Canine Anterior Uveitis

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Abstract: Canine anterior uveitis can be a debilitating, painful, vision-threatening disease. Several local and systemic diseases can cause anterior uveitis. Because the eye is limited in its ability to respond to injury, different diseases produce similar clinical signs, making an etiologic diagnosis difficult but imperative to improve the likelihood of a successful outcome. A thorough history and complete ocular and physical evaluations are necessary to ensure timely and accurate diagnosis. This article reviews the pathophysiology, most common causes, diagnostic recommendations, current therapeutic options, potential complications, and prognosis for canine anterior uveitis.

Anterior uveitis is a painful, inflammatory disorder that is one of the most frequently observed ocular diseases in dogs. Intrinsic ocular abnormalities and multiple systemic diseases can trigger its development. Establishing the etiology is essential because inappropriate therapy may result in loss of vision. Appropriate therapy can be curative but sometimes is, at best, long term and palliative. Complications are common.

Anatomy of the Uveal Tract

The uvea is the highly vascular middle layer of the eye, located immediately beneath the sclera. It comprises the iris, ciliary body, and choroid. The iris and ciliary body make up the anterior uveal tract, and the choroid composes the posterior uveal tract. Uveitis is any inflammatory condition involving all or a portion of these tracts. Iritis and cyclitis refer to inflammation of the iris and ciliary body, respectively. Anterior uveitis, or iridocyclitis, is present when both the iris and ciliary body are inflamed. Posterior uveitis denotes inflammation of the ciliary body and choroid. Further classification is based on duration (acute, chronic, recurrent), pathology (e.g., granulomatous, suppurative), and cause (e.g., traumatic, infectious, neoplastic, immune-mediated).

The blood–aqueous barrier (BAB) plays an important anatomic role in the development of anterior uveitis. Normally, this selectively permeable barrier prevents the influx of blood and proteins into the aqueous humor. It is formed by the nonpigmented epithelium of the ciliary body and the endothelium of the iridal blood vessels. Tight junctions joining these cells maintain the continuity of the barrier. When the BAB is breached as a result of uveal inflammation, protein and blood cells leak into the fluid medium of the eye, resulting in aqueous flare.

Pathophysiology of Ocular Inflammation

Anterior uveitis develops as a result of injury to the anterior uveal tract. Pathophysiologic mechanisms responsible for this tissue injury include damage by organisms or neoplastic cells spread through the bloodstream from distant anatomic sites or directly to the eyes from adjacent tissues (e.g., meninges, optic nerve, upper respiratory tract), tissue damage from exposure to environmental or microbial
Canine Anterior Uveitis

TABLE 1 Differential Diagnosis of Canine Anterior Uveitis

<table>
<thead>
<tr>
<th>Condition</th>
<th>Ocular Redness</th>
<th>Miosis/Mydriasis</th>
<th>Pain</th>
<th>Discharge</th>
<th>Intraocular Pressure</th>
<th>Aqueous Flare</th>
<th>Fluorescein Dye Uptake</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uveitis</td>
<td>Intense ciliary flush just posterior to the limbus</td>
<td>Miosis of affected eye</td>
<td>Present in affected eye</td>
<td>Thin to no discharge</td>
<td>Decreased</td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>Glaucoma</td>
<td>Diffuse congestion of large, deep episcleral vessels; some congestion of superficial conjunctival vessels</td>
<td>Mydriasis of affected eye</td>
<td>Present in affected eye</td>
<td>Thin to no discharge</td>
<td>Elevated</td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>Ulcerative keratitis</td>
<td>Similar to pattern described for uveitis</td>
<td>Normal pupil if simple; miosis if severe and secondary uveitis is present; mydriasis if secondary glaucoma is present</td>
<td>Present in affected eye</td>
<td>Profuse, thick discharge</td>
<td>Normal to decreased if severe</td>
<td>Can be present if keratitis is severe</td>
<td>Present</td>
</tr>
<tr>
<td>Con junctivitis</td>
<td>Diffuse reddening of the conjunctiva between small superficial vessels with thickening and folding of conjunctiva; small superficial vessels move with conjunctival manipulation; vessels blanch with topical epinephrine</td>
<td>Normal pupil size</td>
<td>Present in affected eye</td>
<td>Profuse, thick discharge</td>
<td>Normal</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>Horner's syndrome</td>
<td>Superficial conjunctival hyperemia may be present</td>
<td>Miosis, ptosis, enophthalmos, prolapsed third eyelid</td>
<td>Absent</td>
<td>Absent</td>
<td>Normal</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>Episcleritis</td>
<td>Hyperemia localized to inflamed area with local thickening of episclera and congestion of vessels deep to conjunctiva</td>
<td>Normal pupil size</td>
<td>Present in affected eye</td>
<td>Excessive lacrimation</td>
<td>Normal</td>
<td>Absent</td>
<td>Absent</td>
</tr>
</tbody>
</table>

Toxins, immune-mediated mechanisms (FIGURE 1), primary intraocular neoplasms, trauma, corneal ulceration, and cataract formation. Tissue injury and the continued presence of bacteria or viruses or their genetic material results in inflammation. This inflammation, if left unresolved, can damage delicate ocular tissues.

The inflammatory mediators that can incite classic ocular changes associated with anterior uveitis (i.e., aqueous flare, photophobia, hyperemia, miosis, decreased intraocular pressure [IOP]) are the arachidonic acid metabolites—prostaglandins, thromboxanes, and leukotrienes. Arachidonic acid is released from cell membrane phospholipids through the action of phospholipase A2 after tissue injury. Cyclooxygenase converts arachidonic acid to prostaglandins, thromboxanes, and prostacyclins, whereas lipoxygenase converts arachidonic acid into leukotrienes and hydroperoxy and hydroxyeicosatetraenoic acids. In response to the release of these metabolites from cell membrane phospholipids, inflammatory cells infiltrate the uveal tract. Platelet-activating factor (PAF) released from damaged cells, leukocytes, and mast cells results in platelet aggregation, polymorphonuclear cell chemotaxis, increased vascular permeability, and smooth-muscle contraction with subsequent miosis. Histamine, prostaglandins, and kinins further increase vascular permeability. Prostaglandins are powerful mediators of intraocular inflammation and can cause miosis, hyperemia, and alterations in IOP. Inflammatory mediators (particularly prostaglandins) cause miosis by their direct effects on the iris sphincter.

Leukocyte chemotaxis, phagocytosis, and degradation are stimulated by complement, the clotting/fibrinolytic systems, and, most importantly, leukotrienes. Tissue destruction is further enhanced by release of leukocyte granules and enzymes.

Clinical Signs
Clinical signs of ocular pain (photophobia, blepharospasm, elevation of the nictitating membrane, epiphora) are frequently observed with anterior uveitis. Aqueous flare, miosis, corneal edema, conjunctival hyperemia, and scleral blood vessel congestion are also commonly documented. The presence of protein and cells in the aqueous humor (flare) is pathognomonic for anterior uveitis.

Other acute
signs include keratic precipitates, iridal swelling, hypopyon, and hyphema.\textsuperscript{1} Chronic anterior uveitis results in accumulation of toxic wastes and inflammatory mediators within the aqueous humor. These substances damage corneal endothelial cells and disrupt the normal metabolism of the corneal stroma, leading to corneal edema.\textsuperscript{1} Inflammatory debris can accumulate in the aqueous humor drainage channels and increase IOP, predisposing the patient to glaucoma.\textsuperscript{1} Preiridal fibrovascular membrane formation also contributes to secondary glaucoma. These membranes originate as endothelial buds from anterior iridal stroma that mature into fibrous or fibrovascular membranes and can result in hyphema and glaucoma.\textsuperscript{11} They are rarely detected clinically and likely form in response to angiogenic factors released by an ischemic retina, neoplasms, or leukocytes involved in ocular inflammation.\textsuperscript{11} As the pupillary margin becomes adhesive due to chronic inflammation, anterior and posterior synechiae may form. Iris hyperpigmentation, cataracts, and deep corneal vascularization can also be consequences of chronic inflammation of the anterior uvea.\textsuperscript{1} Ocular redness, miosis, pain, and discharge can have many other causes, including glaucoma, ulcerative keratitis, conjunctivitis, Horner’s syndrome, and episcleritis. Therefore, a thorough ocular examination consisting of a Schirmer tear test (STT), fluorescein dye application, tonometry, pupillary dilation (if IOP is not elevated), slit lamp biomicroscopy, and funduscopy is necessary to distinguish between these diseases and anterior uveitis. Reductions in IOP can be an early but subtle indication of anterior uveitis.\textsuperscript{6} The decrease in IOP results from reduced production of aqueous humor due to cyclitis. Concomitantly, increases in uveoscleral aqueous humor outflow further decrease IOP. The type of vessels involved (superficial, mobile conjunctival versus deeper, immobile scleral), magnitude of increase or decrease of IOP from the normal range, presence of fluorescein dye uptake on the cornea, presence of aqueous flare, presence or absence and consistency of ocular discharge, and presence or absence of photophobia (pain) all aid in differentiating anterior uveitis from the other diseases\textsuperscript{8} (TABLE 1).

**Diagnostic Testing**

In addition to performing a complete physical and ocular examination, clinicians must obtain a detailed and thorough history.\textsuperscript{12} The client should be asked about the patient’s travel history, vaccination status, tick exposure/prophylaxis, trauma, and heartworm prophylaxis. Appropriate tests include hemogram, a serum biochemistry panel, urinalysis, and serologic testing (if infectious disease is suspected) as dictated by the history, physical and ocular findings, geographic location, and travel history.\textsuperscript{12} Aqueocentesis may be considered as a final diagnostic option after exhausting other testing modalities. This is a low-yield test that is contraindicated in a sighted eye with active inflammation, as it may further exacerbate inflammation. Aqueous humor obtained by aqueocentesis can be used for cytologic examination, microbial culture and sensitivity testing, genetic evaluation with polymerase chain reaction (PCR), and antibody titer determination.\textsuperscript{13}

**Etiology**

Causes of anterior uveitis can be noninfectious or infectious\textsuperscript{1,6,14–16} (BOXES 1 and 2). Noninfectious disease processes account for most known causes of anterior uveitis.\textsuperscript{1} Lens-induced uveitis (LIU), trauma, idiopathic anterior uveitis, intraocular neoplasia, corneal ulceration, pigmentary uveitis of golden retrievers, and uveodermatologic syndrome are examples of noninfectious causes of anterior uveitis. Many of these etiologies can be identified by evaluation of signalment, history, and results of thorough physical and ocular examination.

Investigation into possible infectious causes can be frustrating because it is difficult to make an etiologic diagnosis by ocular examination alone. Appropriate diagnostic testing can be performed based on the most likely diseases or syndromes for each case. Geographic location should also be considered when ranking etiologies, as some infectious diseases are more prevalent in certain areas. For example, blastomycosis is more common in young adult dogs in the Mississippi and Ohio River valleys, whereas coccidioidomycosis is more prevalent in the desert regions of the southwestern United States and protothecosis in the southeastern coastal regions.\textsuperscript{17}

**BOX 1**

**Noninfectious Causes of Canine Anterior Uveitis\textsuperscript{1,6,14–16}**

- Lens-induced uveitis
- Trauma
- Idiopathic uveitis
- Primary ocular neoplasia
  - Melanocytic tumors
  - Ciliary body tumors
- Secondary ocular neoplasia
  - Lymphoma
  - Hemangiosarcoma
  - Mammary carcinoma
  - Oral malignant melanoma
- Corneal ulceration
- Pigmentary uveitis of golden retrievers
- Uveodermatologic syndrome

**TABLE 1**

**BOXES 1 and 2.** Noninfectious disease processes account for most known causes of anterior uveitis.\textsuperscript{1} Lens-induced uveitis (LIU), trauma, idiopathic anterior uveitis, intraocular neoplasia, corneal ulceration, pigmentary uveitis of golden retrievers, and uveodermatologic syndrome are examples of noninfectious causes of anterior uveitis. Many of these etiologies can be identified by evaluation of signalment, history, and results of thorough physical and ocular examination.

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Noninfectious Causes of Anterior Uveitis

**Lens-Induced Uveitis**

LIU is an inflammatory response of the ocular uvea to lens protein. Under normal conditions, a low concentration of circulating lens protein is chronically present in the eye to maintain immunologic tolerance to lens antigen by T cells.\(^{18}\)

Two distinct types of LIU exist in dogs, phacolytic and phacoclastic.\(^{8,19}\) Phacolytic uveitis involves slow leakage of small amounts of lens protein through an intact lens capsule of a resorbing cataract (FIGURE 2).\(^{8,15}\) This incites a mild lymphocytic–plasmacytic anterior uveitis that can clinically resemble idiopathic uveitis.\(^{19}\) A presumptive etiologic diagnosis can be made by considering the history of cataract formation with subsequent development of anterior uveitis. This type of LIU is frequently observed in dogs presenting for cataract surgery and often responds well to antiinflammatory therapy.\(^{19}\)

Trauma

Uveal contusion and intraocular hemorrhage may occur secondary to blunt or penetrating ocular trauma. Additional lesions include conjunctival hyperemia, corneal edema, iris

Infectious Causes of Canine Anterior Uveitis\(^{1,6,14–16}\)

**Rickettsial**
- *Ehrlichia canis*
- *Rickettsia rickettsii*

**Mycotic**
- *Blastomyces dermatitidis*
- *Histoplasma capsulatum*
- *Coccidioides immitis*
- *Cryptococcus neoformans*
- *Aspergillus spp*

**Algal**
- *Prototheca zopfii*
- *Prototheca wickerhamii*

**Bacterial**
- *Leptospira spp*
- *Borrelia burgdorferi*
- *Brucella canis*
- *Bartonella vinsonii subsp berkhoffii*
- *Bacteremia/septicemia*\(^{6}\)

**Parasitic**
- *Dirofilaria immitis*\(^{14}\)
- *Leishmania spp*\(^{15,16}\)
- *Toxocara spp*\(^{1,6}\)

**Viral**
- *Infectious canine hepatitis*\(^{1}\)
vascular congestion, miosis, fibrin and cellular debris in the anterior chamber, and hypotony. The physical and ophthalmologic examination, a detailed history, and ultrasonographic imaging (if available) can aid in establishing the extent of ocular trauma.

**Idiopathic**

Idiopathic uveitis is diagnosed in almost 60% of dogs evaluated for anterior uveitis unrelated to trauma, hypermature cataract, neoplasia, or infectious disease. These dogs are generally middle-aged, spayed or neutered, and have no evidence of systemic disease. Unilateral ocular involvement is more likely with idiopathic anterior uveitis than with neoplastic or infectious causes.

Idiopathic anterior uveitis with concurrent exudative retinal detachment has also been documented in dogs. This syndrome results in blindness; acute, severe bilateral choroiditis, and variable anterior uveitis with exudative retinal detachment. The etiopathogenesis of this syndrome is unknown, but it has been successfully treated with high dosages of corticosteroids. Ultimately, many patients require additional immunosuppressive therapy such as azathioprine or cyclosporine in combination with corticosteroids to control clinical signs (TABLE 2). A thorough diagnostic evaluation is necessary before initiating corticosteroid/immunosuppressive treatment to prevent exacerbation of an underlying infectious etiology or neoplastic process.

**Neoplasia**

In one study, almost 25% of dogs evaluated for uveitis from 1989 to 2000 were diagnosed with neoplasia-associated uveitis. Older dogs make up this population; rottweilers are most commonly affected, followed by golden retrievers, Labrador retrievers, German shepherds, and mixed breeds. Ocular inflammation is a possible sequela of any intraocular neoplasm. Aqueous flare was the most common clinical sign observed in the study, but corneal edema, hyphema, and keratic precipitates were also documented.

Although relatively rare, primary and secondary ocular neoplasms can cause anterior uveitis. Tumors of melanocytic origin are the most common primary ocular tumors in dogs, followed by epithelial tumors of the ciliary body. Melanocytic tumors may have a heritable basis in Labrador retrievers. Recent evidence has suggested that limbal melanomas, caudal anterior uveal melanomas, and ocular melanosis in golden retrievers may also be partly heritable, with the same genetic mutation(s) causally associated with melanocytic disease at different ocular sites. Uveal melanomas, whether benign or malignant, almost always arise from the anterior uveal tract and have a low incidence of metastasis. Iridal and ciliary body neoplasms are usually heavily pigmented and have a low risk of metastasis.

Lymphoma is the most common secondary neoplasm of the canine globe, followed by hemangiosarcoma, mammary carcinoma, and oral malignant melanoma. Lymphoma may cause inflammation, iridal thickening, hypopyon, hyphema, and glaucoma. Cytologic samples for diagnosis may be procured via aqueocentesis or hyalocentesis if thorough staging or peripheral lymph node aspiration does not suffice. Alternatively, tissue may be submitted for histopathologic evaluation following enucleation. Other tumors

### TABLE 2: Drugs Used to Treat Canine Anterior Uveitis

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Drug</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Topical drugs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>Prednisolone acetate</td>
<td>q1–12h</td>
</tr>
<tr>
<td></td>
<td>(1% suspension)</td>
<td></td>
</tr>
<tr>
<td>NSAIDs</td>
<td>Flurbiprofen (0.03% solution)</td>
<td>q6–12h</td>
</tr>
<tr>
<td></td>
<td>Suprofen (1% solution)</td>
<td>q6–12h</td>
</tr>
<tr>
<td></td>
<td>Ketorolac (0.5% solution)</td>
<td>q6–12h</td>
</tr>
<tr>
<td></td>
<td>Diclofenac (0.1% solution)</td>
<td>q6–12h</td>
</tr>
<tr>
<td>Mydriatic/cycloplegic drugs</td>
<td>Atropine sulfate (0.5% and 1% solution and ointment)</td>
<td>q8–24h</td>
</tr>
<tr>
<td><strong>Oral drugs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>Prednisone or prednisolone</td>
<td>0.5 to 1 mg/kg bid</td>
</tr>
<tr>
<td>Immunosuppressive drugs</td>
<td>Cyclosporine</td>
<td>5 mg/kg bid; adjust dose pending 12-h whole blood trough level 48 h after initiation of therapy</td>
</tr>
<tr>
<td></td>
<td>Azathioprine</td>
<td>2 mg/kg q12h for 2 weeks, then every other day for 2 weeks, then taper to 1 mg/kg every other day</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>Carprofen</td>
<td>≤2.2 mg/kg q12–24h PRN</td>
</tr>
<tr>
<td></td>
<td>Meloxicam</td>
<td>≤0.2 mg/kg once, then ≤0.1 mg/kg q24h thereafter</td>
</tr>
<tr>
<td></td>
<td>Etodolac</td>
<td>≤15 mg/kg q24h</td>
</tr>
<tr>
<td></td>
<td>Deracoxib</td>
<td>≤4 mg/kg q24h</td>
</tr>
</tbody>
</table>
known to metastasize to the eye include seminoma, transitional cell carcinoma of the urinary bladder and/or urethra, transmissible venereal tumor, anaplastic fibrosarcoma, neurogenic sarcoma, rhabdomyosarcoma, and pheochromocytoma. Bilateral ocular involvement may occur, and varying degrees of anterior uveitis and its sequelae may be the presenting signs. One case of intraocular osteosarcoma causing anterior uveitis in a 10-year-old German shepherd has been documented.

### Corneal Ulceration

Anterior uveitis may occur as an extension of a local process such as scleritis or keratitis. It has been proposed that an axonal reflex mechanism may be responsible for vasodilatation and inflammation of the uvea when ulcerative keratitis is present.

### Breed-Specific Uveitis

Pigmentary uveitis of golden retrievers is presumed to be an inherited form of anterior uveitis. It presents as adhesions between the iris and lens or peripheral iris and cornea, with pigment dispersion across the anterior lens capsule. This form of anterior uveitis is not associated with any systemic disorder or infectious etiology. The most frequently observed early clinical sign is pigment on the anterior lens capsule. Other clinical signs associated with this disorder include aqueous flare, uveal cysts, fibrin in the anterior chamber, posterior synechiae, secondary glaucoma, corneal ulcer, hyphema, iris bombé, phthisis bulbi, retinal degeneration or detachment, and uveal neoplasia. Diagnosis is based on exclusion of other underlying etiologies. The prognosis is guarded because this disease is progressive and predisposes to secondary glaucoma.

### Uveodermatologic Syndrome

Uveodermatologic syndrome is a debilitating disease resulting in blindness in many affected dogs. Due to its similarities to Vogt-Koyanagi-Harada (VKH) syndrome in humans, this disease is commonly known as VKH-like disease. The cause is unknown, but an immune-mediated etiology is strongly suspected. A slightly greater incidence in males has been suggested, with a likely immunogenetic predisposition, evidenced by occurrence of this disease in Akitas, Samoyeds, Siberian huskies, and Shetland sheepdogs.

Ocular signs are usually the first abnormality noted, with most patients being referred for acute-onset blindness or chronic anterior uveitis. Ocular findings range from bilateral anterior uveitis to severe panuveitis, retinal detachment, posterior synechiae, secondary glaucoma, cataract, and vision loss. Depigmentation of the hair and skin usually follows the onset of ocular signs. The eyelids, nasal planum, lips, scrotum, and footpads are often affected; depigmented areas can be generalized or restricted to the face. Some patients develop generalized vitiligo and/or poliosis. Rapidly depigmenting areas tend to become ulcerated and crusted. Ocular histopathology primarily reveals panuveitis, retinal separation, and prominent pigment-containing macrophages. Skin histopathology reveals interface dermatitis with a primarily lichenoid pattern, large histiocytic cells, plasma cells, and small mononuclear cells.

Treatment involves topical or subconjunctival corticosteroids, cycloplegics (atropine), and systemic corticosteroids (prednisone, 1 to 2 mg/kg/d PO) to treat inflammation and dermatologic signs. Recurrence is common, and combination therapy consisting of oral corticosteroids and other immunosuppressive drugs (e.g., azathioprine, 2 mg/kg/d) may be necessary. Oral cyclosporine is a reasonable alternative to azathioprine when combined with corticosteroids to control inflammation. Topical administration of cyclosporine can be considered, but this drug cannot penetrate an intact cornea.

### Infectious Causes of Anterior Uveitis

In a recent retrospective study of dogs with anterior uveitis, 17.6% were diagnosed with an infectious etiology. In general, tick-borne, fungal, algal, and bacterial agents should be suspected when evaluating a patient for infectious causes of anterior uveitis. Other systemic signs may accompany ocular manifestations, such as generalized lymphadenopathy, pancytopenia, thrombocytopenia, diarrhea, and draining skin lesions. Standard-of-care therapy for these etiologic agents is briefly discussed here; a more thorough discussion of treatment can be found in veterinary internal medicine or canine infectious disease texts.

### Tick-Borne Disease

Canine monocytic ehrlichiosis is a tick-borne disease caused by the rickettsial pathogen *Ehrlichia canis*. *E. canis* is transmitted primarily by the brown dog tick (*Rhipicephalus sanguineus*) and the American dog tick (*Dermacentor variabilis*). Ocular lesions are common, and the severity of signs varies. Ocular signs include conjunctivitis, conjunctival/iridal petechiae and ecchymoses, corneal edema, panuveitis, hyphema, secondary glaucoma, optic neuritis, and retinal hemorrhage with detachment. Diagnosis of ehrlichiosis requires visualization of morulae, detection of *E. canis* antibodies, or PCR amplification of *E. canis* DNA. Ocular manifestations can also occur with Rocky Mountain spotted fever (RMSF). RMSF is caused by *Rickettsia rickettsii*, a gram-negative, obligate intracellular cocccobacillus transmitted primarily by the *D. variabilis* tick in the eastern United States and *Dermacentor andersonii* in the western United States and Canada. Ocular involvement occurs secondary to vasculitis. Clinical signs include conjunctival vascular injection, anterior uveitis, petechial hemorrhages of the iris stroma, and bilateral hyphema.
An immunofluorescence assay (IFA) detects IgM and IgG and is the “gold standard” in the diagnosis of RMSF. A single IFA titer of 1:64 or higher for IgM with concurrent clinical signs is considered diagnostic. A fourfold rise in IgG between acute and convalescent specimens acquired 3 to 4 weeks apart is also considered diagnostic.

Standard therapy of ehrlichiosis and RMSF consists of routine supportive care and doxycycline at a minimum dose of 10 mg/kg/d for 28 days, but 7 days of administration has been shown to be sufficient for RMSF. Tetracyclines and fluoroquinolones are also effective in treating RMSF.

Fungal Disease
Systemic mycoses can cause anterior or posterior uveitis or panuveitis. Infection with Blastomyces dermatitidis is the systemic mycosis most commonly associated with ocular lesions. Approximately 30% to 43% of dogs with systemic blastomycosis have clinical signs of ocular involvement. Common ocular abnormalities include conjunctival hyperemia, corneal edema, aqueous flare, iritis, iridocyclitis, vitritis, retinitis, chorioretinitis, serous or granulomatous retinal separation, optic neuritis, secondary glaucoma, and blindness. Other fungal organisms proved or suspected to cause anterior uveitis in dogs include Coccidioides immitis, Cryptococcus neoformans, Aspergillus fumigatus, and Histoplasma capsulatum. All disseminated mycoses result in posterior segment disease, but coccidioidomycosis and cryptococcosis predominantly cause posterior segment disease without anterior segment involvement.

Organisms can be detected by cytopathology of body fluids, lymph node aspirates, vitreous humor, or impression smears of skin lesions or by histopathologic examination of various tissues, including enucleated eyes. Direct visualization of the organism remains the gold standard for diagnosis, but serology may be useful to aid in supporting a diagnosis when organisms cannot be identified.

Systemic blastomycosis with ocular involvement is treated with itraconazole at a dose of 5 mg/kg/d PO for a minimum of 60 to 90 days or at least 30 days beyond resolution of clinical signs. Treatment durations of 6 to 12 months are not unusual. Enucleation may be necessary if severe secondary glaucoma develops. Histoplasmosis can be treated with itraconazole (10 mg/kg/d PO) or with amphotericin B. Fluconazole is the initial drug of choice for coccidioidomycosis (10 mg/kg PO bid) and cryptococcosis (2.5 to 5 mg/kg PO or IV daily or bid).

Protothecosis
Prototheca spp are colorless algae related to the green algae of the genus Chlorella. Of the four recognized or proposed species, Prototheca zopfii and Prototheca wickerhamii have been found to be pathogenic. In dogs, protothecosis usually presents as a systemic infection, with protracted hemorrhagic enteritis as the most common clinical sign. However, canine protothecosis can present with acute blindness as the only sign.

In one study, ocular involvement was present in 77% of cases of systemic protothecosis. Aquous flare, iritis, episcleral injection, epiphora, conjunctival hyperemia, low IOP, and hyphema have also been documented. Diagnosis is confirmed by direct visualization of the organism, cytologic examination of rectal scrapings, aqueocentesis, or histopathologic examination of tissue specimens from the colon or regional lymph nodes.

Successful therapy has yet to be discovered for protothecosis. Amphotericin B has been successful in slowing disease progression but has not been curative. Amphotericin B (1 mg/kg IV three times weekly to a cumulative dose of 12 mg/kg) used in combination with ketoconazole, fluconazole, or itraconazole (5 to 10 mg/kg/d PO) is an option for long-term therapy of P. zopfii infection, but the prognosis remains grave.

Bacterial and Protozoal Disease
Leptospirosis has been documented as a cause of panuveitis in one case, with mild hyphema, aqueous flare, and partial serous retinal detachments bilaterally. Diagnosis can be obtained by evaluation of acute and convalescent microscopic agglutination titers (MATs) for the various Leptospira serovarieties. PCR can be performed on blood and urine to detect leptospiral genetic material. Appropriate clinical signs with elevated serum MATs are the gold standard in diagnosis. Penicillin (25,000 to 40,000 U/kg q12–24h IV or IM for 14 days), ampicillin (22 mg/kg PO, SC, or IV q8–12h for 14 days), or amoxicillin (22 mg/kg PO q8h for 14 days) is given.

Key Facts
- Canine anterior uveitis is a common ocular disorder that is usually idiopathic but can be associated with multiple, serious systemic diseases.
- It can be difficult to distinguish among the various etiologies of canine anterior uveitis because the eye is limited in its ability to respond to injury.
- A thorough history, physical and ocular examinations, and routine database (complete blood cell count, serum chemistry analyses, urinalysis) should be obtained to direct subsequent diagnostic testing and establish a definitive diagnosis.
- Immediate, aggressive therapy is necessary to stop inflammation, prevent and control complications secondary to inflammation (glaucoma, cataract formation, retinal degeneration), relieve pain, and preserve vision.
Canine Anterior Uveitis

to eliminate leptospirosis, followed by doxycycline (5 to 10 mg/kg PO bid) for 14 days to eliminate the organism from the renal tubular cells.50,51 Appropriate therapy is essential because infected animals pose a zoonotic threat to human caretakers.50

Animals infected with *Borrelia burgdorferi* can present with anterior uveitis.52 Uveal inflammation should therefore prompt the clinician to evaluate for borreliosis if other common causes are eliminated. *Brucella canis*, a gram-negative coccobacillus found in the vaginal fluid or urine of infected dogs, can also produce anterior uveitis.53 Serology can be employed in the diagnosis of either borreliosis or brucellosis. Doxycycline (10 mg/kg q24h PO for 21 to 28 days) or β-lactam antibiotics such as amoxicillin (22 mg/kg q12h PO for 21 to 28 days) are effective treatments.54

*Bartonella* spp have been implicated in causing anterior uveitis.55 In one case, a 2-year-old, spayed spaniel mix was evaluated for bilateral anterior uveitis. All infectious disease titers were normal, except for a 1:512 antibody titer to *Bartonella vinsonii* subsp *berkhoffi*. Ocular changes attributable to borreliosis include optic neuritis, anterior uveitis, vitritis, pars planitis, focal and multifocal retinal vasculitis, retinal white dot syndrome, branch retinal artery occlusion, and venous occlusions, focal choroiditis, serous retinal detachments, papillitis, and peripapillary angiomatosus lesions.55 Clinical improvement was linked with a posttreatment decrease in anterior uveitis regardless of its cause because failure to control inflammation leads to serious complications. Topical or systemic administration depends on drug formulation, severity of clinical signs, and location of inflammation.13 Anterior uveitis is initially treated topically, but if the inflammation remains poorly controlled by topical treatment alone, systemic therapy may be required.58

Corticosteroids are the drugs most commonly used to control ocular inflammation, but they are contraindicated in the presence of ulcerative or infectious keratitis.59 Topical corticosteroids can be used to treat anterior uveitis associated with systemic infectious disease without significant exacerbation of the infectious process.59 Prednisolone acetate achieves a high intraocular concentration and is the drug of choice for anterior uveitis.59 Topically, it is administered as a 1% suspension. Frequency of administration depends on the severity, location, and etiology of the disease process. One to six times daily up to hourly administration has been advocated for the suspension.53,59 Effective treatment results in normalization of IOP and decreased photophobia, blepharospasm, discharge, keratitis, and aqueous flare.59

Systemic corticosteroids may be necessary to supplement topical therapy when treating severe cases of anterior uveitis. These drugs have minimal effects on most forms of keratitis and control intraocular inflammation when topical corticosteroids are contraindicated.60 Although not previously reported, I (E. A.) have observed several cases of melting corneal ulcers in dogs receiving immunosuppressive doses of systemic corticosteroids. These patients should be monitored for the development of ulcerative keratitis. Therapy is instituted at a higher dose to suppress inflammation, followed by drug tapering for long-term maintenance. The recommended initial dose is 0.5 mg/kg PO bid for antiinflammatory effects, up to 1 mg/kg PO bid for immunosuppressive effects.59 The dose can then be decreased incrementally based on patient response. When an infectious disease is suspected, systemic corticosteroids should be used with caution because of their immunosuppressive effects. Appropriate antimicrobial therapy is recommended if systemic corticosteroid administration is required in the presence of a bacterial infection.

Available topical ophthalmic NSAIDs include suprofen (1%), diclofenac (0.1%), flurbiprofen (0.03%), and ketorolac (TABLE 2).

Antiiinflammatory drug therapy (corticosteroids and NSAIDs) is an extremely important consideration in treating anterior uveitis regardless of its cause because failure to control inflammation leads to serious complications. Topical or systemic administration depends on drug formulation, severity of clinical signs, and location of inflammation.13 Anterior uveitis is initially treated topically, but if the inflammation remains poorly controlled by topical treatment alone, systemic therapy may be required.58

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(0.5%). Flurbiprofen and suprofen are similar in their ability to reduce ocular inflammation.62 Flurbiprofen is well absorbed into ocular tissues, concentrates in the cornea, and has low systemic absorption.63 It can be used in conjunction with topical corticosteroids. Adverse effects include topical irritation and possible hemorrhage as a result of interference with platelet aggregation.64

Choices for injectable or oral NSAIDs include aspirin, acetaminophen, piroxicam, ketoprofen, meloxicam, carprofen, etodolac, and deracoxib. These drugs are commonly used for treatment of anterior uveitis when corticosteroids are contraindicated.65 Gastrointestinal effects and hepatopathy are the most significant adverse effects of their use.66 Keratoconjunctivitis sicca has been reported in dogs receiving oral etodolac.67

Cycloplegic drugs relieve pain by preventing ciliary body and iris muscle spasms, whereas mydriatic drugs prevent or break down posterior synecchia by dilating the pupil and decreasing iris-lens contact.13 Cycloplegia and mydriasis can be accomplished by using a parasympatholytic agent such as atropine sulfate. Atropine is a direct-acting parasympatholytic agent that blocks the postganglionic cholinergic receptor response, resulting in mydriasis, cycloplegia, and decreased tear production.59 It is often the drug of choice in management of inflammation of the anterior segment.59 Much of the pain associated with anterior uveitis is a result of inflammation and subsequent spasm of the iridal and ciliary body musculature.59 Atropine paralyzes these muscles, decreasing discomfort. Atropine also stabilizes the BAB.5,60 Topical atropine sulfate is formulated in a 1% ointment or solution. Duration and frequency of application depend on the severity of inflammation. Mild inflammation may require once-daily administration, whereas severe inflammation may require treatment three to four times a day.13 Atropine is contraindicated in glaucoma; therefore, IOP should be measured during the course of atropine therapy and immediately discontinued if evidence of glaucoma is observed.5,59

**Complications and Prognosis**

Intraocular inflammation can have many deleterious sequelae; therefore, treatment should be prompt, aggressive, and appropriate. Synecchia formation can lead to glaucoma by obstructing aqueous humor flow through the pupil or iridocorneal angle. Development of secondary glaucoma should be suspected when IOP is >10 mm Hg in eyes with anterior uveitis.13 Anterior uveitis may cause cataracts, the extent of which depends on the severity and duration of inflammation. Corneal endothelial damage from chronic anterior uveitis can cause corneal edema, often followed by deep corneal vascularization and scarring.8

The prognosis depends on the location, extent, and duration of inflammation; underlying cause; secondary complications; and timeliness/adequacy of treatment.12 Chances of recovery are greatest when the inflammation is mild to moderate and a treatable underlying cause can be found. Severe, recurrent anterior uveitis typically carries the poorest long-term prognosis.12 Systemic spirochetal and rickettsial infections have a good prognosis if treated promptly and aggressively, whereas the prognosis for systemic mycotic/algal infections and uveodermatologic syndrome is guarded to poor.12 The prognosis is good for most canine primary intraocular neoplasms because they are usually benign, whereas the outlook for multicentric or metastatic intraocular neoplasia remains guarded.6,12

**Conclusion**

Canine anterior uveitis is a complex ocular disorder with several etiologies. Understanding the pathophysiology, clinical signs, and potential etiologies can guide clinicians to a prompt, accurate diagnosis and appropriate therapy. Proper treatment is essential to alleviate patient discomfort, produce rapid recovery, and prevent secondary complications and permanent undesirable sequelae that may result in blindness or enucleation.
Canine Anterior Uveitis

30. Ocular Disorders Presumed to be Inherited in Purebred Dogs. 2nd ed. Phoenix, AZ: Genetic Committee of the American College of Veterinary Ophthalmologists; 1996.
1. Canine anterior uveitis
   a. presents with distinctive clinical signs.
   b. is almost always associated with a systemic infectious disease.
   c. is commonly idiopathic.
   d. can be treated effectively, easily, and with a low risk of complications.

2. The BAB
   a. is impermeable to constituents within blood and plasma.
   b. is not affected in patients with anterior uveitis.
   c. is composed of loosely adherent cells of the ciliary body and iridal blood vessels.
   d. leaks fluid, protein, and cells into the aqueous humor when compromised by inflammation, resulting in aqueous flare.

3. Which of the following is not a common mechanism responsible for ocular tissue injury resulting in anterior uveitis?
   a. damage to ocular tissue by infectious organisms
   b. topical drug administration
   c. immune-mediated mechanisms
   d. neoplastic invasion

4. __________ is not a diagnostic differential for anterior uveitis.
   a. Endothelial dystrophy
   b. Glaucoma
   c. Ulcerative keratitis
   d. Conjunctivitis

5. Which statement regarding aqueous flare is true?
   a. It is caused by increased protein and/or cells in the aqueous humor as a result of a disrupted BAB and is pathognomonic for anterior uveitis.
   b. It does not occur in dogs.
   c. It is caused by BAB breakdown in the iridocorneal angle.
   d. It occurs only when glaucoma is present.

6. The most common secondary ocular neoplasm in dogs is
   a. hemangiosarcoma.
   b. osteosarcoma.
   c. malignant melanoma.
   d. lymphoma.

7. Ocular blastomycosis
   a. can be ruled out by serology.
   b. can be treated cheaply and rapidly.
   c. is best diagnosed by direct visualization of fungal organisms.
   d. always results in enucleation of the affected eye.

8. Which statement regarding treating uveitis is true?
   a. Nonspecific therapy should never be employed until a definitive diagnosis is made.
   b. The primary goal should be to stop inflammation, relieve pain, and prevent or control complications.
   c. Oral corticosteroids are preferred over topical corticosteroid administration.
   d. Atropine is always recommended to relieve ocular discomfort.

9. Which statement regarding topical drug therapy for treating canine anterior uveitis is false?
   a. Prednisolone acetate suspension (1%) is a potent topical corticosteroid used in the treatment of canine anterior uveitis.
   b. Topical NSAIDs can be used in conjunction with topical corticosteroids.
   c. Atropine relieves ocular pain by relaxing uveal muscle spasm.
   d. Hemorrhage due to interference with platelet aggregation is not a side effect of topical NSAID application.

10. Which statement regarding complications of anterior uveitis is true?
    a. Anterior uveitis rarely results in the development of glaucoma.
    b. Development of secondary glaucoma should be suspected when IOP is >10 mm Hg in eyes with anterior uveitis.
    c. Anterior uveitis does not cause cataracts.
    d. Development of blindness is a concern only with chorioretinitis, not anterior uveitis.