Feline Uveitis

Angelie K. Shukla, BSc, DVM
Chantale L. Pinard, DVM, MSc, DACVO
University of Guelph

Abstract: Uveitis is defined as inflammation of the vascular tunic of the eye, the uvea. Although inflammation can affect the entire uvea, clinical signs may present predominantly in either the anterior or the posterior chamber. Anterior uveitis lesions may affect the cornea, anterior chamber, iris, and lens, whereas posterior uveitis anomalies may be located in the vitreous and fundus. Uveal inflammation is often a sentinel finding indicative of underlying systemic pathology. Causes of feline uveitis are numerous, with infectious disease being the most common. Clinical signs are often nonspecific, and recurrence of disease is common, posing the challenges of accurate diagnosis and appropriate treatment.

Uveitis is a common form of feline ocular disease that may result in permanent blindness if not identified and treated properly1–3 (BOX 1). Potential causes of uveitis in cats are numerous; ocular signs typically indicate an underlying systemic disease process. An underlying or associated systemic disease was linked to up to 70% of cases of feline uveitis in one report.4

Etiologies of feline uveitis can be broadly categorized into infectious, immune-mediated, neoplastic, traumatic, and idiopathic. Of identified causes, infectious disease is by far the most common.5 I (C. P.) have also found trauma to have a significant causal relationship compared with idiopathic and infectious causes when evaluating etiologic risk factors of feline uveitis compared with a control population. However, in as many as 62% to 70% of cases, no underlying cause is identified.4,6

Ocular effects of uveitis can be severe and may have a number of devastating sequelae, such as iris bombé with secondary glaucoma, lens subluxation/luxation, cataract formation, and blindness.3,7,8 Uveitis has been reported to be the leading cause of feline glaucoma.9

Anatomy

The uvea is the vascular tunic of the eye. It is located deep to the sclera and sandwiched between the retina and sclera in the posterior segment of the eye (FIGURE 1). It is composed of three discrete parts: (1) the iris and (2) the ciliary body, making up the anterior uvea, and (3) the choroid, making up the posterior uvea. The iris is composed of sphincter and dilator muscles that control the amount of light entering the eye. The ciliary body contains epithelial cells that produce aqueous humor (AH). It is also the site of the blood-aqueous barrier (BAB), which regulates the entry of molecules into the eye. The BAB is composed of an endothelial barrier and an epithelial barrier, which prevent proteins and inflammatory cells from entering the AH; this results in the protein concentration of the AH being much lower than that of plasma. The choroid, continuous with the ciliary body, provides a vascular supply to the retina, which is located on its inner surface. The reflective tapetum covers the choroid in the dorsal aspect of the globe.

Box 1. Types of Uveitis

- Anterior uveitis or iridocyclitis: inflammation of the iris and ciliary body
- Posterior uveitis or choroiditis: inflammation of the choroid
- Panuveitis: inflammation of both anterior and posterior chambers of the eye

Figure 1. Anatomy of the eye. The uveal tract is composed of the iris and ciliary body in the anterior segment and of the choroid (between retina and sclera) in the posterior segment of the eye. The tapetum covers the inner aspect of the choroid in the dorsal aspect of the posterior segment of the eye.
**Pathophysiology**

Although inciting causes of uveitis are numerous, the sequence of events that occur as a result of insult to the uvea is similar regardless of etiology. Following uveal damage, the BAB is disrupted and prostaglandins and leukotrienes (which mediate vasodilation and increase vascular permeability) leak into the eye.10 The breakdown of the BAB also allows the entry of proteins, other inflammatory mediators (cytokines), and inflammatory cells into the eye.10 These events lead to the clinical signs associated with uveitis.

**Clinical Signs**

The clinical presentation of uveitis is variable and usually nonspecific to etiology. The hallmark signs of ocular pain, namely blepharospasm, enophthalmos, photophobia, and epiphora, are common.1,7,11 Additionally, signs of anterior uveitis can include one or more of the following: conjunctival hyperemia (chronic or recurrent), corneal edema (perilimbal, focal, or diffuse), aqueous flare (inflammatory cells and/or protein deposits in suspension within the anterior chamber; **Figure 2**), hyphema (**Figure 3**), hypopyon, keratic precipitates (inflammatory cells and/or protein deposits on the inner aspect of the corneal endothelium), miosis (caused by prostaglandin release), iris thickening (iritis), iris color change (in chronic cases, due to proliferation of melanocytes), and posterior synechiae (adherence of pupillary margin to anterior lens capsule).1,7,11,12 Aqueous flare and keratic precipitates can be challenging to detect even for experienced practitioners; although direct ophthalmoscopy can be used, slit lamp biomicroscopy has superior optics to visualize these lesions.

Low intraocular pressure (IOP) is a common feature of uveitis. An IOP <10 mm Hg or a difference in IOP of 10 mm Hg between the affected eye and the normal eye is suggestive of uveitis. A low IOP is expected because inflammation of the ciliary body results in decreased AH production13 as well as an increase in AH outflow through the uveoscleral route in response to prostaglandins.14 However, the reliability of finding a low IOP depends on the presence of concurrent secondary ocular pathologies, specifically glaucoma.4 Glaucoma can be caused by buildup of inflammatory debris and cells in the iridocorneal angle, leading to impaired AH flow within the eye, or by mechanical disruption of AH flow through the pupil from development of posterior synechiae.3,15

Signs of posterior uveitis include cellular infiltrate in the vitreal body (vitritis), chorioretinal inflammation (focal or generalized hemorrhage, exudate or transudate leading to retinal detachment, subretinal granulomas; **Figure 4**), and, in severe cases, blindness.1,2,12

**Diagnostic Tests**

A minimum ophthalmic database includes the following:

- A thorough history
- A neuro-ophthalmic examination that assesses the following:
  - **Dazzle reflex**: A bright light is shone into each eye; the normal response is a blink
E3

—Menace response: An abrupt gesture is made toward each eye; the normal response is a blink
—Pupillary light reflexes: A bright light is shone into each eye; the normal response is for the illuminated pupil to constrict (direct reflex) and the contralateral pupil to constrict equally (indirect reflex)
—Palpebral reflexes: The medial and lateral canthi of the eye are touched; the normal response is a blink
• A Schirmer tear test
• Fluorescein staining
• Tonometry
• Examination of all ocular structures with direct and indirect ophthalmoscopy

As long as the IOP is <25 mm Hg, dilation of the pupil with 1% tropicamide is recommended to best visualize the fundus. If the IOP is ≥25 mm Hg, dilation of the pupil is not recommended, as mydriasis may cause glaucoma due to compression of the iridocorneal angle. In most cases, it is advisable to build a minimum systemic database consisting of a comprehensive physical examination, a complete blood count (CBC), a serum biochemistry panel, and urinalysis. More advanced and specific testing is recommended depending on the suspected underlying etiology, including serologic titer measurement (on blood, aqueous, or vitreal samples), thoracic radiography, and abdominal ultrasonography (TABLE 1).

Etiology
Specific etiologies of feline uveitis are numerous and may be broadly categorized into endogenous (immune mediated or neoplastic), exogenous (infectious or traumatic), and idiopathic.

Infectious Causes
Feline Immunodeficiency Virus
FIV, a retrovirus, exists endemically in all domestic feline populations. The disease is typically contracted via bite wounds; therefore, outdoor male cats are more likely to become infected. Infected individuals may never develop disease or may not develop it until 4 to 6 years of age or older. Viral damage commonly causes concurrent conjunctivitis and anterior uveitis. Other ocular signs may include chorioretinitis secondary to another infectious agent, glaucoma, lens luxation, and pars planitis (inflammation at the junction of the ciliary body and retina). The prognosis varies depending on stage and expression of immunodeficiency. All positive FIV ELISA results should be confirmed using a more specific test (e.g., Western blot, immunofluorescent antibody [IFA], virus isolation [VI]). Cats should not be euthanized based on a positive test result, as individuals may remain asymptomatic for years after diagnosis.

Euthanasia is not recommended for cats with clinical signs of FIV if the signs can be medically managed and pain control established. However, if severe uveitis with glaucoma is unresponsive to medication, enucleation should be performed. Clients should be aware that FIV-positive cats are more likely to develop infections and may be prone to immune-mediated diseases and neoplasia.

Feline Leukemia Virus
Feline leukemia virus (FeLV), another retrovirus, may infect cats through mutual grooming and sharing of water or food bowls, but it is most often transmitted via saliva into bite wounds. Recent research suggests that unvaccinated cats exposed to the virus remain infected for life, previously, it was believed that up to two-thirds of individuals were eventually able to clear the infection. Cats may be able to revert to an aviremic state (also termed regressive infection) in which no antigen is detectable in blood, but FeLV proviral DNA may still be detected by a polymerase chain reaction (PCR) assay. Alternatively, cats may develop progressive infection due to an insufficient immune response to the virus. These cats are expected to develop clinical disease, with systemic effects expected to be fatal within a few years. Hence, clinical signs become apparent at a younger age than in cats infected with FIV. The manifestation of this disease includes uveitis. Ophthalmic findings can include uveal lymphoma, iridocyclitis, hypopyon, keratic precipitates, and chorioretinitis. Most persistently viremic cats develop systemic signs of disease, with 70% to 90% of individuals surviving between 1.5 and 3 years after the development of clinical signs. Similar to FIV, cats should not be euthanized based on a positive test result, as individuals may remain asymptomatic for years after diagnosis; all positive ELISA results should be confirmed using a more specific test (IFA, VI). Clients should be aware that FeLV-positive cats are more likely to develop infections and may be prone to immune-mediated diseases and neoplasia.

Feline Infectious Peritonitis
FIP is an immune-mediated disease that may affect any feline infected with feline coronavirus. Purebred cats are proposed to be at increased risk for FIP. Approximately 5% to 13% of seropositive cats develop clinical signs of FIP; cats less than 1 year of age are at the highest risk. Manifestation of FIP may be effusive (wet) or noneffusive (dry). The dry form is more commonly associated with intraocular disease. Ocular manifestations of the disease include panuveitis with fibrin deposition in the anterior chamber, granulomatous chorioretinitis, retinal vasculitis (perivascular infiltration of white blood cells), retinal detachment, and optic neuritis. The prognosis is grave, as the disease is invariably fatal. More recently, a study involving three cats examined the effects of polyprenyl immunostimulant as a new therapy in the treatment of uveitis.

Key Points
• Uveitis is a common feline ocular disease that may result in blindness if not identified and properly treated.
• The causes of feline uveitis are numerous, and specific diagnostic tests may be required to arrive at a diagnosis.
• Aggressive symptomatic and, when appropriate, specific therapy is necessary to decrease pain and inflammation and to preserve vision.
• The prognosis varies depending on the underlying etiology. If no causative agent is identified, clients should be advised that recurrence of uveitis is possible.
noneffusive FIP; although the results were promising, additional studies are needed to assess efficacy. Postmortem analysis should be performed on cats with suspected FIP that are euthanized; confirmation of the disease should be discussed with the owner along with preventive measures to limit exposure to other cats.

**Feline Herpesvirus**

Ocular disease is a common manifestation of feline herpesvirus (FHV-1) infection, with the virus inducing conjunctivitis and dendritic or superficial geographical corneal ulcers via cytopathic effects on conjunctival and corneal epithelial cells. Corneal
ulcerative keratitis may induce a “reflex uveitis” through stimulation of the trigeminal nerve. More recently, it has been postulated that endogenous FHV-1 is also a causative pathogen of uveitis.17,26 Transient uveitis was detected after experimental inoculation of specific-pathogen-free kittens with FHV-1. Feline herpesvirus DNA has also been isolated from AH in cats with uveitis when no other agent was identified.26 The prognosis is variable because latency of the virus is common and infected cats may experience recurrence of clinical signs, typically induced by stress.27

Bartonella henselae
A gram-negative bacterium, Bartonella henselae is known to commonly infect cats and humans; it causes chronic uveitis in both species, and the cat is considered the organism’s main host.28 The bacterium replicates in endothelial cells and survives within erythrocytes.28 Depending on geographic location, up to 93% of cats may have been exposed to the organism; therefore, a diagnosis of Bartonella-induced uveitis is suggested (not confirmed) by exclusion of other causes along with serologic findings, including response to appropriate therapy.28,29 The usefulness of serum and AH antibody testing for Bartonella spp is limited because antibodies can be detected in healthy cats as well as in cats with uveitis.28 Recent work suggests that diagnosis requires confirmation using (1) enriched blood culture followed by PCR and (2) DNA sequencing involving PCR detection of Bartonella spp DNA in addition to enrichment culture of blood and serum samples in Bartonella alpha Proteobacteria growth medium.28 Uveitis may be chronic due to the propensity of B. henselae to survive intracellularly for several years.28,31

Fungal Disease
Histoplasma capsulatum, Cryptococcus neoformans, and, less commonly, Coccidioides immitis and Blastomyces dermatitidis are systemic fungal agents that have been associated with ocular disease in cats.30–33 Typical ocular presentations include granulomatous foci appearing clinically as keratic precipitates, highly cellular hypopyon, retinal granulomas, and retinal detachment. A recent report involving three cases of feline coccidiomycosis indicates that enophthalmos, conjunctival hyperemia, chemosis, and corneal neovascularization may also be observed.36 Treatment with antifungal therapy should continue for 1 month beyond the resolution of clinical signs regardless of cost concerns. For example, in the three cases mentioned above, long-term therapy was continued in all patients, resulting in administration of fluconazole for more than 12 months in one cat.36 The disease may manifest as a focal lesion; however, the disease is typically disseminated by the time lesions are detected.37 The prognosis varies depending on the extent of tissues involved, owner finances, and time commitment.

Parasitic Causes
Toxoplasma gondii
Toxoplasma gondii is a common zoonotic intracellular parasite for which cats are the only definitive hosts. Infected cats shed oocysts in their feces; the oocysts become infective after exposure to the environment.38 The estimated prevalence of toxoplasmosis in the cat population worldwide is 30% to 40%.38 Clinical signs of disease include anterior and posterior uveitis.39 The classic findings in Toxoplasma-induced uveitis include grey iridal nodules (FIGURE 5), multifocal dark grey lesions in the tapetal fundus, and fluffy white infiltrates in the nontapetal fundus.39 Treatment of toxoplasmosis can be challenging because current therapies suppress replication of the tachyzoites; therefore, complete elimination of the organism is unlikely.40

Other Parasites
Rarely, uveitis may be the result of aberrant parasite migration of Cuterebra and Toxocara larvae.41 Cuterebra larvae or track lesions of Cuterebra and Toxocara organisms may be visualized on fundic examination; histology reveals parasitic track lesions and/or coagulation necrosis and hemorrhage in affected areas such as the optic nerve head.41 Patients affected by ocular larval migrans may also present with neurologic signs, including behavioral changes, depression, and blindness due to migration of the parasite through the central nervous system.41

Immune-Mediated Causes
Although immune-mediated cases of feline uveitis are numerous, often making the search for an etiology difficult, a diagnostic workup is still recommended. Well-recognized forms of immune-mediated uveitis include phacolytic uveitis (chronic form of lens-induced uveitis) and phacoclastic uveitis (acute form of lens-induced uveitis). In phacolytic uveitis, cataractous lens proteins slowly leak across an intact lens capsule. In phacoclastic uveitis, the lens capsule ruptures (e.g., after perforating trauma), allowing a large amount of protein to leak rapidly from the lens. Phacoclastic uveitis may ultimately result in posttraumatic intraocular sarcoma.42 The prevalence of cataracts in the feline population is low; therefore, concurrent uveitis should be suspected when cataracts are observed.37
Neoplastic Causes

Diffuse iridal melanoma is the most common neoplastic cause of feline uveitis. This tumor appears as a flat, brown-black, freckle-like lesion within the iris (FIGURE 6). It is important to note that not all freckle-like lesions are melanomas: iris melanosis and uveal cysts remain important diagnostic differentials. Differentiation between iris melanoma and melanosis can be challenging. Without definitive confirmation via an iridal biopsy, the velvety appearance of the hyperpigmented lesion, the coalescing nature of the lesions over time, and a unilateral presentation of areas of iris hyperpigmentation (iris melanosis) can be suggestive of iris melanoma. Invasion of the sclera and iridocorneal angle with resulting glaucoma is highly indicative of iris melanoma. Frequent reevaluation (i.e., every 3 to 4 months) to track these lesions by taking photos is a reasonable initial approach unless malignancy is suspected early on. The metastatic rate of this malignancy may be as high as 63%; therefore, enucleation of the affected eye is typically recommended, especially in cases with glaucoma or scleral invasion. A highly effective treatment for canine uveal melanoma is diode laser ablation; however, this therapy has not yet been shown to be efficacious in feline patients.

Ocular sarcomas, which are typically associated with trauma, are also primary ocular tumors that may have epithelial or mesenchymal features. Although their origin is difficult to elucidate, it has been suggested that they may arise from lens epithelium. Although their origin is difficult to elucidate, it has been suggested that they may arise from lens epithelium. As metastasis of this tumor is expected, early enucleation of the affected eye is recommended.

The most common secondary neoplasm affecting the eye is lymphoma, which also typically causes unilateral uveitis.

Trauma

Perforating or blunt trauma is a common cause of uveitis. Uveitis may also manifest secondary to ocular surgical procedures (i.e., corneal surgery, cataract surgery) and corneal ulceration. While blunt trauma is less common than perforating trauma, it typically results in more damage to the globe. Ocular ultrasonography may be a useful adjunctive diagnostic tool, especially if the anterior chamber cannot be visualized. Treatment of trauma-induced uveitis follows the same general principles of symptomatic therapy for uveitis; however, the effects of trauma to other ocular structures must be considered. Corneal injury subsequent to trauma is common, making topical steroids an inappropriate choice for therapy. Topical and systemic NSAIDs are occasionally used in lieu of steroids in patients with endocrinopathies (e.g., diabetes mellitus), lymphosarcoma, or systemic infectious diseases; however, the risk of precipitating the progression of an existing corneal ulcer is not eliminated by using topical NSAIDs. Examples of commercially available topical NSAID ophthalmic solutions include diclofenac and flurbiprofen. Topical antibiotics are also indicated when corneal injury exists. The prognosis for vision and viability of the eye depends on the nature and extent of the trauma; if significant intraocular hemorrhage exists, the prognosis is guarded at best.

Idiopathic Uveitis

Reportedly, in as many as 70% of feline uveitis cases, no underlying etiology is identified. A complete diagnostic database is nevertheless recommended to allow for prompt and specific therapy if a specific underlying systemic disease can be found. In cases of idiopathic uveitis, aggressive symptomatic treatment is recommended and the prognosis may be guarded, as recurrence is common.

Symptomatic Treatment of Feline Uveitis

Regardless of cause, the goals of treatment are to stabilize the BAB, decrease inflammation, treat ocular pain, minimize potential ocular sequelae, and preserve vision. When miosis is observed, administration of a mydriatic (atropine, tropicamide) is indicated to help prevent development of posterior synechiae, as well as to provide analgesia via cycloplegia (paralysis of the ciliary muscle). Dilution of the pupil should be maintained until clinical improvement of uveitis is observed; this may entail one to three times daily administration if the pupil is persistently miotic to administration every other day (or third day) if the dilated pupil relapses into miosis. Atropine accumulates in the eye and can have a long-lasting effect, but it is highly effective at improving visual acuity, decreasing pain, and minimizing ocular sequelae.

Clinical Pearls

- To help rule in/out causes of feline uveitis, the ocular examination should include a neuro-ophtalmic examination, fluorescein staining, and tonometry.
- Uveitis is the most common cause of glaucoma in cats.
- Long-term therapy may be required in cases of uveitis caused by FIV or intraocular neoplasia and in cases of idiopathic uveitis.
- Chronic or recurrent conjunctivitis is often caused by underlying uveitis in cats.
duration of action (e.g., the pupil may remain dilated for several days to weeks after the last dose of atropine). Prolonged pupillary dilation is not of concern as long as the IOP remains below 25 mm Hg. Clients should be informed that cats may salivate after administration of atropine because of its bitter taste. Tropicamide can also be used but requires frequent administration (e.g., every 6 to 8 hours) because its duration is not as long as that of atropine.

The inflammatory nature of uveitis dictates the use of topical and systemic antiinflammatory pharmaceuticals when corneal trauma is not present. Topical corticosteroids are recommended to suppress inflammation and help decrease protein leakage and deposition. Depending on the degree of inflammation, topical corticosteroids may initially be administered as frequently as once every hour until clinical improvement is observed. Systemic corticosteroids may resolve within 1 or 2 weeks of therapy; however, severe posterior uveitis requires systemic administration of corticosteroids, possibly for an extended period of time (weeks). Additional therapeutic options for specific causes of feline uveitis are summarized in Table 3. The choice of medication and frequency of administration depend on the severity of the case. For example, mild anterior uveitis may require only once-daily administration of a topical steroid or twice-daily administration of a topical NSAID and may resolve within 1 or 2 weeks of therapy; however, severe posterior uveitis requires systemic administration of steroids, possibly for an extended period of time (weeks). Additional therapeutic options for specific causes of feline uveitis are summarized in Table 3.

**Conclusions**

Uveitis can be challenging to diagnose and treat in feline patients. Identifying the underlying cause allows better tailoring of therapy to alleviate patient discomfort, avoid or minimize sequelae, and, ultimately, improve prognosis for the patient. Recent advances in diagnostic tests and therapies allow for improved outcomes in feline uveitis.
Acknowledgments
The authors thank Dr. Ellison Madson (University of Wisconsin-Madison), Dr. Dennis Brooks (University of Florida), Kevin Hogg (University of Guelph), and Peter Jaspers-Fayer (University of Guelph) for their assistance with the figures and images in this article.

References
**Feline Uveitis**

1. Other than idiopathy, the most common cause of feline uveitis is
   a. an immune-mediated condition.
   b. neoplasia.
   c. trauma.
   d. infection.

2. Aqueous flare is caused by
   a. a hyperreflective tapetal fundus.
   b. a cataract.
   c. the presence of proteins within the anterior chamber.
   d. liquefaction of the vitreous.

3. Uveitis can result in
   a. glaucoma.
   b. diabetes mellitus.
   c. systemic hypertension.
   d. corneal ulcer.

4. Which statement regarding treatment of feline uveitis is true?
   a. Topical and systemic antiinflammatory drugs are recommended when corneal trauma is not present.
   b. Use of topical corticosteroids is always indicated, regardless of underlying cause.
   c. Topical tropicamide has a longer duration of action than topical atropine.
   d. Topical atropine or tropicamide is indicated only when a dilated pupil is observed.

5. Which of the following statements is correct with respect to FIV?
   a. It is found in North American cat populations only.
   b. All infected, unvaccinated cats develop signs of systemic disease.
   c. Euthanasia of all seropositive asymptomatic cats should be recommended.
   d. Cats are typically infected via bite wounds.

6. Which of the following statements is incorrect with respect to uveitis in cats?
   a. In as many as 70% of uveitis cases, no underlying etiologic agent is identified.
   b. If symptomatic treatment for uveitis is instituted quickly, recurrence is unlikely.
   c. Uveitis is a common feline ocular disease that can result in permanent blindness if not treated aggressively and quickly.
   d. Uveitis may involve any and all parts of the feline uvea, including the iris, ciliary body, and choroid.

7. Ocular clinical signs suggestive of feline anterior uveitis include
   a. scleral hyperemia, blepharospasm, and retinal detachment.
   b. aqueous flare, miosis, and low IOP.
   c. intraocular hemorrhage, elevated IOP, and retinal granuloma.
   d. corneal ulcer, mydriasis, and cataract.

8. Which statement is correct with regard to toxoplasmosis in cats?
   a. Recurrence of disease is unlikely with appropriate therapy.
   b. The parasite is transmitted through shared food and water bowls.
   c. Ocular signs of *Toxoplasma*-induced uveitis include multifocal, dark grey lesions in the tapetal fundus.
   d. The prevalence of toxoplasmosis in the feline population is estimated at 75%.

9. Which is the most common type of primary ocular neoplasia resulting in uveitis in cats?
   a. ciliary body adenoma
   b. lymphosarcoma
   c. sarcoma
   d. iris melanoma

10. Which statement regarding trauma-induced uveitis in cats is true?
    a. It can be caused by blunt or perforating trauma.
    b. It is only a consideration in cases of bilateral uveitis.
    c. It is uncommon except after ocular surgical procedures.
    d. It is easy to treat and has an excellent prognosis.