitis treatment should be aggressive, with judicious tapering of antiinflammatory and cycloplegic



FIGURE 29-46 Bilateral uveitis in a cat. Rubeosis iridis and keratic precipitates are visible in the right eye. Mydriasis and buphthalmos of the left eye are due to glaucoma, which has developed secondary to uveitis. There is also a cataract in the left eye, likely caused by the uveitis. This case reinforces the need for early and aggressive therapy of uveitis in cats, with slow tapering of therapy based only on reduction of clinical evidence of uveitis. Unrecognized or inadequately treated uveitis is associated with severe and blinding sequelae. (Image courtesy UC Davis Veterinary Ophthalmology Service.)

agents based on clinical improvement. Recheck examinations should be frequent and at increasing intervals as signs abate. Initial rechecks may need to be as frequent as twice weekly to manage complications should they arise. Patients should also be rechecked beyond the time that all medications are completely discontinued on account of the potential for recurrence. Owners should also be warned that patients who have experienced past bouts of uveitis are at risk of future episodes. Some patients, particularly those diagnosed with idiopathic uveitis, may require lifelong low-dose antiinflammatory medications to control clinical signs, reduce complications, and minimize recurrence of disease.

In some cases uveitis may prove intractable. Secondary complications in these patients are common. The most important sequelae of chronic uveitis in cats are glaucoma, lens luxation, cataract, and retinal detachment^{43,147} (Figure 29-46). Should glaucoma arise, treatment with the carbonic anhydrase inhibitor dorzolamide, twice or thrice daily, should be instituted. Unfortunately, glaucoma can be challenging to treat and may ultimately necessitate enucleation of the affected eye. Cataract formation and lens luxation are other common complications of uveitis that may be difficult to treat. An advanced cataract may exacerbate ocular disease by inciting phacolytic uveitis; however, most cats are not candidates for phacoemulsification because of the severity of ocular pathology. Similarly, surgical removal of a luxated lens carries a poor prognosis if uveitis is ongoing. In many patients with these sequelae to uveitis, a blind and painful globe eventuates, and enucleation is necessary



FIGURE 29-47 Note the anisocoria in this patient. Pupillary light reflexes were also abnormal, and the degree of anisocoria changed over time. These features are suggestive of feline spastic pupil syndrome, which is thought to be due to neuritis of cranial nerve 3, induced by feline leukemia virus. (Image courtesy UC Davis Veterinary Ophthalmology Service.)

to reduce pain, permit cessation of medical therapy and frequent recheck examinations, minimize risk of intraocular sarcoma development (discussed later in this chapter), and allow a histologic diagnosis that may permit more appropriate treatment of the opposite eye.

Spastic Pupil Syndrome

Spastic pupil syndrome (SPS) is a condition unique to cats in which clients report anisocoria, which may sometimes be transient and independent of ambient light levels (Figure 29-47). Clinically, cats with SPS appear to be healthy, are visual, and have no ocular abnormalities besides unusual behavior of the pupils. Clinical examination reveals anisocoria, failure to achieve complete mydriasis in dark conditions, and sluggish PLRs; however, examination findings can be normal because signs may be transient. It is claimed that all cats with SPS test positive for FeLV, although this is not always the case at the initial examination. The lesion is proposed to result from virally induced neuritis involving cranial nerve 3. No treatment is possible, and the prognosis for long-term survival is poor.¹⁷⁴

Uveal Neoplasia

Few primary intraocular tumors have been documented in cats. These include iridociliary epithelial tumors,¹⁴⁵ melanoma,¹⁴³ feline ocular sarcoma (FOS),⁴⁹ and perhaps extramedullary plasmacytoma.¹²⁶ Ultimately, an eye with a suspected primary neoplastic process should be removed after a thorough physical examination and diagnostic workup are performed to rule out obvious systemic metastasis. However, both diffuse iris



FIGURE 29-48 Multiple, diffuse to coalescing areas of iridal hyperpigmentation, highly suggestive of diffuse iris melanoma. At this stage, where the only ocular change is iridal hyperpigmentation, determining if these lesions are due to benign melanosis or malignant melanoma is highly challenging. Referral is recommended. (Image courtesy UC Davis Veterinary Ophthalmology Service.)

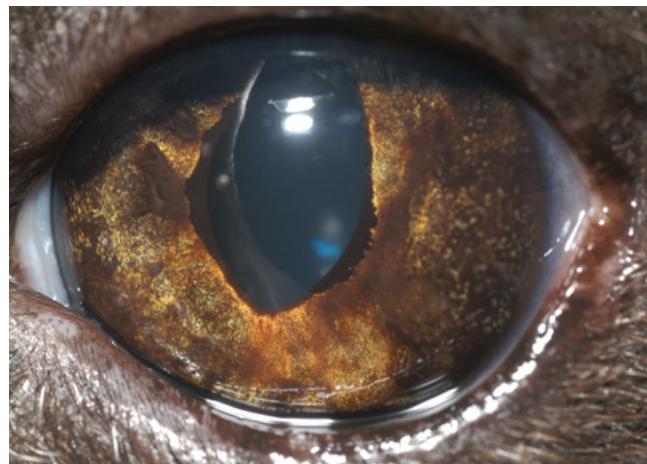


FIGURE 29-49 Diffuse iris melanoma. Although histology is ultimately required to confirm a diagnosis, the raised nature of the melanotic lesions and the dyscoria are highly suggestive of a malignant process. (Image courtesy UC Davis Veterinary Ophthalmology Service.)

melanoma (DIM) and FOS have special considerations that warrant specific discussion. They are considered to be the two most common and most significant primary intraocular tumors in cats. FOS is discussed in the upcoming section on diseases of the lens.

Iris Melanoma

DIM is the most common primary intraocular tumor in cats.¹³⁰ Unlike dogs with intraocular melanoma, which typically develop a discrete raised mass on their anterior iris face, cats most commonly demonstrate diffuse and insidious iridal melanosis with little or no projection above the iris surface (Figures 29-48 and 29-49). Clinical recognition in the early stages of disease can be difficult

because of the similar appearance of benign iris melanosis, a common aging change in cats.⁵⁰ Definitive diagnosis is further complicated by the difficulty of obtaining an iris biopsy, as well as the potential for benign areas of melanosis to later undergo transformation into malignant melanoma.^{56,130} Until better methods to differentiate these syndromes are discovered, practitioners and owners must sometimes elect to remove an eye that potentially has only benign melanosis or risk metastatic disease by delaying removal of an eye containing neoplastic cells.

No breed or gender predilection exists, but the average affected cat is middle-aged to older, presenting at an average age of 11 years.^{12,143} DIM usually first appears as a focal area of brown iridal hyperpigmentation.^{1,50,53,130} In the early stages distinguishing between DIM and benign iris melanosis is sometimes impossible.⁵⁰ The appearance of early DIM may remain static for months or years, but it is ultimately progressive, resulting in visible enlargement of iridal discoloration.^{1,56} Although DIM has no pathognomonic clinical features, thickening of the iris, hyperpigmentation extending beyond the anterior iris surface, and alterations of pupillary function increase the suspicion for melanoma.^{12,130} Without treatment, there is progressive infiltration of the anterior uvea and ocular drainage pathways, eventually resulting in uveitis and secondary glaucoma.^{53,130,200}

Diode laser photocoagulation, as reported for the treatment of focal areas of iridal hyperpigmentation in dogs,³³ has not been recommended for cats because of incomplete destruction and potentially dispersal of neoplastic cells and tissue. One reasonable management approach is to monitor areas of iris color change over time. Photographic documentation of such lesions is extremely helpful. However, because of the risk of metastatic disease, enucleation is ultimately the recommended treatment for enlarging iridal hyperpigmentation.^{53,56,98,130}

Latency times of up to a few years have been reported for metastatic disease, with documented metastatic rates as high as 62.5%.¹⁴³ The liver is the most common site for metastatic disease; however, lungs, regional lymph nodes, and other sites may also be affected.^{14,56,130,143} A thorough diagnostic workup is therefore recommended before surgery. Enucleation should be performed early in the disease course.⁹⁸ Although this may risk removal of eyes with subsequent histologically diagnosed benign iridal melanosis, this risk should be weighed against treatment delay, given the fact that survival time decreases with progressive tumor infiltration into the uvea.⁹⁸ Compared with a control group, equivalent survival times were achieved when enucleation was performed while the melanoma was confined to the iris stroma.^{56,98} In contrast, tumor infiltration into the ciliary body or drainage pathways, especially with development of glaucoma, strongly correlates with markedly

decreased survival time.^{56,98} Although increased metastatic rate is associated with high mitotic index and evidence of scleral invasion,^{56,98} cellular characteristics such as cell shape, nucleus to cytoplasm ratio, number of nucleoli, and melanin content do not appear to be of value for determining prognosis.⁵⁶

Amelanotic DIM has been described and presents similarly to the classical DIM except that the discoloration appears gray rather than brown.¹⁷ Clinical progression and potential for metastasis should be considered to be the same as for classical DIM. A second variant, atypical ocular melanoma, has also been reported. Unlike DIM, atypical ocular melanoma originates from multiple areas within the uveal tract and may have a more aggressive clinical course.⁸¹ Cats with atypical ocular melanoma had neoplastic infiltration of the entire uveal tract and sclera at the time of initial presentation,⁸¹ whereas in DIM neoplastic cells remain in the anterior uvea. At this time it is not clear if the advanced nature of disease at presentation was due to more aggressive behavior at the cellular level or a result of tumor arising from the posterior, rather than anterior, uvea.

Iris melanoma can be experimentally induced after anterior chamber inoculation with FeLV and feline sarcoma virus (FeSV), leading to speculation that these viruses may play a role in the development of DIM.^{4,5} An association has been documented between naturally arising DIM and FeLV/FeSV; however, this was seen in a minority of cases of one study only.¹⁷⁵ At this time there is no evidence that FeLV or FeSV is involved in the pathogenesis of DIM.³⁷

Secondary Intraocular Neoplasia

Any systemic neoplastic process has the potential to metastasize to the eye. Intraocular metastases secondary to SCC, pulmonary adenocarcinoma, hemangiosarcoma, and lymphosarcoma have been documented.^{32,34,68,99} Of these, lymphosarcoma is by far the most common²⁰⁴ (**Figure 29-50**). Because hematogenous spread appears to be the main route into the eye, metastatic intraocular neoplasia first affects the uvea.^{27,54,68} In cats choroidal metastases may occur more often than metastases to the anterior uvea.⁵⁴ A discrete uveal mass is possible; however, more diffuse metastases with signs of uveitis are more common.^{34,54} In fact, uveitis may be the first clinical sign of underlying systemic neoplasia.³⁴ For this reason systemic neoplasia should always be considered when evaluating a patient presenting with uveitis. Thorough physical examination and diagnostic investigation are essential, as for all other cases of uveitis. Ocular ultrasound is useful when intraocular structures are not easily seen on clinical examination. Although rare, intraocular metastasis of pulmonary adenocarcinoma warrants special mention because of its unique presentation in cats. In addition to the nonspecific signs of uveitis,



FIGURE 29-50 Dyscoria due to an iridal mass in the right eye of a cat. The histopathologic diagnosis was lymphosarcoma. (Image courtesy WCVM Ophthalmology service.)

this tumor causes characteristic wedge-shaped areas of fundic discoloration resulting from ischemic chorioretinopathy.²⁷

Treatment for metastatic intraocular neoplasia should include both nonspecific treatment for uveitis as well as treatment of the underlying neoplastic process. With tumors that are responsive to chemotherapy (in particular, lymphosarcoma), the reduction in uveitis tends to correlate well with response of the tumor at extraocular sites and is often dramatic. By contrast, ocular tissues do not tolerate irradiation, and so radiation-responsive intraocular tumors often necessitate enucleation as a palliative measure.

DISEASES OF THE LENS

Cataract and Lens Luxation

The most common diseases of the feline lens are cataract and lens luxation, both of which occur as primary syndromes much less frequently in cats than in dogs⁷⁰ (Figure 29-51). Rather, in cats both diseases tend to occur as a result of chronic uveitis; therefore patients should be thoroughly examined for signs of uveitis and its causes. Diabetic cats rarely develop cataracts, presumably because of decreased aldose reductase centrations in the feline lens compared with the canine lens.¹⁵⁹ Congenital cataracts have been reported in conjunction with such ocular abnormalities as eyelid agenesis, microphakia, and Chédiak-Higashi syndrome but are also considered to be uncommon.^{2,31,128} Primary lens luxation is believed to occur in cats, but peer-reviewed descriptions do not exist and a breed predilection has not been reported. Instead, lens dislocations in the cat occur secondary to other ocular disease, such as uveitis, glaucoma, and senile zonular degeneration¹⁶⁵ (Figure 29-52). Treatments for cataracts and lens luxation are similar to

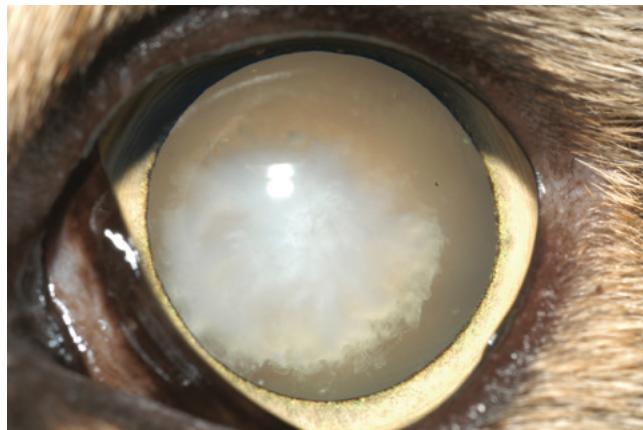


FIGURE 29-51 Incomplete cataract involving the lens nucleus. (Image courtesy UC Davis Veterinary Ophthalmology Service.)



FIGURE 29-52 Complete cataract and anterior lens luxation in the left eye of a cat. The lens is seen anterior to the iris. Note the superficial corneal vessels, which are commonly seen with lens luxation. Serology indicated that this cat was positive for feline immunodeficiency virus. Lens luxation in cats is associated with uveitis, cataract, and glaucoma and should initiate referral. If the eye is irreversibly blind, enucleation with histopathology should be performed. (Image courtesy UC Davis Veterinary Ophthalmology Service.)

those for dogs and require referral to a veterinary ophthalmologist.

Feline Ocular Sarcoma

FOS is an aggressive ocular tumor resulting in tumor-related death of the majority of affected cats. Because of this, many ophthalmologists strongly recommend enucleation of blind and painful feline globes, regardless of cause, to prevent subsequent malignant transformation to FOS. For these reasons, this tumor warrants special mention here.

Most cats diagnosed with primary ocular sarcoma have a known history of trauma to the affected eye



FIGURE 29-53 An intraocular mass has caused glaucoma, buphthalmos, and rupture of the right eye of this cat. Histopathology identified this tumor to be feline ocular sarcoma that had migrated into the orbit. The orbit was exenterated as a palliative measure, but the owner was warned to expect tumor recurrence and death as a result of local invasion and recurrence. (Image courtesy UC Davis Veterinary Ophthalmology Service.)

several years prior.* For this reason FOS is sometimes referred to as *posttraumatic intraocular sarcoma*. Chronic uveitis and intraocular injections have also been reported as precursors to the development of FOS.¹⁸⁰ Quite often, the affected eye has been blind for several years, and the reason for presentation is a change in the appearance of the eye.^{52,77} Cats rarely show overt signs of discomfort at the time of presentation.^{49,51} Clinical examination often shows an opaque cornea.^{49,52,77} An anterior chamber mass can sometimes be appreciated, but intraocular structures are often difficult to discern^{52,77,180} (Figure 29-53). Ultrasound may be useful for confirmation of an intraocular mass when clinical examination is limited. The affected globe may also have an abnormal shape; quite frequently, the globe is phthisical or buphthalmic.^{9,52}

Histologically, there is obliteration of normal architecture of globes from cats with FOS.[†] Neoplastic cells tend to invade the sclera, preferentially exiting the globe at the posterior pole/optic nerve and the limbus.^{49,52,146} Severe pathology of the lens, particularly lens rupture, has been found in almost all cases.^{49,52,146} Although the origin of FOS was unknown for years, it is now accepted that the tumor arises from lens epithelial cells.^{26,55,209} It is believed that the anterior epithelium of the lens undergoes a malignant transformation in response to trauma in a manner similar to the development of fibrosarcoma at sites of vaccination.²⁰⁹ FeLV and FeSV are not believed to play a role in the pathogenesis of FOS.³⁷

Given the relationship between FOS and lens rupture, cats with perforating lens injury should be referred for

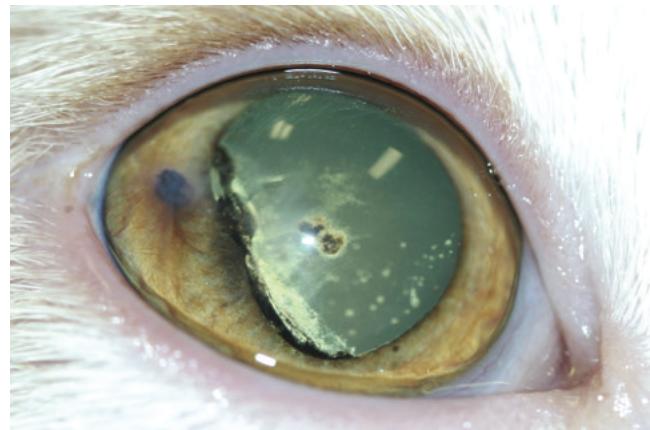


FIGURE 29-54 Clinical signs of globe perforation. Note the anterior synechiae at the 9 o'clock position, indicating corneal perforation. Dyscoria is a result of posterior synechiae along the lateral pupillary margin, consistent with uveitis. The presence of melanin on the anterior lens capsule and within the lens as well as early cataract are highly suggestive of lens capsule perforation. This cat is at risk of developing of developing feline ocular sarcoma. (Image courtesy WCVM Ophthalmology Service.)

treatment immediately and followed up rigorously for life. Treatment options include medical management, phacoemulsification, or enucleation. A small lens capsule perforation may self-seal and respond to medical management for the associated uveitis; however, the liberation of lens material into the eye necessitates long-term follow-up for these patients. Larger lens capsule ruptures require either phacoemulsification to remove free lens material from the eye or enucleation (Figure 29-54). Development of FOS has been reported in cats that previously underwent surgical lens extraction.⁵⁵ Although development of FOS has not been reported after phacoemulsification specifically, its development is theoretically possible, thus necessitating long-term follow-up.

Likewise, cats with a known history of ocular trauma should also be monitored closely because of the potential for FOS. Clinical suspicion of an intraocular mass or observation of a phthisical globe in a cat, especially one known to have undergone ocular trauma, should prompt the clinician to recommend enucleation after diagnostic investigation for metastatic disease. Although it is not known if early enucleation decreases the mortality rate, treatment should not be delayed because of the aggressive nature of the disease. In the vast majority of reported cases, patients died from tumor-related disease within months of enucleation as a result of local invasion of the orbit, extension along the optic nerve into the central nervous system, or metastatic disease.^{9,49,52,77,146} At this time, there are no reports of adjunctive treatments, such as radiation or chemotherapy, for the management of FOS.

*References 9, 49, 52, 55, 77, 146.

†References 9, 52, 53, 77, 146, 180.

GLAUCOMA

It is essential to measure IOP during every ophthalmic examination to avoid overlooking a diagnosis of glaucoma, especially because glaucoma can be a very subtle and insidious disease in cats. In contrast to dogs, glaucoma occurs infrequently in the cat, and secondary glaucoma is far more common than primary glaucoma.^{18,160,200} In addition, the rare aqueous humor misdirection syndrome (AHMS) arises naturally in cats but has not yet been reported in dogs. Although any animal can be affected, the typical feline patient with glaucoma is middle-aged or older.^{18,41,78,160,190}

Because clinical signs of feline glaucoma tend to develop gradually rather than acutely, irreversible blindness is frequently present by the time of presentation for ophthalmic evaluation.^{18,160} Cats often do not develop obvious corneal edema or overtly red eyes in the same manner that dogs do. Instead, the most common findings on initial presentation include absent menace response, absent PLR, and buphthalmos.¹⁸

A diagnosis of glaucoma is made on the basis of IOP measurements greater than 25 to 30 mm Hg combined with evidence of ocular abnormalities (Figure 29-55). A single elevated IOP reading, in the absence of clinical signs, should not be used to make a diagnosis of glaucoma. Tonometry technique, excessive neck pressure, diurnal variation, and fractious patients can all contribute to elevated readings.^{45,102} Eyes should be re-evaluated if IOP is greater than 25 mm Hg or there is a greater than 12 mm Hg difference between eyes.¹⁰² As mentioned previously in this chapter, the neuro-ophthalmic examination will be abnormal. Retinal degeneration may be present if disease is advanced. Optic disc cupping, a feature of canine glaucoma, is often difficult to appreciate in the cat because of the unmyelinated nature of the feline optic disc. Because the vast majority of feline glaucoma is secondary to anterior uveitis and intraocular neoplasia,^{18,200} abnormalities such as aqueous flare, cataract, intraocular mass, or iris discoloration are often also present. Primary glaucoma is possible if such clinical findings are absent, although this condition is rare.^{18,96,200} Referral for gonioscopy is necessary to make the diagnosis of primary glaucoma.

AHMS is a rare condition arising from misdirection of aqueous humor into the vitreous cavity instead of into the posterior then anterior chambers and out through the iridocorneal angle. The pathogenesis for this condition is not well understood. It is hypothesized that a defect of the anterior hyaloid membrane acts as a one-way valve, allowing aqueous humor to enter, but not exit, the vitreous cavity. As pressure builds up within the vitreous, the lens and anterior uvea are anteriorly displaced. As a consequence of this shift, there is increased iris-lens contact, producing mydriasis and

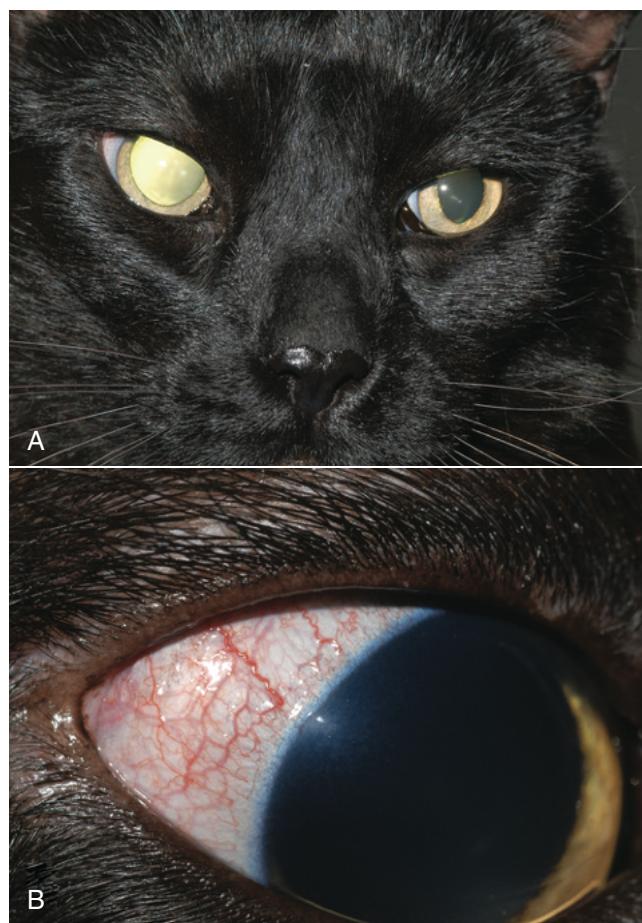


FIGURE 29-55 **A**, Uveitis and marked secondary glaucoma in the right eye of a cat. Despite the intraocular pressure in the right eye being 73 mm Hg, the signs of discomfort, mydriasis, and visible ophthalmic abnormalities are minimal. Signs to look for in this cat are mydriasis, subtle corneal edema, and episcleral injection, none of which can be associated with conjunctivitis alone. Note too that buphthalmos is evident only when the entire head is viewed and symmetry of the globes is assessed. **B**, Finally, note the difference in tapetal reflection between the eyes. This subtle change is sometimes the most obvious sign of ophthalmic disease, usually indicates serious intraocular disease, and should therefore never be ignored. (Image courtesy UC Davis Veterinary Ophthalmology Service.)

reduced flow of aqueous humor to the anterior chamber as a result of “pupillary block,” which further exacerbates ocular hypertension. Patients with AHMS present with similar neuro-ophthalmic examination abnormalities as cats with other forms of glaucoma.⁴¹ Ophthalmic findings required for diagnosis of AHMS include intact lens zonules, juxtaposition of the ciliary body, consolidated anterior vitreous face, narrow approach to the iridocorneal angle, and a uniformly shallow anterior chamber.⁴¹ Compared with the other examination findings, a uniformly narrow anterior chamber is more easily recognized in a general practice setting and is the characteristic sign of AHMS⁴¹ (Figure 29-56). The uniform narrowing helps differentiate between AHMS and glaucoma due to other causes. In other forms of glaucoma,

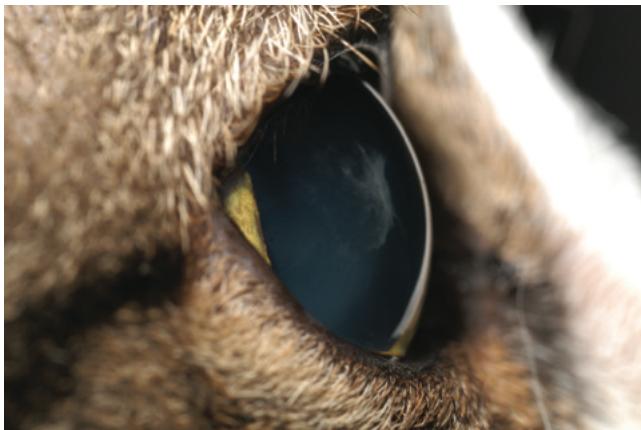


FIGURE 29-56 A narrow anterior chamber is characteristic of aqueous humor misdirection syndrome. The slit beam of the direct ophthalmoscope helps identify the narrowed distance between the bright reflections off the cornea and the anterior lens capsule. In this cat the presence of an anterior cortical cataract also helps demonstrate forward displacement of the lens. This cat's intraocular pressure was 40 mm Hg but responded well to phacoemulsification and anterior vitrectomy. (Image courtesy UC Davis Veterinary Ophthalmology Service.)

buphthalmos causes deepening of the anterior chamber. With iris bombé, the peripheral anterior chamber narrows but the central anterior chamber remains deep. The IOP in patients with AHMS is elevated, sometimes markedly so. However, unlike most other forms of glaucoma wherein pharmacologic mydriasis causes a further elevation in IOP, the IOP of some patients with AHMS may be reduced by pupil dilation because of a reduction in pupillary block. AHMS may occur unilaterally at first but often becomes bilateral.

Regardless of cause, treatment of glaucoma should always address the underlying disease if identified. Because many of these primary conditions are intractable, feline glaucoma is usually advanced at presentation, and few antiglaucoma medications are effective in the cat, feline glaucoma is particularly challenging to treat. Medical control of IOP is achieved in 21% to 58% of treated eyes.^{18,160} The carbonic anhydrase inhibitor dorzolamide appears to be one of the most useful antiglaucoma drugs for cats. Topical carbonic anhydrase inhibitor therapy is preferred over systemic therapy because of the susceptibility of cats to adverse systemic effects. Dorzolamide is effective for lowering IOP when applied twice daily; however, 4 or 5 days of therapy are needed to reach a reliable decrease.¹⁵⁴ Dorzolamide may also be administered in combination with timolol twice daily, although the additional benefit of timolol appears to be marginal.⁴⁶ The carbonic anhydrase inhibitor brinzolamide is ineffective in cats,⁷⁴ as are the prostaglandin analogs bimatoprost, unoprostone, and latanoprost, which are quite successful in dogs.^{10,183} The hypotensive effect of travoprost in cats is not known. Although prostaglandin analogs do not effectively decrease IOP, they

do induce miosis in cats as they do in dogs. Pilocarpine also has hypotensive effects in cats²⁰¹; however, on account of its propensity to induce uveitis,¹⁰¹ as well as systemic side effects, its use is generally discouraged.⁴¹

Mydratics are generally contraindicated in glaucoma. Although atropine therapy is a vital component of the treatment of aqueous misdirection in humans, beneficial effects of mydriatic therapy for AHMS have not been demonstrated. In one study application of tropicamide was followed by an increase in IOP.⁴¹ Use of miotics such as pilocarpine and timolol may worsen glaucoma associated with AHMS and should therefore be avoided.

Unfortunately, cyclodestructive procedures appear to provide limited benefit in cats, perhaps because they exacerbate or fail to address the underlying inflammation present in most cases.^{78,160} A combination of lensectomy by phacoemulsification in association with posterior capsulotomy and anterior vitrectomy appears to permit redirection of aqueous from the vitreous and correct pupillary block and narrowing of the anterior chamber and holds promise for the control of IOP in AHMS.⁴¹ When medical and surgical interventions fail to control IOP, enucleation should be performed for all blind globes that appear to be causing pain.

CHORIORETINAL DISEASE

Hypertensive Chorioretinopathy

Because it is an end organ, the eye is susceptible to damage resulting from systemic hypertension. Specifically, persistently elevated blood pressure causes pathology to the retina, choroid, and optic nerve. *Hypertensive retinopathy* is a blanket term used to describe all the ocular lesions arising from damage to these structures. Incidence of ophthalmic lesions in hypertensive cats has been estimated to be as high as 60% to 77%.^{57,176}

A short review of anatomy may assist in understanding pathogenesis (Figure 29-57). Briefly, vessels are located in only the innermost layers of the feline retina. The outermost retina is highly metabolically active but avascular. The choriocapillaris is a network of capillaries supplying choroidal blood to the outer retina. Although the choroidal vasculature is permeable to most substances, the blood–ocular barrier prevents entry of solutes and fluid into the retina from the choroid and systemic circulation. Exclusion of substances from the retina assists in maintaining retinal attachment.

Hypertensive ocular lesions ultimately arise from ischemic injury to vessel walls. In the face of chronically elevated blood pressure, autoregulatory mechanisms within the retina become deranged and there is leakage of angiotensin II into both the extracellular choroidal space and optic nerve. Consequently, there is vasoconstriction of the retinal vessels, choriocapillaris, and

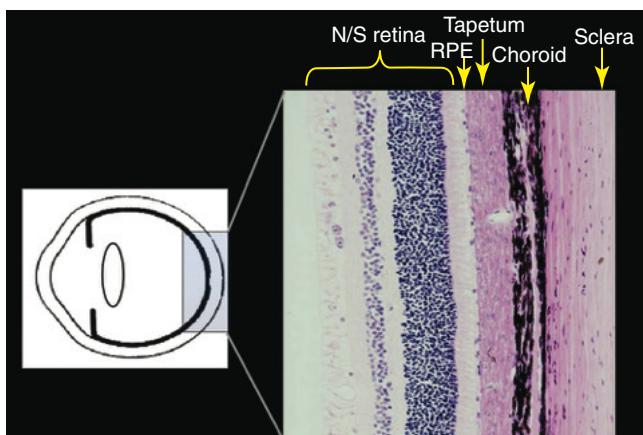


FIGURE 29-57 Normal anatomy of the feline fundus, including the sclera, choroid proper, tapetum (which is actually part of the choroid), retinal pigment epithelium, and neurosensory retina. The blood-retinal barrier normally prevents solutes and fluid from entering the potential space between the retinal pigmented epithelium and the neurosensory retina. Leakage of substances from the choroidal vasculature into this potential space results in retinal detachment.

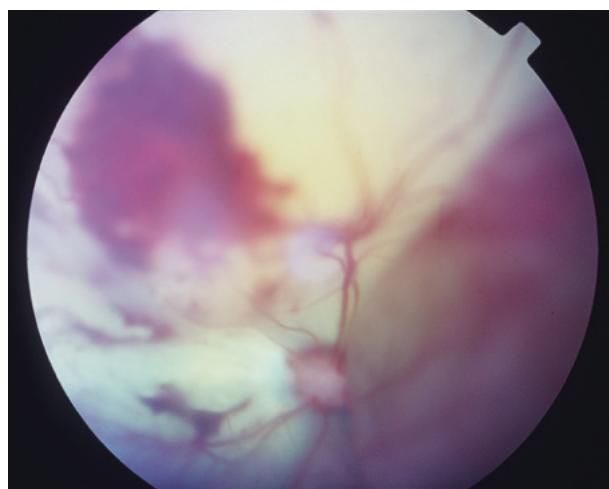


FIGURE 29-59 Complete retinal detachment and multiple retinal hemorrhages are characteristic findings in cats with systemic hypertension, with vision loss being the most frequent reason for presentation to a veterinarian. (Image courtesy UC Davis Veterinary Ophthalmology Service.)



FIGURE 29-58 Evidence of retinal detachment can often be seen during retroillumination, before performing the fundic examination. In this patient complete, bilateral retinal detachment has resulted in mydriasis, and the retinal vessels can be seen in focus immediately posterior to the lens. (Image courtesy WCVM Ophthalmology Service.)

vessels supplying the optic nerve. The ischemic damage resulting from prolonged vasoconstriction causes vessel wall necrosis and leakage of fluid from these vessels. Clinically, these changes are manifested as retinal edema, retinal hemorrhage, and serous retinal detachment (Figures 29-58 and 29-59). Papilledema, seen in other species, has not been reported in cats.³⁵

The magnitude and duration of blood pressure elevation required to induce ocular lesions is not known. In one study hypertensive ocular lesions were associated with systolic blood pressure measurements above 168 mm Hg¹⁶⁴; however, the majority of studies show the systolic blood pressure in most cats with hypertension-induced ocular lesions to be above 200 mm Hg.^{107,129,163,191}

Ocular lesions may be more likely to develop after pronounced hypertension of prolonged duration, and hypertensive cats with ocular lesions have significantly higher blood pressure than hypertensive cats without ocular lesions.^{29,129} For cats with ocular lesions, no significant difference was found between systolic blood pressure of cats presenting with retinal detachment (and acute blindness) compared with that of cats that did not present with acute blindness.⁵⁷ Hypertensive cats with ocular lesions are likely to have more severe cardiac pathology than hypertensive cats without ocular lesions.²⁹

The typical cat with systemic hypertension is older than 10 years of age.^{107,129,164,176} Gender predilections have been suggested but not confirmed.^{107,164} The most common reason for presentation is acute blindness.^{57,107,163} In fact, in many patients ocular disease is the first indicator of systemic disease.¹⁸⁶ Serous retinal detachment, usually accompanied by retinal hemorrhage, is the most common examination finding, supporting the notion that choroidal pathology accounts for the majority of ocular lesions in cats.¹¹³ Other common examination findings include resting mydriasis, slow to absent PLRs, hyphema, iris hemorrhage, retinal edema, and retinal vessel tortuosity (see Figure 29-59).

Systemic hypertension should be considered in all cats presenting with intraocular hemorrhage or retinal detachment. A thorough diagnostic work up is essential. Diagnosis of hypertensive retinopathy is confirmed when systolic blood pressure measurements exceed 160 to 170 mm Hg and potential causes of posterior uveitis have been excluded. Chronic renal failure is the most common underlying disease associated with systemic hypertension.^{107,113,129,176} Primary hypertension and

hypertension associated with hyperthyroidism, diabetes mellitus, and hyperaldosteronism should also be considered, but these occur less frequently.^{113,176,193}

Antiinflammatory treatment should be considered in cats with anterior segment disease. Corticosteroids are preferred over NSAIDs, which can exacerbate bleeding. To prevent potential systemic effects of corticosteroid therapy, these should be administered topically.¹⁵⁰ Ultimately, the most important components of treating hypertensive retinopathy are control of blood pressure and treatment of any underlying disease. Medical control of blood pressure will allow for improvement of hypertensive ocular lesions in the majority of patients.^{57,107,113,129,191}

In recent years the calcium channel blocker amlodipine besylate has emerged as a successful treatment for systemic hypertension and related ocular lesions. At doses ranging from 0.625 to 1.25 mg orally, every 12 to 24 hours, amlodipine may be more effective than other classes of drugs for reduction of intraocular hemorrhage and retinal edema and reattachment of serous retinal detachments.¹¹³ For further discussion about the treatment of systemic hypertension, please see Chapter 20.

Prognosis for return to vision depends on both duration and severity of ocular lesions. Mild retinal edema and hemorrhage, without retinal detachment, may completely resolve with successful control of blood pressure.¹¹³ Prognosis becomes guarded if retinal detachment is present. Histologically, retinal degeneration is visible within 1 hour of detachment, and extensive photoreceptor damage occurs within 2 weeks.⁶⁰ Therefore, although retinal reattachment is possible with medical management, many cats remain blind or visually impaired due to the retina becoming irreversibly degenerated while detached.^{113,129} Prognosis is also guarded in cats with intraocular hemorrhage, particularly hyphema, because of the increased potential of secondary glaucoma.¹⁶³

Enrofloxacin Toxicity

Accounts of blindness in association with enrofloxacin administration in cats were rare until almost a decade after Baytril was first approved by the Food and Drug Administration for use in dogs and cats; these reports appeared to coincide with a labeling change that allowed higher doses to be given to cats. Subsequent toxicologic studies have confirmed that retinal degeneration is dose related rather than idiosyncratic and led to a maximum recommended oral dose of 5 mg/kg per day for cats. Blindness of rapid onset, sometimes as soon as 4 days into treatment, and mydriasis are the typical signs noted by owners. Clinical findings included absent menace responses, sluggish to absent PLRs, variable degrees of tapetal hyperreflectivity, and retinal vascular attenuation⁶⁴ (Figure 29-60). Electroretinography has confirmed reduction in retinal function as early as 24 hours after initiation of therapy at 50 mg/kg per day.⁶³ No common

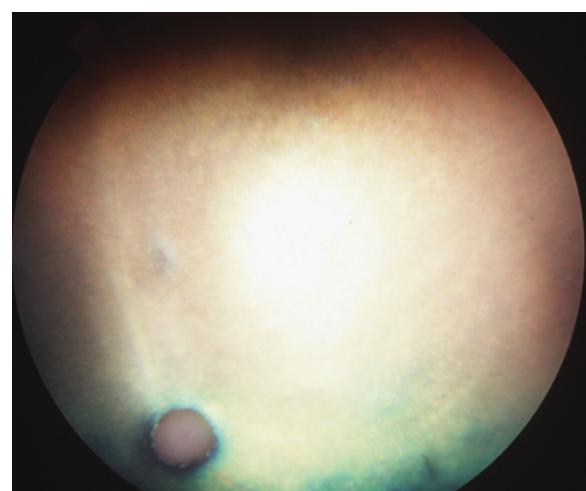


FIGURE 29-60 Tapetal hyperreflectivity and marked retinal vascular attenuation are indicators of advanced retinal degeneration in this cat. Although these signs are pathognomonic for retinal degeneration, they do not permit definitive diagnosis of a cause, which may include taurine deficiency, progressive retinal atrophy, enrofloxacin toxicity, glaucoma, and severe and prolonged previous retinal detachment from any cause. Reaching an etiologic diagnosis requires a complete history and ophthalmic and general physical examination. (Image courtesy UC Davis Veterinary Ophthalmology Service.)

signalment, duration of therapy, or underlying medical condition for which enrofloxacin was prescribed has been noted.⁶⁴ In one study oral enrofloxacin doses ranged from 4.6 mg/kg once daily to 27 mg/kg twice daily.⁶⁴ After cessation of treatment, a limited amount of vision was preserved or regained in four cats. At higher doses (50 mg/kg daily), some cats also demonstrate neurologic signs.⁶³ Although the exact mechanism by which enrofloxacin exerts its effects is not known, hypertensive retinopathy does not appear to be a contributing cause.⁶³

Although a dose of 5 mg/kg daily is in accordance with the manufacturer's recommendations, retinal degeneration may still be possible at this dose.⁶⁴ Several factors, such as large drug doses or plasma drug concentrations, rapid intravenous infusion, prolonged treatment, and advanced patient age, may increase the risk of toxicity.¹⁹⁹ In particular, cats older than 12 years are more likely to experience adverse effects than are cats younger than 9 years, perhaps because of a higher incidence of hepatic or renal disease causing impaired drug clearance.¹⁹⁹ Exposure to ultraviolet A light during treatment, drug interactions, and drug accumulation (secondary to impaired metabolism or clearance) may also increase the likelihood of retinal degeneration.¹⁹⁹

A study conducted in 2- to 8-week-old kittens found that oral administration of enrofloxacin at a dose of 5 mg/kg daily failed to achieve therapeutic plasma concentrations but that parenteral administration was successful in achieving target plasma concentrations.¹⁶⁹ This study also suggested that doses higher than 5 mg/kg per day were necessary. This was attributed to the

differences in volume of distribution and drug clearance in kittens compared with adult cats. No ocular lesions were found in this study. It is worth noting, however, that at this time the manufacturer's label indicates that enrofloxacin should not be used in kittens younger than 12 weeks of age and that parenteral administration is not licensed in cats.

Because there is no treatment for enrofloxacin toxicity and the vast majority of cats remain permanently blind, practitioners must exercise caution when dispensing fluoroquinolones to cats. Selection of a fluoroquinolone should be made only after culture and sensitivity testing confirms that alternative antibiotics are not suitable. A complete ophthalmic examination, including a fundic examination, should be performed before and after treatment. Owners should be warned of the potential for adverse effects. Should signs of mydriasis, altered PLRs, or visual impairment be noted, treatment should be stopped immediately and the cat brought in for evaluation. Enrofloxacin oral doses in cats should never exceed a maximum of 5 mg/kg per day, and duration should not exceed the manufacturer's recommendation of 2 to 3 days beyond cessation of clinical signs. Caution is especially warranted in patients of advanced age or those with concurrent medical conditions that may impair drug metabolism or elimination. Enrofloxacin is not approved for parenteral use in cats; therefore off-label use of injectable enrofloxacin should be avoided.

Taurine-Deficient Retinopathy

In the 1970s several authors demonstrated that cats fed taurine-deficient diets showed funduscopic evidence of retinal degeneration and decreased retinal function. In the following years, naturally arising cases of taurine-deficient retinopathy were documented. In particular, this syndrome was recognized in cats fed dog food, which tends to have minimal taurine concentrations.³ Since then, the practice of feeding dog food to cats has largely stopped, and because most cat foods contain adequate levels of taurine,¹⁷⁸ retinopathy secondary to dietary taurine deficiency is relatively rare. However, with the increased interest in homemade pet diets, the potential for resurgence of this condition remains. Recognition of this condition is important not only for prevention of blindness but also for prevention of dilated cardiomyopathy; another disease associated with taurine deficiency.¹⁴⁸

Because the half-life of retinal taurine is protracted, it may take several months of dietary deficiency for retinal degeneration to occur.^{167,168} Early signs of taurine-deficient retinopathy are similar to those of early progressive retinal atrophy. The first abnormality is a granular appearance to the area centralis, followed by the development of hyperreflectivity¹⁶⁷ (Figures 29-61 and 29-62). If taurine deficiency is corrected, this is the



FIGURE 29-61 A focal, elliptical area of tapetal hyperreflectivity dorsolateral to the optic disc is one of the early signs of taurine-deficient retinopathy. This would be considered stage 2 degeneration in a 5-stage scaling system. (Image courtesy UC Davis Veterinary Ophthalmology Service.)

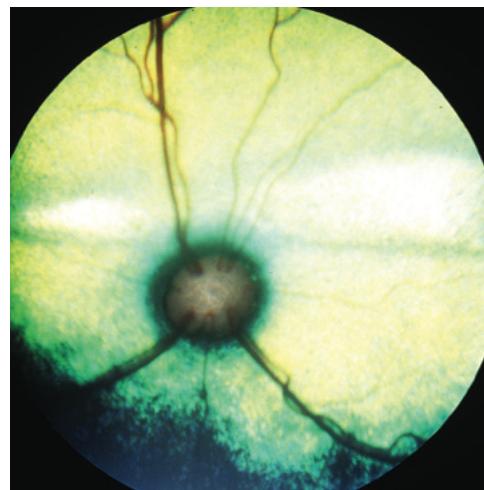


FIGURE 29-62 Prolonged taurine deficiency has led to stage 3 retinal degeneration with hyperreflective regions dorsolateral and dorsomedial to the optic disc. Continued dietary deficiency will lead to complete retinal degeneration (stage 5). (Image courtesy UC Davis Veterinary Ophthalmology Service.)

limit of the fundic changes; however, with continued dietary deficiency, extension of degeneration to the midperipheral retina is possible. Should the clinician suspect dietary taurine deficiency in a cat with retinal degeneration, confirmation of low plasma taurine is warranted. If plasma taurine is demonstrated to be low, dietary supplementation is required. With supplementation partial reversal of retinal degeneration is possible in cats with mild to moderate stages of disease, but prevention of further progression is the major therapeutic goal.^{85,86}

Progressive Retinal Atrophy

Inherited retinal degeneration or dysplasia (often grouped together as progressive retinal atrophy) occurs in cats, particularly the Abyssinian and Persian breeds.^{39,134,153} An autosomal recessive, early onset retinal photoreceptor dysplasia is seen in Persian cats and as an autosomal dominant condition in Abyssinian cats as early as 2 to 3 weeks of age.^{39,153} In the Persian the earliest ocular abnormalities are subtly diminished PLRs at 2 weeks of age, progressing to minimal PLRs and resting mydriasis by 17 weeks of age. Funduscopic signs of retinal degeneration, such as retinal vascular attenuation, tapetal hyperreflectivity, and optic nerve head darkening, are minimal at 4 to 5 weeks but marked by 17 weeks of age. In the Abyssinian early onset retinal degeneration is a result of an autosomal dominant photoreceptor dysplasia.³⁹ As with the Persian, abnormal PLRs are first noted at approximately 2 to 3 weeks of age, but the terminal stage of disease is not reached until approximately 1 year of age.³⁹ Nystagmus accompanies this form of retinal degeneration.³⁹ A later onset autosomal recessive retinal degeneration also occurs in the Abyssinian. Early ophthalmoscopic evidence of retinal degeneration is visible at approximately 1.5 to 2 years of age, in the form of a gray discoloration of the peripapillary fundus and the area centralis in particular.¹³⁴ Disease progression is much slower than for early onset disease, with terminal stages being reached at approximately 3.5 to 4 years of age.¹³⁴ No treatment is possible for any of these conditions. Affected animals should not be bred.

Resources for Cat Owners

<http://www.petplace.com/cats/living-with-a-blind-cat/page1.aspx>

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