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“Ocular Emergencies”

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Objectives of the Presentation

- Be able to recognize congenital and inherited orbital diseases of domestic animals.
- To recognize the clinical signs associated with orbital disease.
- To formulate an appropriate diagnostic plan for affected animals.
- To determine medical and surgical options to treat orbital disease.

General Key Points

- Orbital disease is common in dogs and cats. It is frequently misdiagnosed and subsequently may be treated inappropriately.
- It is important to understand the general orbital anatomy to diagnose conditions that affect the orbit.
- The bony orbit is comprised of the frontal, lacrimal, zygomatic, presphenoid, basisphenoid and palantine bones.
- Differential diagnosis for orbital disease is based on orbital/peri-orbital anatomy. A limited number of structures are involved.
- Diseases of the sinuses (frontal, maxillary), teeth (upper fourth premolar, first and second molar) and ramus of the mandible may compress or invade the orbit.
- Intraorbital structures include the globe, cranial nerves (II-VII), blood vessels, gland of the third eyelid, lacrimal gland, zygomatic salivary gland, extraocular muscles, masticatory muscles, fat and periorbita.
- Alterations in any of the bony or soft tissues in the orbit may affect the position of the eye.
- Advanced diagnostic procedures are available to determine the extent and location of the lesion.

Key Clinical Diagnostic Points

- Obtain a complete history. This is essential to complete the work-up of all ophthalmic and orbital abnormalities. The onset and duration of the condition, clinical signs, eating behaviour, temperament and visual performance should be investigated.
- A change in the volume of contents of the orbit will affect the position of the globe. The orbit is examined indirectly. The eyelids, globe, function and appearance of the globe may change with orbital disease. (See Figure 1)
- Palpate the periocular tissues. Note any changes in colour, palpation and evidence of discomfort. Examine the ears.
- Retropulse the globe and compare to the normal eye.
- Examine the oral cavity. (See Figure 2) Dental radiographs may be indicated if gross abnormalities are not observed.
- Perform a neuro-ophthalmic exam.
- Three primary signs of orbital disease are exophthalmos, enophthalmos and strabismus.
- Secondary signs of orbital disease include changes in vision, ocular movements, eyelid and nictitating membrane position, pupillomotor function, sensation, vascular engorgement, corneal or conjunctival exposure and pain upon opening the mouth.
- Clinically, conjunctival hyperaemia, chemosis, elevation of the nictitating membrane (See Figure 3), lagophthalmos, exposure keratitis, abnormal papillary light reflexes and scleral inflammation may be noted.
- Key diagnostic tests include CBC, serum biochemical profile, cytological examination of fine needle aspirates, radiographs, ocular ultrasound, Computerized Tomography (CT) and Magnetic Resonance Imaging (MRI). (See Figure 4)
- Aspiration cytology is often necessary to obtain an accurate diagnosis. Damage to important orbital structures, infection, failure to obtain a representative sample and possible need for anaesthesia or sedation are disadvantages.
- Radiographs are useful if bony or sinus disease is expected. Films may be difficult to interpret and general anaesthesia is necessary for proper positioning.
- B-scan ultrasonography is helpful in soft tissue disease but bony structures are not imaged well.
- Advanced diagnostics are generally necessary for appropriate surgical planning.
Surgical exploration of the orbit may be necessary if less invasive techniques fail to yield a diagnosis. Surgery may be therapeutic and diagnostic. Disadvantages include the need for anaesthesia, advanced surgical training, infection, damage to vital structures and expense. (See Figure 5)

Key Etiologic and Pathophysiologic Points

- Orbital disease is classified as inflammatory, neoplastic or cystic.
- Congenital and inherited conditions include microphthalmos, divergent strabismus in brachycephalics and convergent strabismus (autosomal recessive in the Siamese cat).
- Acquired orbital diseases that cause exophthalmos include proptosis, orbital cellulitis, retrobulbar abscess, eosinophilic myositis, extraocular polymyositis, neoplasia, orbital emphysema, zygomatic mucocele, retrobulbar haemorrhage, granuloma and pseudotumor.
- Causes of enophthalmia include ocular pain, dehydration, emaciation myopathies, periorbital fraction or trauma, Horner’s syndrome, microphthalmia or ptosis bulbi and space occupying lesions anterior to the globe.
- Proptosis--exophthalmia with contracture of the eyelids behind the globe. Animals hit by cars and bite wounds are the most common causes.
- Orbital cellulites/retrobulbar abscess--these conditions are most common in dogs which chew on bones or sticks. Physical exam may allow for a diagnosis: swelling caudal to the fourth premolar and the presence of pain upon opening the mouth.
- Eosinophilic myositis--German Shepherds, Shetland sheepdogs, Golden Retrievers and Weimaraners. Enophthalmia may occur in long standing cases from post-inflammatory fibrosis. The diagnosis is made by the breed, pain on opening the mouth, bilaterally swollen extraocular muscles and muscle biopsy.
- Extraocular polymyositis--bilateral exophthalmia in dogs due to localized swelling and inflammation of the extraocular muscles. (See Figure 6) The condition is presumed to be immune-mediated and is responsive to steroids. The Golden Retrievers, Doberman and Springer Spaniels are predisposed. Dogs are generally young (8 months).
- Neoplasia--primary, metastatic or an extension from adjacent tissues. CT scan or MRI may be necessary for surgical planning. The prognosis is usually poor as lesions are often malignant.
- Orbital emphysema--may occur after fracture or trauma to a sinus or following orbital surgery.
- Zygomatic mucocele--may cause exophthalmos or enophthalmos. A fluctuant cyst may be aspirated.
- Retrobulbar haemorrhage--secondary to trauma, patients with bleeding disorders or neoplasia.
- Retrobulbar granuloma/pseudotumor--due to parasite migration, foreign body or fungal infection.

Figure 1. Exophthalmos in a cat due to retrobulbar tumor.

Figure 2. Extension of orbital disease into the oral cavity of a cat.
Figure 3. Elevated nictitans due to change in volume of the orbital contents in the left eye of this dog.

Figure 4. CT scan of a dog with clinical signs of exophthalmos. A hyperechoic cystic structure is noted ventral to the zygomatic arch.

Figure 5. Illustration of a lateral orbitotomy in a dog. The zygomatic arch has been transected and reflected dorsally.

Figure 6. Extraocular polymyositis in a Golden Retriever. Bilateral exophthalmos is noted.

Key Therapeutic Points

Identifying the cause of orbital disease is essential to determining an appropriate medical or surgical plan.

- Enucleation--removal of only the globe. An orbital prosthesis may be placed to reduce indentation of the soft tissues. A prosthesis is contraindicated when infection or neoplasia are present.
- Exenteration--removal of all the orbital contents and the globe. This is indicated when orbital neoplasia or infection are suspected. An orbital prosthesis is not recommended.
- Evisceration and intraocular prosthesis--the intraocular contents are removed and a silicone cosmetic implant is placed inside the corneo-scleral shell. Contents of the glove should be submitted for histopathology. This procedure is contraindicated when infection, neoplasia, corneal ulcer, dry eye or other inflammatory disease is present.
Orbitotomies--surgical approaches to the orbit ranging from superficial dissection of the anterior orbit through the conjunctiva to extensive lateral approaches involving reflection of the zygomatic arch. Damage to sensitive ocular structures may occur and may lead to vision loss or altered ocular motility.

Orbital cellulitis and abscess are treated by identifying the affected tissues and establishing surgical drainage, local irrigation and antibiotic therapy. Diseased teeth should be extracted. The wound should be left to heal by second intention.

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Masticatory myositis--treatment involves administration of immunosuppressive doses of corticosteroids (2mg/kg q 12 h) for 14-21 days. Azathioprine (2 mg/kg PO q 24 h) may be effective as adjunct therapy.

Extraocular polymyositis--corticosteroids (2 mg/kg q 12 h) +/- Azathioprine (2 mg/kg PO q 24 h).

Cystic orbital disease--broad spectrum antibiotic therapy with surgical intervention in certain cases.

Key Prognostic Points

Inflammatory conditions generally have a favourable prognosis if identified early in the disease process and appropriate antimicrobial or anti-inflammatory therapy is administered.

Any retrobulbar inflammatory process may cause vision loss due to damage of the optic nerve.

Frequent lubrication is necessary to reduce progressive corneal disease.

Retrobulbar tumours generally are malignant and either requires enucleation or orbitotomy as a salvage procedure. Recurrent disease is possible as adjacent tissues may be affected.

Secondary sequelae or orbital disease may include dry eye, prolapsed gland of the nictitans, deviated globe position, vision loss and corneal scarring.

Overview of the Issue

Diseases affecting the orbit may cause severe alteration to ocular function. Recognizing the clinical signs of exophthalmos, strabismus, decreased retropulsion of the globe, reduced mobility of the temporomandibular joint, vision loss and inflammation of the adjacent tissues are important factors for the best opportunity to save vision and the globe. A thorough history, complete physical and ophthalmic exam, diagnostic procedures to include ultrasound, aspiration cytology, CT or MRI may be necessary to characterize the lesion. Targeted specific antimicrobial therapy for susceptible organisms and anti-inflammatory therapy for immune-mediated processes help to restore ocular function. Surgical drainage of infectious processes may be necessary. Orbital surgery may be performed in cases where the globe must be removed due to extensive disease or orbitotomies to permit the most tissue to be salvaged.

Summary

Animals that present with clinical signs of orbital disease require a meticulous and thorough work-up to offer the best prognosis. Advanced diagnostic techniques are available to help localize the lesion in order to determine the recommended therapeutic approach. A combination of medical and surgical modalities are used to treat conditions that affect the orbit.

References

Objectives of the Presentation

What do I need to know about the anterior intraocular portion of the eye? How do you diagnose, differentiate and treat diseases affecting the lens and anterior uvea? Should your practice have a Tonopen® or Tonovet®? Anterior segment disease are among the most common and devastating diseases of the canine and feline eye.

General Key Points

- All red eyes should have their intraocular pressure determined.
- Every small animal practice should be able to accurately determine IOP in a reliable manner.
- All diabetic dogs will get cataracts. The incidence is 80% within the first year of onset of diabetes.

Key Clinical Diagnostic Points

- Glaucoma should be divided into acute vs. chronic and primary vs. secondary.
- Primary glaucoma has a 50% risk of becoming bilateral within 2 years of the first eye becoming affected.
- Anterior uveitis may be a manifestation of a systemic disease and a complete physical examination and lab work are often indicated.
- Cataracts are not an isolated event. If left untreated they can result in lens-induced uveitis, lens luxation, glaucoma and retinal detachment.
- In general, canine cataracts are considered inherited unless another aetiology is apparent.

Key Etiologic and Pathophysiologic Points

- The blood flow to the eye is amongst the highest by mass of any organ in the body. This makes the eye highly susceptible to hematogenously disseminated diseases such as neoplasia, mycotic infections, and septicaemia. Also vascular disorders such a hypertension, IHA and ITP may manifest as ocular conditions.
- Diabetic cataracts with an acute onset can experience spontaneous lens capsule rupture and acute phacoanaphylaxis.

Key Therapeutic Points

- While the anterior segment of the eye can be reached by selected topical therapy, systemic therapy may be indicated and is required if there is involvement of the vitreous, retina and choroid.
- The contralateral, at risk eye, should be monitored and treated in dogs with primary glaucoma.
Additional Detail

Cataracts

1. Any opacity of the lens without regard to aetiology
2. Causes of cataracts in dogs:
   a. Inherited is the number 1 cause!!!!
   b. Diabetes mellitus
   c. Nutritional disorders:
      i. Arginine or other amino acid deficiencies
      ii. Xylose excess: rats
      iii. Galactosemia: kangaroos, wallabies fed cow’s milk
   d. Progressive Retinal Atrophy (PRA) - dialdehyde toxins are released from the degenerating retina causing subcapsular and cortical lens opacities
   e. Electrolyte/mineral imbalances: hypocalcaemia
   f. Trauma
   g. Inflammation (uveitis) = especially cats and horses
   h. Electric cord shock
   i. Irradiation (radiation therapy for cancer)
   j. Toxins or drugs - corticosteroids in humans, disophenol (DNP), naphthalene in dogs, hygromycin in sows; DMSO: transient
   k. Senility - may refer to time of onset and aetiology (not nuclear sclerosis)
   l. Persistent vascular remnants
3. Classification of cataracts:
   a. By age of onset (does not imply aetiology):
      i. Congenital: Present at birth
      ii. Juvenile: Few months to 6 years
      iii. Senile: Dog >6 years
   b. By location (determined by slit lamp biomicroscopy):
      i. Capsular
      ii. Subcapsular (anterior, posterior, equatorial)
      iii. Cortical
      iv. Nuclear
      v. Axial
      vi. Polar
   c. By degree of maturation:
      i. Incipient (less than 10% of tapetal reflection obstructed)
      ii. Early Immature (10 to 50% of tapetal reflection obstructed) - refer at this stage to increase success of the surgery
      iii. Late Immature (51 to 99% of tapetal reflection obstructed)
      iv. Mature (100% of tapetal reflection obstructed)
      v. Hyper-mature (cortical lens material may undergo liquefaction and part of the tapetal reflex may be seen; the lens capsule may be wrinkled with multifocal dense white plaques, the anterior chamber depth may be increased, may see signs of lens-induced uveitis)
4. Tendency to progress:
   a. Nuclear: often static
   b. Cortical: variable, often progressive
   c. Equatorial: often progressive
5. Sequelae to cataracts:
   a. These dogs should not be used in a breeding program
   b. If selling animal, the buyer must be told!
   c. The dog will probably lose vision
   d. Chronic or hyper-mature cataracts will develop lens-induced uveitis, may develop secondary glaucoma and retinal detachment
6. Treatment of cataracts:
   a. Rule out diabetes mellitus
b. There is no medical therapy for cataracts!

c. Surgery is the treatment of choice - phacoemulsification with intraocular lens implantation

d. Surgical success rates: best outcome (>95% success) if the cataract is immature, success decreases to
>85% if cataracts is hyper-mature

7. Surgical techniques:
   a. Phacoemulsification with intraocular lens prosthesis placement
   b. There is no laser treatment for cataracts!!! ND:YAG laser is used often in human patients for secondary
      cataracts (we call this posterior capsular opacification, PCO)
   c. If the cataract is subluxated or luxated, it will require intracapsular extraction (ICCE) and a sulcus intraocular
      lens prosthesis can be sutured into the eye
   d. Lifelong monitoring post-surgery for uveitis, glaucoma and retinal detachment - RDVM/ophthalmologist

**Lens Subluxations and Luxations**

1. Aetiology (all involve degeneration or damage to the ciliary zonules):
   a. Primary/inherited - most terrier breeds
   b. Secondary to glaucoma (buphthalmia causes the zonules to break)
   c. Secondary to chronic uveitis (especially in cats)
   d. Associated with hyper-mature cataracts
   e. Trauma (uncommon)

2. Clinical signs:
   a. Aphakic crescent (a portion of the pupil is devoid of the lens)
   b. Iridodonesis and phacodonesis (quivering of the iris and lens, respectively)
   c. Deep anterior chamber if lens is posteriorly displaced
   d. Shallow anterior chamber if lens is anteriorly displaced
   e. Blepharospasm, corneal edema and increased intraocular pressure especially if anterior lens luxation;
      usually acute
   f. Complications of lens luxation: corneal endothelial damage (corneal edema), glaucoma, anterior uveitis

3. Treatment of lens luxation:
   a. Surgical intervention: intracapsular lens extraction (ICLE)
   b. This is a surgical emergency if the lens is anteriorly luxated
   c. Even a posterior luxation requires removal because leaving the lens will predispose the eye to chronic
      uveitis, glaucoma and retinal detachment
   d. Prognosis is dependent on the cause, duration of the luxation and extent of secondary damage

**Nuclear Sclerosis**

1. Aging change due to compression of nucleus by cortical fibers

2. Age of onset:
   a. Dog: 6 years
   b. Cat: 9 years
   c. Horse: 15 years

3. Diagnosis is made by dilating the pupil and seeing the fundic reflex

4. If this progresses to the point where the dog is blind and the fundic reflex is not visualized, then this has become a
   nuclear cataract

5. Treatment: None

**Anterior Uveitis**

1. Clinical signs: Miosis, flare, redness, photophobia, pain, keratitic precipitates, hypotony

2. Etiologies. The etiologies of anterior uveitis can be either ocular or systemic.
   a. Ocular:
      i. Corneal ulceration - can result in a neurogenic reflex anterior uveitis.
      ii. Lens-induced - a hypermature cataract can result in anterior uveitis as a result of the leakage of
         lens protein into the anterior chamber.
      iii. Ocular trauma - penetrating or blunt trauma.
      iv. Neoplasia - primary.
Ocular Emergencies

b. Systemic: In general any systemic neoplasia, bacteremia, viremia, or septicemia can result in anterior uveitis. A complete physical examination is therefore essential.
   i. Dog: Infectious: Ehrlichiosis, Rocky mountain spotted fever, Mycoses (Blasto, Crypto, Histo, Toxo), Lyme disease, Prothecosis, Brucellosis, Distemper, Infectious hepatitis, Autoimmune: SLE, Uveodermatologic syndrome (VKH)
   ii. Cat: FeLV, FIP, FIV, Toxo, Mycotic, Bartonella

3. Diagnostic tests:
   a. History:
      i. Duration, progression of disease
      ii. Other physical changes such as weight loss, anorexia, vomiting, diarrhea are very important
      iii. Environment? Does this animal have exposure to other animals? to mycotic organisms etc?
   b. Physical examination - a complete physical examination must be performed on all animals with anterior uveitis. Carefully evaluate the lymph nodes, liver, spleen, auscultate the chest, take the temperature, etc.
   c. Complete blood count:
      i. WBC count? Differential?
      ii. Platelet count? If low consider rickettsial agents.
      iii. Biochemical profile
      iv. Serology:
         1. Blasto, Histo, Crypto
         2. RMSF, Ehrlichia canis/platys, Lymes, ICH, Distemper
         3. FeLV, FIV, Bartonella
         4. Toxo - request IgG, IgM, and Toxo antigen tests
   e. Ultrasound of the eye to examine the posterior portions if they are not visible by ophthalmoscopy
   f. Cytology/histopathology

4. Treatment of anterior uveitis: As you can see from the extensive list of etiologies it is impossible to give you one treatment that will apply to every case. We therefore divide treatment into specific and non-specific therapy.
   a. Specific:
      i. Directed towards the inciting cause
      ii. Requires you to correctly diagnose the etiology and, if possible, eliminate it
   b. Non-specific:
      i. Topical antiinflammatories:
      ii. Atropine 1%
      iii. Corticosteroids
      iv. Non-steroidal
      v. Systemic antiinflammatories:
      vi. Corticosteroids
      vii. Non-steroidal

5. Sequelae of anterior uveitis:
   a. Anterior &/or posterior synechia
   b. Cataract
   c. Glaucoma
   d. Blindness
   e. Phthisis bulbi

Glaucoma

1. Glaucoma, by definition, is an increase in the IOP to a level that is incompatible with the health of the eye
   a. Increased IOP - always the result of a decrease in outflow
   b. Decreased IOP - always the result of a decrease in production (uveitis)

2. All red eyes have glaucoma until proven otherwise

3. When presented with a glaucomatous eye the next questions to ask yourself are:
   a. Is the glaucoma primary or secondary?
   b. Is it acute or chronic?

4. The answers to these questions will help you to select the therapy of choice

5. Primary vs. secondary glaucoma:
   a. Primary:
      i. Not associated with any other ocular disease. No antecedent cause.
ii. This is generally seen in predisposed breeds:
   1. Poodle
   2. Basset hound
   3. American & English Cocker Spaniel
   4. Beagle
   5. English Springer Spaniel
   6. Chow Chow
   7. Arctic breeds - Husky, Elkhound, etc.
   8. Afghan
   9. Shar-Pei
   10. Other

iii. Further classified based on gonioscopy into open and narrow angle glaucoma. Without a goniolens you will not be able to subdivide into the various categories so you only need to be able to decide if the glaucoma is primary or not.

iv. These patients are unfortunately predisposed to bilateral involvement. Therefore if you are presented with a unilateral primary glaucoma it is essential that the other eye is evaluated and closely monitored. To the best of our knowledge the incidence of bilateral involvement is 50% within 2 years.

v. In addition to routine monitoring, the unaffected eye requires preventive therapy in the form of either systemic medication given to treat the affected eye which will also treat the predisposed eye, or topical medication administered to the predisposed eye

vi. Suggest repeated measurements of the intraocular pressure in the predisposed eye every 3–4 months for life or until the eye becomes glaucomatous

b. Secondary:
   i. The result of some other event in the eye which results in a decrease in aqueous humor access to the drainage angle or a decrease in outflow
   ii. It is essential to ascertain the cause for the glaucoma as therapy will vary according to etiology and in addition some of the inciting causes are systemic diseases that will threaten the life of the animal
   iii. With the exception of breed-related anterior lens luxation there is no predisposition to bilateral involvement
   iv. Etiologies:
      1. Anterior lens luxation
      2. Anterior uveitis
      3. Chronic retinal detachment
      4. Synechia
      5. Abnormal aqueous contents:
         a. Hyphema
         b. Hypopyon
      6. Neoplasia

6. Acute vs. chronic glaucoma:
   a. Acute:
      i. The acute glaucoma patient is rare to see, but if you are not certain if the eye has acute or chronic glaucoma always err on the side of acute and treat aggressively.
      ii. These patients are true medical &/or surgical emergencies. Hours make the difference between seeing and being blind.
      iii. Clinical signs:
         1. Corneal edema
         2. Sluggish PLR, pupil dilated
         3. Decreased to absent menace
         4. Pain - epiphora, blepharospasm
         5. Episcleral vessels engorged
      iv. Treatment:
         1. Medical therapy:
            a. Osmotic agents
            b. Carbonic anhydrase inhibitors - systemic and topical
            c. Prostaglandin analogues
            d. Autonomic agents
2. Surgical therapy
   a. All of these are referral procedures
   b. If you have attempted medical control of the glaucoma and have been unsuccessful then now is the time to contact the local veterinary ophthalmologist and discuss referral for surgical intervention
   c. Laser surgery:
      i. Cyclophotoablation
      ii. Endocyclophotoablation
   d. Filtering procedures
b. Chronic:
   i. These are not emergencies as is the case with the acute patient. These eyes are blind and the damage is irreversible.
   ii. Treatment of choice is generally surgical in order to effect the most rapid and cost effective cure
   iii. Clinical signs:
      1. Corneal edema
      2. Absent PLR, pupil dilated
      3. Absent menace response
      4. +/- Pain - epiphora, blepharospasm
      5. Episcral vessels engorged
      6. Corneal striae
      7. Retinal degeneration
      8. Cupped optic disc
      9. Buphthalmia - enlarged globe
   iv. Treatment:
      1. Surgical therapy:
         a. Evisceration with prosthesis - remove the internal contents of the globe leaving the fibrous tunic (cornea, sclera) behind. Insert a 19mm silicone sphere into the globe and suture the globe closed. Avoid trauma to the cornea.
            i. Post-surgery the cornea will vascularize over the next 2–4 weeks
         b. Enucleation
Glaucoma

Definition [<Gr. glaukos, gray, glistening]: A group of diseases characterized by increased intraocular pressure (IOP), resulting in damage to the ganglion cells and optic nerve.

It is the most frequent cause of irreversible blindness in dogs.

Anatomy and Physiology

The aqueous humor (AH) is the transparent fluid that fills the anterior and posterior chamber. It supplies the inner cornea and lens with nutrients.

AH is formed by three mechanisms; diffusion, ultrafiltration (hydrostatic pressure difference between capillaries in the ciliary body and the posterior chamber) and active secretion. Active secretion is the most important mechanism in AH formation. Carbonic anhydrase catalyzes the reaction: \( \text{CO}_2 + \text{H}_2\text{O} \rightleftharpoons \text{HCO}_3^- + \text{H}^+ \). The bicarbonate ion is followed by water into the posterior chamber.

The AH is produced at a relatively constant rate and flows into the posterior chamber. From there it moves into the anterior chamber then into the iridocorneal angle (the area between the cornea and the iris). The pectinate ligaments span the ICA.

The AH then flows either through the conventional or unconventional pathway. In the conventional route, the AH flows into the trabecular meshwork then into the scleral venous plexus and into the circulation (1) and (2) (ciliary, conjunctival and vortex veins). The unconventional route (3) is independent of IOP and accounts for a small amount of the aqueous humor outflow (15% in dogs and 3% in cats). The AH flows into the stroma of the iris, ciliary body and choroid, then into the systemic circulation. The rate of AH production equals AH outflow in normal dogs.

Causes

The IOP elevation is due to decreased aqueous humor outflow. Decreased aqueous humor outflow is caused by either primary or secondary ICA abnormalities as viewed by gonioscopy.

Primary ICA abnormalities are:

1. Goniodysgenesis: A continuous sheet of tissue bridging across the ICA in place of pectinate ligaments. Usually a few flow holes are present.
2. Narrow angle glaucoma: The ICA progressively narrows and causing the IOP to rise. As the IOP increases the ICA narrows and may collapse which results in a sudden increase in IOP.
3. Open angle glaucoma: Most common cause of glaucoma in humans but rarely seen in dogs.

Primary glaucomas are considered to be inherited condition that is ultimately bilateral. The list below is the most common breeds that I have documented primary glaucoma. Primary glaucoma is rarely seen in cats.

**Breeds Predisposed to Primary Glaucoma**

<table>
<thead>
<tr>
<th>Breed</th>
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<tbody>
<tr>
<td>Akita</td>
<td>Dalmatian</td>
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<tr>
<td>Alaskan Malamute</td>
<td>German Shepherd</td>
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<tr>
<td>Bassett Hound</td>
<td>Great Dane</td>
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<tr>
<td>Beagle</td>
<td>Norwegian Elkhound</td>
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<tr>
<td>Boston Terrier</td>
<td>Poodle</td>
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<tr>
<td>Bouvier des Flanders</td>
<td>Samoyed</td>
</tr>
<tr>
<td>Bull Mastiff</td>
<td>Shih Tzu</td>
</tr>
<tr>
<td>Cocker Spaniel</td>
<td>Shar Pei</td>
</tr>
<tr>
<td>Chow Chow</td>
<td>Siberian Husky</td>
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Secondary ICA abnormalities are:

1. Anterior lens luxation: The lens causes collapse of the ICA. Considered to be an inherited condition in terriers, Border collie and Shar Pei.
2. Anterior uveitis: Glaucoma occurs acutely due to blockage of the ICA with inflammatory cells and fibrin or in chronic cases by peripheral anterior synechiae or posterior synechiae (iris bombé). Most common cause of glaucoma in cats.
3. Intraocular neoplasia
4. Hyphema

**Clinical Signs**

Clinical signs of glaucoma can be very subtle in the early stages and can be interpreted as simple conjunctivitis. Injection of the episcleral vasculature is a result of venous blood shunting to more superficial vessels. The endothelial cells of the cornea are responsible for maintaining the cornea is a relatively dehydrated state. The elevated pressure damages these cells and hydrostatic pressure forces aqueous into the corneal stroma causing corneal edema. Blepharospasm indicates pain from stretching the nociceptive nerves in the choroid/sclera. The iris sphincter muscle undergoes ischemic necrosis and mydriasis results. Mild aqueous flare is evident in cases due to damage to the epithelial cells in the ciliary body allowing leakage of protein into the posterior chamber. Vascular and mechanical injury to the retinal ganglion cells and optic nerve cause decreased vision/blindness.

Chronic changes include the above clinical signs as well as the ones listed below. The sclera is able to stretch with chronicity and buphthalmia is clinically noted. Due to buphthalmia the zonules holding the lens rupture and lens subluxation is noted. Usually the lens is posteriorly luxated and incomplete (subluxation - as seen by an aphakic crescent). Optic disc cupping occurs with loss of ganglion cells and mechanical compression on the lamina cribrosa. The pressure may eventually return to normal due to extensive damage to the ciliary body.

**Diagnosis**

Normal IOP is between 15 to 25 mm Hg based on determining accurate IOP via tonometry. The Schiotz tonometer places a known weight on the cornea and the distance that weight can indent the eye is measured. The force resisting indentation
which is the IOP) can be calculated from the calibration tables. The applanation tonometer is more accurate and better for monitoring response to treatment. This device measures how much force is required to flatten the cornea in a given area.

There are a few things that will help you get consistent results. Elevated IOP will occur with overzealous restraint (occlusion of the jugular vein) or excessive eyelid restraint (excessive pressure placed on the globe). A normal area of the cornea should be assessed since scarring will artificially elevate the corneal resistance. The applanation tonometer only requires very slight touching of the cornea and aggressive pressure readings will be record elevated IOP. The condom on the applanation tonometer should be placed on snugly but not too tight. Both tonometers should be cleaned regularly.

Some cases of glaucoma will have intermittent blindness described by owners and on examination the pressure is normal. If it a case where glaucoma is suspected IOP curves should be recommended. This involves IOP checks every 2 hours for 12 to 24 hours. Some cases only have one pressure spike in 24 hours. This pressure spike over the long term can eventually cause significant retinal and optic nerve damage or turn into an acute glaucoma crisis.

Gonioscopy is performed to assess the ICA. Usually done on the “normal” eye since the cornea can be edematous or the pupil dilated, obscuring the ICA, making examination difficult. The ICA in one eye looks like the other eye.

**Therapy**

Once the diagnosis is established the potential to restore or preserve vision must be assessed in order to plan a course of treatment. Obviously if vision is present the ability to maintain vision is very good. If vision is absent it is necessary to determine how long the pressure has been elevated (are signs of chronicity present - very, very poor prognosis). Glaucoma can cause irreversible vision loss in a matter of days depending on the severity of IOP elevation. A study has shown necrosis and apoptosis of ganglion cells in retinas affected ≤ 1 day and end-stage retinal atrophy by day 7 in primary glaucoma cases.

In cases for potential preservation of vision, medical therapy should be instituted to lower the IOP as quickly as possible. The goal is to reduce the pressure to < 10 mmHg (the lower the better). I am not happy getting the pressure < 25 mm Hg. Emergency therapy for primary glaucoma cases that I use is as follows:

1. Xalatan 1 gtt: Check IOP in 30 minutes
2. If IOP < 25 mm Hg - recheck IOP 2 h
   >30 mm Hg - Cosopt 1 gtt q 15 min x 4 tx and 2.5–5 mg/kg Methazolamide
   PO - Check IOP in 30 minutes
3. If IOP > 30 mm Hg: Go to # 4 or Try IV Mannitol 1–2 mg/kg over 30 minutes
   Check IOP in 30 minutes - probably will not work
4. If IOP > 30 mm Hg: Surgery to save vision

Continue medical therapy to maintain pressure in normal range. Medical therapy is often temporary (patients become refractory) or may not be effective so long term reduction of IOP nearly always requires surgical intervention. If surgery is an option it should be done before significant optic nerve damage has been done.

Medical therapy should also be initiated on the apparently normal eye in primary glaucoma cases since this eye is a very high risk of developing glaucoma. Prophylactic therapy has been show to delay the onset of glaucoma, on average, to 31 months after the initial visit. Patients not receiving any medications developed glaucoma, on average, 8 months after the initial visit. Prophylactic therapy also forces the owner to examine the eye twice daily and hopefully this will allow for earlier detection of any abnormalities.

In cases of glaucoma secondary to lens luxation lens, removal is indicated on an emergency basis. Glaucoma secondary to anterior uveitis is best managed with medical therapy to control the inflammation (topical +/- oral corticosteroids) and the pressure (this can be a very unrewarding experience). If the anterior uveitis is secondary to lens induced uveitis then immediate removal of the cataractous lens is indicated.
Medical Therapy

The following is a list of the most commonly used anti-glaucoma medications, mechanism of action, side effects, clinical application, trade names and dosage recommendations:

1. Prostaglandin Analogues
   a. Mechanism of action: Reduce IOP by increasing unconventional outflow. Can be very effective in lowering IOP.
   b. Side effects: Miosis (can be very pronounced), conjunctival irritation and may worsen uveitis. Do not use in anterior lens luxations since it may result in pupillary blockade and worsening of the glaucoma. This is an expensive medication.
   c. Clinical application: Can be used for acute glaucoma (the only negative is that it can make examination of the optic nerve difficult post treatment) and long term management of glaucoma.
   d. Latanoprost (Xalatan®): Once daily is fine for most patients but resistant cases may require twice daily regimen. Acute glaucoma cases can respond within 30 minutes.
   e. Travoprost (Travatan®): Once daily to twice daily.
   g. Unoprostone isopropyl (Rescula®): Once daily.

2. ß-Blockers
   a. Mechanism of action: Reduce IOP by decreasing the formation of aqueous humor. Very weak IOP lowering effects.
   b. Side effects: Miosis (very mild) and reduces ability to heal epithelial defects (therefore do not use with corneal ulcers). Contraindicated in patients with lower airway disease or heart failure.
   d. Timolol (Timoptic®): Use the 0.5% solution not the 0.25% solution. Two times daily application.

3. Carbonic Anhydrase Inhibitors (CAI)
   a. Mechanism of action: Reduce IOP by decreasing the formation of aqueous humor (reduces active secretion by the non-pigmented epithelium of the ciliary body).
   b. Side effects: Topical medications are well tolerated but may exacerbate anterior uveitis (unexplained phenomena) and can cause ocular irritation. Oral CAIs cause GI disturbance and metabolic acidosis (panting resolves within the first few weeks of starting treatment).
   c. Clinical application: Acute glaucoma and long term management.
   d. Dorzolamide (Trusopt®): Three times daily application.
   e. Brinzolamide (Azopt®): Three times daily application.
   f. Methazolamide (Neptazane®): 2.5 mg/kg to 5 mg/kg orally two to three times daily.
   g. Dorzolamide + Timolol (Cosopt®): Two times daily application. I use this more frequently than dorzolamide alone.

4. Parasympathomimetics
   a. Mechanism of action: Reduce IOP by increasing outflow through the conventional pathway. Opens up the iridocorneal angle thereby decreasing resistance to aqueous humor passage.
   b. Side effects: Miosis (can be severe) and local irritation due to low pH. May exacerbate anterior uveitis. Do not use in anterior lens luxations since it may result in pupillary blockade and worsening of the glaucoma. GI disturbance can also occur.
   d. Pilocarpine (0.5% to 8%): Three to four times daily.

5. Hypersmotics
   a. Mechanism of action: Decreases ultrafiltration by the ciliary body. Reduces volume of the vitreous and aqueous humor with resultant decrease in IOP. Due to the volume loss in the vitreous the iris face moves posteriorly and thereby opens up the iridocorneal angle.
   b. Side effects: May overload cardiovascular system due to fluid overload with resultant pulmonary edema. Cerebral dehydration manifested as nausea, vomiting and altered consciousness. Avoid in patients with renal failure. Less effective if uveitis present since manitol will leak into the vitreous and aqueous humor.
   c. Clinical application: Acute glaucoma and secondary glaucoma due to anterior lens luxation.
   d. Mannitol: 1 to 2 g/kg IV over 20 to 30 minutes. Works within 30 minutes to one hour. Do not give water for 2 to 3 hours.

6. Calcium Channel Blockers
   a. Mechanism of action: Retinal ganglion cells (RGC) are injured in glaucoma due or mechanical and/or ischemic insults. The RGC release intracellular glutamate, which over stimulates glutamate receptors on
surrounding RGC causing calcium homeostasis (levels in the cell increase) to be disrupted. This RGC dies and the cycle continues. Therefore, once the damage begins it can be difficult to halt.

b. Side effects: Hypotension, therefore monitor blood pressure.
c. Clinical application: Acute glaucoma as a neuroprotective agent. May protect against glutamate-mediated excitotoxicity.
d. Amlodipine besylate (Norvasc®): 0.2 mg/kg once daily (use for the first few days).

Surgical Techniques to Save Vision

Surgical therapy is most effective if employed before significant optic nerve and ganglion cell damage has been done. The following surgeries can be done separately or in conjunction with each other.

1. Laser Cyclophotocoagulation (Laser CPC)

   The theory is to destroy part of the ciliary body with subsequent decrease in aqueous humor production. The pigmented cells of the ciliary body absorb the energy from the laser (780 to 850 nm) and coagulation necrosis occurs. A contact diode laser is applied to the sclera 4 mm posterior to the limbus (approximately 30 spots using 1000 mW for 5000 ms). Complications include uveitis, cataracts and corneal ulceration. The pressure may increase initially so frequent IOP recordings are needed immediately post-op (I will keep them in the hospital until the pressure stabilizes). Can take one to two weeks for the full effect to be appreciated. Can be very successful treatment. If the IOP spikes again it can be repeated.

2. Gonioimplant

   A shunt is placed in the anterior chamber and exits under the conjunctiva (increases aqueous humor outflow). Main complication is fibrosis over the tube under the conjunctiva, which prevents fluid outflow. Fibrosis needs to be resected and the implant will function again. The implants I place are mainly to control the IOP in the immediate post-op period after laser CPC.

Surgical Techniques for the Blind Eye

The following procedures are recommended only for non-visual eyes. In humans IOP over 35 mm Hg is considered painful so if the IOP is greater than 35 mm Hg I recommend one of the procedures listed below.

1. Enucleation

   Should be 100% successful. Procedure can be viewed in most surgical texts. Transpalpebral technique used for cases with corneal infection to decrease risk of post-operative infection. Should send eye in for histopathology to determine diagnosis.

2. Evisceration

   Can be used for chronic primary glaucoma and lens luxation cases. A 120° incision through the dorsal conjunctiva (approximately 3 to 5 mm behind the limbus). Incise sclera for 120° (do not incise the uveal tract). Insert cyclodialysis spatula between uvea and sclera and rotate to separate. Note - there will be bleeding in this procedure. Remove uvea (should only be attached at the optic nerve), lens and retina. Place silicone ball (2 mm larger than limbus to limbus diameter of normal eye) into globe with sphere introducer. Close sclera and conjunctiva (6-0 vicryl). Complications include corneal ulcers, infection and wound dehiscence. Procedure done for cosmetic results. Do not use if secondary glaucoma suspected due to bacterial or fungal infections or neoplasia. Post-operative medications include topical ophthalmic ointment, oral antibiotics and anti-inflammatory.

3. Pharmacologic Ciliary Body Ablation

   Inject 25 mg gentamicin (do not exceed the patient’s daily dose) and 1 mg dexamethasone into vitreous (20 gauge needle inserted 6 to 8 mm posterior to limbus directed towards the optic nerve). Can try to aspirate 1 cc of vitreous
prior to injection but I usually find the vitreous too viscous. Variable results, from phthisis bulbi (10%) to inadequate pressure control (effective in lowering pressure in 65% of cases). Chronic inflammation may result. May take a month for the pressure to lower. Do not use for intraocular neoplasia or infection. Less effective in primary lens luxation cases. I reserve for patients that are at risk for complications with general anaesthesia.

References

Anatomy/Physiology

1. Aqueous Humor Dynamics

- The aqueous humor is normally under pressure in the eye. This is termed the intraocular pressure (IOP) and is measured in mmHg. It can be measured clinically using a Schiotz tonometer or a Tonopen in private practice.
- Remember the pressure is evenly distributed in the eye. The pressure on the inner cornea = the pressure on the retina.
- Normal IOP--15-25mmHg
- Glaucoma-->25-30mmHg
- Anterior uveitis--<10-15mmHg
- Anterior uveitis & secondary glaucoma--<10 to >30mmHg

2. Production

- The ciliary body, specifically the epithelial cells of the folds of the pars plicata, is the site of the production of aqueous humor. These cells are separated from the systemic circulation by tight junctions that serve as part of the Blood-aqueous barrier. This is a barrier to the passage of larger molecules and cells into the aqueous.
- The aqueous humor is produced by a combination of:
  - Active production--50% of the production
  - Passive diffusion
  - Ultrafiltration
- The active portion of secretion is dependent on the enzyme carbonic anhydrase, ATP, glucose, and the local environment (temp, pH, osmolality, etc). Interference with any of these will decrease the production of aqueous.
- The enzyme carbonic anhydrase can be inhibited pharmacologically. This is used clinically in the management of glaucoma.
- Anterior uveitis will alter the local environment, changing pH, glucose concentration, etc, and resulting in a decrease in aqueous production. This is the reason for the low IOP seen in anterior uveitis.
- It would appear that the rate of aqueous production is also under some degree of neuronal control as various autonomic agents are capable of decreasing production.

3. Outflow

- The aqueous circulates from the ciliary epithelium, between the iris and lens (posterior chamber), through the pupil, and into the anterior chamber. From here it travels peripherally to the junction of the base of the iris and the cornea. This is the iridocorneal angle and is the site of entry of the aqueous into the outflow pathway. At the iridocorneal angle the base of the iris is connected to the cornea by the Pectinate ligaments.
- Once through the iridocorneal angle the aqueous enters the trabecular meshwork which it must percolate through in order to reach the blood venous system. The trabecular meshwork is the site of resistance to outflow and the reason the pressure inside the eye does not equal that outside.
- The trabecular meshwork is part of the ciliary musculature and as such is under parasympathomimetic control. Parasympathomimetic agents (pilocarpine) will result in contraction of this muscle, decreasing the resistance to outflow, and lowering the IOP. Conversely, parasympatholytic agents (atropine) will paralyze this muscle, increasing resistance and decreasing outflow.
The iridocorneal angle is not just a histologic term. The angle can be seen clinically in the normal cat and horse with a penlight. In the dog and human a contact lens, termed a goniolens, is used to aid in visualization of the drainage angle. The technique is termed **Gonioscopy**.

### Diagnostic tests

1. **Penlight Examination (Private Practice)**
   - Evaluate for pupil size, PLR, corneal transparency, lens position, presence of flare.
   - **Mydriasis**—Dilated Pupil. This is the result of an elevation in IOP >40mmHg paralyzing the iris sphincter (efferent) or, if the increase in the IOP is chronic, retinal degeneration results (afferent).
   - **Miosis**—Constricted Pupil. When seen in combination with increased IOP suggests concurrent uveitis.
   - A sluggish to absent PLR is expected in the glaucomatous eye. Is there a consensual to the unaffected eye? If the answer is yes this indicates some retinal function remains in the glaucomatous eye.
   - Diffuse corneal edema is common with IOP >40mmHg. Edema is the result of endothelial cell damage and the hydrostatic pressure within the eye.
   - If the lens is luxated you must decide if it is primary and causing the glaucoma or secondary as a result of the glaucoma.
   - Flare combined with an increased IOP indicates concurrent uveitis.

2. **Biomicroscopy (Referral Center)**
3. **Fundic Examination**
   - This is very important in the glaucomatous eye. Evaluate the retina for blood vessel size and distribution, look for tapetal hyperreflectivity indicating retinal degeneration, is the optic nerve cupped? atrophic?
   - This examination will provide information that will aid you in staging the glaucoma and giving the owner a prognosis.

4. **Intraocular Pressure Determination (IOP)**
   - This is the only diagnostic test to definitively diagnose glaucoma.
   - You must be able to perform this in practice in order to diagnose and manage glaucoma.
   - The instrument of choice in practice is the **Tonopen**. If not available, a **Schiotz tonometer** may be used.
   - All red, blind, and painful eyes should have their IOP determined.
   - All eyes with fixed and dilated pupils, anisocoria, or anterior uveitis should have their IOP determined.
   - All predisposed breeds should have their IOP determined as part of the routine physical examination.

5. **PLR**
   - **Mydriasis**—Result of elevation in IOP >40mmHg paralyzing the iris sphincter (efferent) or, if the increase in the IOP is chronic, retinal degeneration will result (afferent).
   - **Miosis**—In combination with increase IOP suggests concurrent uveitis.
   - A sluggish to absent PLR is expected in the glaucomatous eye. Is there a consensual to the unaffected eye? This indicates some retinal function remains in the glaucomatous eye.

6. **Menace Response**
   - Remember a lack of menace response initially in the acute patient does not mean permanent blindness. Although it is a poor sign, the retina may simply be ischemic and when the IOP is reduced some vision may return.

### Glaucoma

- Glaucoma, by definition, is an increase in the IOP to a level that is incompatible with the health of the eye.
• **Increased IOP**—Always the result of a decrease in outflow
• **Decreased IOP**—Always the result of a decrease in production (uveitis)
• **All red eyes have glaucoma until proven otherwise**
• When presented with a glaucomatous eye the next questions to ask yourself are:
  o Is the glaucoma primary or secondary?
  o Is it acute or chronic?

The answers to these questions will help you to select the therapy of choice.

*Primary vs Secondary Glaucoma*

1. **Primary**

   • Not associated with any other ocular disease. No antecedent cause.
   • This is generally seen in predisposed breeds:
     o Poodle
     o Basset hound
     o American & English Cocker Spaniel
     o Beagle
     o English Springer Spaniel
     o Chow Chow
     o Artic breeds--Husky, Elkhound, etc.
     o Afghan
     o Shar-Pei
     o Other
   • Further classified based on gonioscopy into open and narrow angle glaucoma. Without a goniolens you will not be able to subdivide into the various categories so you only need to be able to decide if the glaucoma is primary or not.
   • These patients are unfortunately predisposed to bilateral involvement. Therefore if you are presented with a unilateral primary glaucoma it is essential that the other eye is evaluated and closely monitored. To the best of our knowledge the incidence of bilateral involvement is 50% within 2 years.
   • In addition to routine monitoring, the unaffected eye requires preventive therapy in the form of either systemic medication given to treat the affected eye which will also treat the predisposed eye, or topical medication administered to the predisposed eye.
   • Suggest repeated measurements of the intraocular pressure in the predisposed eye *every 3-4 months* for life or until the eye becomes glaucomatous.

2. **Secondary**

   • The result of some other event in the eye which results in a decrease in aqueous humor access to the drainage angle or a decrease in outflow.
   • It is essential to ascertain the cause for the glaucoma as therapy will vary according to etiology and in addition some of the inciting causes are systemic diseases that will threaten the life of the animal.
   • With the exception of breed-related anterior lens luxation there is no predisposition to bilateral involvement.

   a. **Etiologies**
      a. Anterior lens luxation - the lens, when displaced forwards, can obstruct the flow of aqueous humor through the pupil or at the iridocorneal angle. Etiologies for this include:
         i. Breed related—Terriers
         ii. Trauma
         iii. Secondary to glaucoma--Here the luxation is the result of rather than the cause for the glaucoma.
         iv. Displacement by an intraocular neoplasia
         v. Regardless of the etiology, if the lens is resulting in glaucoma, the treatment of choice is surgical removal. This is a referral surgery and is an emergency.
         vi. Remember in the Terrier breeds to always look at the opposite eye, it may also have a lens luxation or subluxation.
vii. Lens luxation as a result of glaucoma is seen only with chronic glaucoma and the eye is permanently blind. Treatment for these is also surgical, but involves either an evisceration with a prosthesis or an enucleation.

b. Synechia - Synechia are adhesions between the iris and the lens (posterior) or cornea (anterior). They are always the result of inflammation of the anterior segment (anterior uveitis). It is essential to try and ascertain the etiology of the inflammation as it might be a symptom of systemic disease. These animals require a complete physical examination, CBC, Biochemical profile, and possibly serologic testing. Treatment of these patients takes 2 forms:
   i. Treatment of the inciting cause of the inflammation
   ii. Treatment of the glaucoma. This is usually unrewarding and most of these eyes will become chronic glaucoma eyes and require surgical removal or a prosthesis. Remember to submit any tissues removed for histology, especially if the etiology is uncertain.
   iii. Avoid treatment with Parasympathomimetics (Pilocarpine) as they will exacerbate the inflammation, or Parasympatholytics (Atropine) as it will exacerbate the glaucoma.

c. Abnormal aqueous contents - Abnormal accumulations of material in the anterior chamber can result in obstruction of the aqueous outflow at the iridocorneal angle. It is essential to attempt to establish the reason this material is in the anterior chamber.
   i. Hyphema = Blood in the anterior chamber, which may be caused by
      1. Clotting disorders
      2. Trauma
      3. Hypertension
      4. Intraocular neoplasia

Hyphema alone does not require treatment. It may result in glaucoma and then treatment is indicated. Also the etiology of the hyphema may require treatment.

   ii. Hypopyon = WBC’s in the anterior chamber. This is usually sterile, and may be caused by:
      1. Corneal ulceration--severe
         a. Septicemia
         b. Bacteremia
      2. Neoplasia – Primary or Secondary

Acute vs. Chronic Glaucoma

Acute

- The acute glaucoma patient is rare to see, but if you are not certain if the eye has acute or chronic glaucoma always err on the side of acute and treat aggressively.
- These patients are true medical &/or surgical emergencies. Hours make the difference between seeing and being blind.

Clinical Signs

- Corneal edema
- Sluggish PLR, pupil dilated
- Decreased to absent menace
- Pain--epiphora, blepharospasm
- Episcleral vessels engorged
Treatment

Medical Therapy

1. Osmotic Agents
   a. This is the first drug of choice in the acute patient.
   b. The osmotic agent of choice is Mannitol:
      i. Mannitol 20%--administered intravenously
      ii. 0.5-1.0 gm/kg (5cc/lb)--given over 15-20 minutes
      iii. Withhold water for 3-4 hours
      iv. IOP reduction begins at 20-30 minutes; 4-6 hour duration of effect.
   c. Effect is to dehydrate the vitreous humor and lower IOP. Requires an intact blood-aqueous barrier to work
      therefore its efficacy is decreased with anterior uveitis.
   d. Alternate drug is oral glycerin--may induce vomiting.

2. Carbonic Anhydrase Inhibitors
   a. Systemic
      i. These affect the enzyme carbonic anhydrase which is required for the active production of aqueous.
         Therefore the rate of aqueous production is decreased.
      ii. The systemic CAI's of choice are Dichlorphenamide (Daranide®) or Methazolamide (Neptazane®)
      iii. Dichlorphenamide 2-5 mg/kg--orally BID-TID
      iv. Side effects:
         1. Metabolic acidosis--panting, depression, vomiting, diarrhea
         2. Hypokalemia
      v. The topical CAI most commonly used is 2% Dorzolamide (Trusopt®)
         1. Topically BID-QID
         2. Choice for prophylaxis?
   b. Topical
      i. This is a more recent form of carbonic anhydrase inhibitor
      ii. Dorzolamide 2% (Trusopt®). Also, Brinzolamide (Azopt®) and Dorzolamide:Timolol combination
         (Cosopt®)
         1. Expensive
         2. BID-QID frequency
         3. Mechanism of action as for systemic CAI’s
         4. Avoids systemic side effects
         5. Consider for prophylaxis in primary glaucoma patient

3. Autonomic Agents
   a. Parasympathomimetics
      i. Pilocarpine 2%
      ii. BID-TID topically
      iii. Increases outflow by constricting ciliary muscles
      iv. May result in miosis
      v. Contraindicated in eyes with anterior uveitis
      vi. Side effect:
         1. Topical irritation
   b. Sympathomimetics
      i. 1% Epinephrine or 0.1% Dipivalyl epinephrine (Propine®)
      ii. BID-TID topically
      iii. Increases outflow
      iv. Side effect:
         1. Topical irritation
   c. Beta-Blockers
      i. 0.5% timolol maleate (Timoptic®)
      ii. BID-TID topically
      iii. Reduces aqueous production
      iv. Side effects:
         1. Potential for Bronchoconstriction
         2. Potential for Bradycardia
   d. Alpha Agonists
i. 0.2% brimonidine (Alphagan®)
ii. 0.5-1.0% apraclonidine (Iopidine®)
iii. Very potent
iv. May make some animals, cats especially very ill, vomiting, etc.

4. Latanoprost 0.005% (Xalatan)
   a. Topical prostaglandin
   b. Associated with iris hyperpigmentation in humans
   c. May result in miosis and some discomfort
   d. BID

Surgical Therapy

- All of these are referral procedures.
- If you have attempted medical control of the glaucoma and have been unsuccessful then now is the time to contact the local veterinary ophthalmologist and discuss referral for surgical intervention.

1. Cyclocryosurgery
2. Laser surgery
   a. Cyclophotoablation—Transscleral or Endolaser
      i. Diode Laser—810 nm
      ii. Absorbed by pigment
      iii. Delivered transclerally
      iv. Start at 1500 mW for a duration of 1500 msec. Listen for 1 "pop" per site
      v. Treat 15-30 sites depending on the severity
   b. ND YAG laser
3. Filtering procedures

Glaucoma Filtration Surgery

Acute glaucoma is a frustrating disease with poor long-term success if treatment relies solely on topical and systemic medication. Canine glaucoma is now generally considered a surgical disease with medication designed to provide short term control or to serve an adjunct role with surgery. Surgical therapy for acute glaucoma includes cyclodestructive procedures such as cryosurgery or laser surgery or procedures designed to increase aqueous outflow, filtering surgery.

Glaucoma filtering surgery is designed to provide an alternate outflow pathway for the aqueous humor. The aqueous is usually redirected to the subconjunctival tissue space either through a filtering hole or through the implantation of a filtering device. Although the initial success with this procedure may be high, most filtering procedures ultimately fail due to fibrosis/occlusion of the new outflow pathway. Filtering procedures work best when used in conjunction with additional medical and surgical therapies and when they are intended only to function for a short time. This is a referral procedure.

Implants used in veterinary medicine:

- Baerveldt
- Krupin-Denver valve
- Molteno implant
- Ahmed™ Glaucoma valve
- Joseph device
- Silastic tube implant

Chronic

- These are not emergencies as is the case with the acute patient. These eyes are blind and the damage is irreversible.
- Treatment of choice is generally surgical in order to effect the most rapid and cost effective cure.
Clinical Signs

1. Corneal edema
2. Absent PLR, pupil dilated
3. Absent menace response
4. +/- Pain--epiphora, blepharospasm
5. Episceral vessels engorged
6. Corneal striae
7. Retinal degeneration
8. Cupped optic disc
9. Buphthalmia--enlarged globe

Treatment

1. Surgical therapy
   a. Evisceration with Prosthesis
      i. Remove the internal contents of the globe leaving the fibrous tunic (cornea, sclera) behind. Insert a
         19mm silicone sphere into the globe and suture the globe closed. Avoid trauma to the cornea.
      ii. Post-surgery the cornea will vascularize over the next 2-4 weeks.
   b. Enucleation

2. Pharmacologic ablation
   a. Involves the intravitreal injection of a substance toxic to the eye (gentamicin, cidofovir (Vistide®)) in the hope
      that this will result in the destruction of the ciliary body, thereby lowering the intraocular pressure. In the
      author’s opinion, this is a potentially dangerous method for the management of glaucoma. This is an
      irreversible, inaccurate, and sometimes painful procedure. A significant portion of the eyes treated in this
      manner will have corneal opacification and will undergo phthisis bulbi. These results are cosmetically
      unacceptable and will often result in enucleation. In addition, many animals referred for a diagnosis of
      glaucoma do not have glaucoma. Intravitreal pharmacologic ablation in these eyes would be a grave error.

Table 1. Clinical signs of acute and chronic glaucoma.

<table>
<thead>
<tr>
<th>Acute</th>
<th>Chronic</th>
</tr>
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<tbody>
<tr>
<td>Pain</td>
<td>Discomfort—often subclinical</td>
</tr>
<tr>
<td>Sluggish PLR</td>
<td>Absent PLR</td>
</tr>
<tr>
<td>Weak—absent Menace</td>
<td>Blind</td>
</tr>
<tr>
<td>Corneal edema</td>
<td>Corneal edema +/- striae</td>
</tr>
<tr>
<td>Episceral hyperemia</td>
<td>Episceral hyperemia</td>
</tr>
<tr>
<td>Mydriasis</td>
<td>Mydriasis</td>
</tr>
<tr>
<td>Epiphora</td>
<td>Buphthalmos</td>
</tr>
<tr>
<td>Blepharospasm</td>
<td>Corneal vascularization</td>
</tr>
<tr>
<td></td>
<td>Retinal degeneration</td>
</tr>
<tr>
<td></td>
<td>Optic nerve cupping</td>
</tr>
</tbody>
</table>
Table 2. Common breeds with primary glaucoma.

- Beagle
- Basset Hound
- American Cocker Spaniel
- Siberian Husky
- Malamute
- Dalmatian
- Bouvier des Flandres
- English Springer Spaniel
- Akita
- Chow Chow
- Shar Pei
- Miniature Poodle
- Norwegian Elkhound
- Samoyed

Table 3. Therapy for acute glaucoma.

<table>
<thead>
<tr>
<th></th>
<th>Dose</th>
<th>Mechanism of action</th>
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</thead>
<tbody>
<tr>
<td><strong>Osmotics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mannitol</td>
<td>0.5 gm/kg IV</td>
<td>Osmotic effect to dehydrate the vitreous and aqueous</td>
</tr>
<tr>
<td><strong>Carbonic Anhydrase Inhibitors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systemic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methazolamide (Neptazane®)</td>
<td>2-5 mg/kg q8-12h</td>
<td>Decrease aqueous production</td>
</tr>
<tr>
<td>Dichlorphenamide (Daranide®)</td>
<td>2-5 mg/kg q8-12h</td>
<td>Decrease aqueous production</td>
</tr>
<tr>
<td><strong>Topical</strong></td>
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<td>Dorzolamide 2% (Trusopt®)</td>
<td>q8h</td>
<td>Decrease aqueous production</td>
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<td>Dorzolamide:Timolol (Cosopt®)</td>
<td>q8h</td>
<td>Decrease aqueous production</td>
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<td><strong>Parasympathomimetics</strong></td>
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<td>Direct acting miotics</td>
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<tr>
<td>Pilocarpine 2% (Isopto-Carpine®)</td>
<td>q8-12h</td>
<td>Increase aqueous outflow</td>
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<tr>
<td>Carbachol 1.5% (Isopto-Carbachol)</td>
<td>q8-12h</td>
<td>Increase aqueous outflow</td>
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<td><strong>Cholinesterase Inhibitors</strong></td>
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<td>Indirect acting miotics</td>
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<td>Demecarium 0.125-0.25%</td>
<td>q12-24h (Humorsol®)</td>
<td>Increase aqueous outflow</td>
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<td>Echothiophate 0.03-0.25%</td>
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<td>Increase aqueous outflow</td>
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<td>(Phospholine Iodide)</td>
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<td><strong>Sympatholytics</strong></td>
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<td>Timolol maleate 0.5% (Timoptic®)</td>
<td>q8-12h</td>
<td>Decrease aqueous production</td>
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<td>Dorzolamide:Timolol (Cosopt®)</td>
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<td><strong>Sympathomimetics</strong></td>
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<td>Epinephrine 1.0% (Epifrin)</td>
<td>q8-12h</td>
<td>Increase aqueous outflow</td>
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<td>Epinephrine 0.1% (Propine®)</td>
<td>q8-12h</td>
<td>Increase aqueous outflow</td>
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<td><strong>Alpha-2 Adrenergic Agonists</strong></td>
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<tr>
<td>Apraclonidine 0.5-1.0% (Iopidine®)</td>
<td>q12h</td>
<td>Decrease aqueous production</td>
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<tr>
<td>Brimonidine 0.2% (Alphagan®)</td>
<td>q8h</td>
<td>Decrease aqueous production</td>
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<td><strong>Prostaglandin Analog</strong></td>
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<tr>
<td>Latanoprost 0.005% (Xalatan®)</td>
<td>q12-24h</td>
<td>Increase uveoscleral outflow</td>
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The eyelids and conjunctiva are immunologically active structures with an extensive presence of blood vessels, lymphatics, and immune cells. Several immune-mediated phenomena can involve these structures either in isolation or in association with systemic clinical features, but, fortunately, they are rare diseases [1–5]. Immune-mediated blepharoconjunctival diseases are divided into two main categories: primary autoimmune disease in which the disease results from an attack against self-antigens and secondary immune-mediated disease in which the disorder results from exogenous material inducing the autoimmune disease. Such causes of secondary immune-mediated disease include infectious agents and drugs [6].

Although the pathogenesis of many ocular autoimmune diseases is known, most of the eye allergic disorders have not been well characterized in veterinary ophthalmology. Although conjunctival disorders used to be diagnosed and treated by ophthalmologists, when the eyelids are affected, the patient can be seen by either an ophthalmologist or a dermatologist. It is always necessary to rule out systemic involvement to coordinate therapy so as to treat the underlying disease rather than only ocular signs. Although clinical signs are different for every disorder, immune-mediated eyelid and conjunctival diseases share some characteristics, including itching, redness, and ocular discharge.

In human medicine, chronic presentation of these conditions can induce abnormal cicatrization leading to significant mechanical alterations as a result of fibrosis. In some chronic cases, the eyelid may need surgery to restore its physiologic function. In veterinary ophthalmology, there are no reports on chronic immune-mediated conjunctival and eyelid lesions without systemic signs. This article reviews the most important autoimmune and immune-mediated eyelid and conjunctival disorders in dogs.

AUTOIMMUNE EYELID AND CONJUNCTIVAL DISORDERS

Medial Canthal Ulcerative Blepharitis

This disease represents a juxtapalpebral disorder, usually affecting the medial canthus. Breeds most often affected include the German shepherd, long-haired...
dachshund, toy and miniature poodle, and others (Fig. 1A) [7,8]. In the German shepherd, the medial canthal blepharitis can be associated with pannus and immune-mediated plasma cell infiltration of the nictitating membrane. In the long-haired dachshund, medial canthal blepharitis may appear concurrently with superficial punctate keratitis. Even if it has not been described as a separated disease, the lateral marginal canthus can also be affected (Fig. 1B).

The condition is usually bilateral. Biopsy reveals lymphocytic and plasma cell infiltrates; sebaceous glandular hyperplasia may be also present. Antibodies against epithelial cells have been demonstrated in selected cases and may suggest a relationship to pemphigus. The condition usually responds to topical ophthalmic antibiotics and corticosteroids [7].

Vogt-Koyanagi-Harada-Like Syndrome
The Vogt-Koyanagi-Harada (VKH) syndrome in humans is an immune-mediated disease in which melanocytes are targeted [9]. The factor or factors responsible for the development of cellular hypersensitivity to melanin have not been elucidated, although specific circulating anti-melanin autoantibodies and melanin-sensitized lymphocytes have been reported in affected patients [10]. The possibility that VKH syndrome has an autoimmune pathogenesis is supported by the statistically significant presence of human leukocyte antigen DR4 (HLA-DR4 or human major histocompatibility complex [MHC] DR4) in affected individuals. This antigen has been commonly associated with other autoimmune diseases [10]. Darkly pigmented human races are predisposed, and there may be a genetic component of the disease as well given the high incidence of the condition among the Japanese. The clinical presentation can include anterior uveitis, chorioretinitis, exudative retinal detachment, poliosis, vitiligo, dysacusis, and meningitis. A similar disease syndrome has been reported in the dog, although meningitis is rarely reported [11]. In dogs the disease has been termed VKH-like syndrome or uveodermatologic syndrome. It has been described in the Akita [12–19], Siberian husky [9,11,18], golden retriever [18], beagle [16], chow chow [14], Old English sheepdog [18], Saint Bernard [18],

Fig. 1. (A) Medial canthal ulcerative blepharitis in a 3-year-old Yorkshire terrier. (B) Lateral canthal affection in a German shepherd with medial canthal ulcerative blepharitis.
Australian shepherd [18], dachshund [20], Brazilian fila dog [20], Shetland sheepdog [21], Irish setter [22], and Samoyed [22]. The breed predisposition in dogs could be also related to the presence of MHC anomalies as in humans (HLA-DR4). To the authors’ knowledge, there are no studies showing a relation between MHC anomalies and VKH-like syndrome in dogs. Dogs are typically affected in adulthood, and ocular lesions usually precede the dermatologic lesions, which are located in the mucocutaneous junctions. The ocular clinical signs in dogs are similar to those in humans. Apart from the intraocular signs, the eyelids are also affected, showing ulceration, hypopigmentation, and crusting (Fig. 2). Often, loss of pigmentation of the eyelids and nose is the primary clinical sign recognized by the owner and is the basis for the initial presentation. A recent study examining ocular and dermatologic tissue from two affected dogs suggested that skin lesions are the result of a Th1-mediated inflammatory response, whereas ocular lesions are the result of a Th2-mediated one [23].

Currently, there is no specific diagnostic test for uveodermatologic syndrome. The diagnosis is made by means of clinical signs and histopathologic examination of skin biopsies [14]. Histology of the eyelid skin reveals lichenoid interface dermatitis with infiltration by histiocytes, lymphocytes, plasma cells, and multinucleated giant cells [22]. Initial therapy involves immunosuppressive doses of oral prednisone (1 to 2 mg/kg/d), possibly in combination with azathioprine (beginning with 2 mg/kg/d and tapering gradually to 0.5 mg/kg/d) or cyclophosphamide (1–2 mg/kg/d), and topical eye treatment [14] consisting of corticosteroids and immunosuppressive drugs. The long-term prognosis is poor.

Pemphigus Complex

The pemphigus complex is a group of uncommon autoimmune diseases described in dogs that is comparable to human disease. In humans, there are at least eight varieties of pemphigus [24]; in dogs, there are five described varieties (vulgaris, foliaceus, erythematous, vegetans, and bullous) [25].

Fig. 2. Vogt-Koyanagi-Harada syndrome in a Saint Bernard 4-year-old male with periocular alopecia, ulcers, conjunctival hyperemia, diffuse corneal edema, and mucopurulent discharge.
In humans, the pemphigus complex is characterized histologically by intraepithelial acantholysis leading to vesicle formation and immunologically by the presence of autoantibodies to different components of the keratinocyte desmosome found in the skin and circulating in the serum [26,27]. In dogs, only pemphigus vulgaris causes an intraepidermal vesicle or bulla. The other forms of pemphigus are typically associated with intraepidermal pustules, a major distinction between human and canine disease [28].

In dogs, facial lesions usually involve mucocutaneous junctions and are characterized by pustules or vesicles that eventually rupture, leaving erosions and ulcers, crusting, scaling, and hypopigmentation. In pemphigus foliaceus, vulgaris, and erythematous, the facial lesions usually involve the eyelids (Fig. 3). The dermatologic clinical signs are due to a type II hypersensitivity reaction [3].

The pemphigus complex is uncommon in dogs, accounting for about 0.6% to 1% of all canine skin disorders diagnosed at referral small animal clinics [29,30]. The most important diagnostic aspects are the history, physical examination, and histopathologic findings (Table 1) [31]. Detection of pemphigus antibody by direct immunofluorescence or immunohistochemical testing may also be helpful. Owing to costs, technical problems, and relatively poor diagnostic sensitivity and specificity, these tests are not routinely recommended.

The prognosis for canine pemphigus varies with the form and severity of the disease [29,32,33]. On the basis of the small number of cases documented in the veterinary literature, pemphigus vulgaris appears to be a severe disease that is often fatal, and, even with treatment, many dogs fail to respond and are euthanized. Pemphigus foliaceus is less severe but, without treatment, may be fatal. In contrast, pemphigus erythematous is usually a benign disorder that rarely produces systemic signs and readily responds to treatment.

The treatment of these diseases requires long-term topical and systemic corticosteroids (prednisone, 1 to 2 mg/kg/d), with additional immune suppression thorough the use of cyclophosphamide (1–2 mg/kg/d) or azathioprine (1–2 mg/kg/d) for refractory cases [7,34]. Side effects of these drugs are common and vary from mild to severe, and close physical and hematologic monitoring of
the patient is critical. Some animals may require medication for life; therefore, the therapeutic regimen must be individualized for each patient, and owner education is essential [3,25]. Occasionally, the cicatricial entropion from these diseases may require corrective blepharoplasty [7,35].

**Lupus Erythematosus**

Lupus erythematosus is a term that encompasses a group of diseases that have different clinical syndromes but share a similar underlying autoimmune process [36]. The terminology and classification system used in humans, described by Sontheimer, is

<table>
<thead>
<tr>
<th>Disease</th>
<th>Histopathologic findings</th>
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<tr>
<td>Pemphigus foliaceus</td>
<td>Intragramular and subcorneal acantholysis is present with resultant cleft and vesicle or pustule formation. Neutrophils or eosinophils may predominate within the vesicle or pustule. Eosinophilic exocytosis and microabscess formation occur within the epidermis or follicular outer root sheath. Acantholytic, dyskeratotic granular epidermal cells are found at the surface of erosions.</td>
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<tr>
<td>Pemphigus vulgaris</td>
<td>Suprabasilar acantholysis is present with resultant cleft and vesicle formation. Basal epidermal cells remain attached to the basement membrane zone like a row of tombstones. The inflammatory reaction may be scant and perivascular or prominent and interstitial to lichenoid.</td>
</tr>
<tr>
<td>Pemphigus erythematosus</td>
<td>Condition is identical to pemphigus foliaceus except for the fact that it often has a lichenoid cellular infiltrate of mononuclear cells, plasma cells, and neutrophils or eosinophils or both.</td>
</tr>
<tr>
<td>Canine discoid lupus erythematosus</td>
<td>Interface dermatitis is present. Findings include focal hydropic degeneration of basal epidermal cells, pigmentary incontinence, focal thickening of the basement membrane zone, apoptotic keratinocytes, and marked accumulations of mononuclear cells and plasma cells around dermal vessels. Dermal mucinosis occurs of variable degrees.</td>
</tr>
<tr>
<td>Canine systemic lupus erythematosus</td>
<td>The dermatohistopathologic changes vary with the type of gross morphologic lesions and may be nondiagnostic. Interface dermatitis occurs involving hair follicle outer root sheaths. Apoptosis of basal and suprabasal cells may occur, and, occasionally, these apoptotic cells are associated with lymphocytic satellitosis. Findings include subepidermal vacuolar alteration, focal thickening of the basement membrane zone, and dermal mucinosis.</td>
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currently being used in veterinary medicine. The basis of Sontheimer’s system is that lupus erythematosus may be systemic or cutaneous (discoid) [37].

Lupus erythematosus is an uncommon autoimmune disorder of dogs, cats, and humans that has polyclonal lymphocytic involvement [29]. The exact etiology is unknown, but, in humans, all forms are characterized by a variety of autoantibodies to nuclear antigens with or without immune complex deposition. It is considered a type III-mediated (antibody-antigen complex-related) hypersensitivity reaction.

Canine discoid lupus erythematosus is a relatively benign cutaneous disease with no systemic involvement [38,39]. A relationship or progression to canine systemic lupus erythematosus has not been reported. Although there is a clear breed predisposition in German shepherd dogs, it has been demonstrated that sun exposure aggravates the disease in about 50% of cases, suggesting that photosensitivity has a role in pathogenesis. The disease is associated with facial dermatitis consisting of crusts, depigmentation, erosions, and ulcers, which predominantly affect the nasal planum and muzzle; eyelid and oral lesions are also described [25]. The diagnosis is based on history, physical examination, and skin biopsy (Table 1). Anti-nuclear antibodies (ANA) test results are not reliable [40]. The prognosis for canine discoid lupus erythematosus is good [29,39]. The disease can be managed by avoiding exposure to intense sunlight and by using topical immunosuppressive drugs (glucocorticoids or 0.2% to 1% cyclosporine A) [25]. In refractory cases, systemic glucocorticoids (2.2 to 4.4 mg/kg of prednisone or prednisolone given orally every 24 hours) may be needed. Therapy will probably need to be continued for life.

The most common presentation of canine systemic lupus erythematosus is fever (constant or irregularly cyclic) with polyarthritis, proteinuria, and skin disease, present in greater than 50% of cases [36,37]. Other relatively common manifestations include anemia, leucopenia, thrombocytopenia, proteinuria, peripheral lymphadenopathy, splenomegaly, and oral ulcers. Cutaneous manifestations of canine systemic lupus erythematosus are extremely diverse and similar to those of canine discoid lupus erythematosus. The disease is so variable in its clinicopathologic presentation that any dogmatic diagnostic categorization is impossible. The diagnosis is based mainly on ANA tests and skin biopsy (Table 1). The ANA test is currently considered the most sensitive serologic test, but its specificity is low [35,41]. The prognosis in systemic lupus erythematosus is generally unpredictable and depends on the organs involved. In general, the earlier the diagnosis is made, the better the prognosis [38,42,43]. Therapy for canine systemic lupus erythematosus must be individualized. The initial agent of choice is probably large doses of systemic glucocorticoids. When systemic glucocorticoids are unsatisfactory, other immunomodulating drugs may be useful [38,42,43].

**IMMUNE-MEDIATED EYELID AND CONJUNCTIVAL DISORDERS**

**Canine Juvenile Cellulitis**

Canine juvenile cellulitis is a well-recognized lymphocutaneous disease that is commonly seen in puppies less than 8 months of age [6,44–48]; however, adult
dogs may become affected by this condition [49,50]. Predisposed breeds include the dachshund, golden retriever, Labrador retriever, Gordon setter, and Lhasa apso [6,44]. Canine juvenile cellulitis is an uncommon granulomatous and pustular disorder of the face, pinnae, and submandibular lymph nodes. Normally, an acute swollen face with particular involvement of the eyelids, lips, and muzzle is accompanied by submandibular lymphadenopathy (Fig. 4). Within 24 to 48 hours, papules and pustules develop around the lips, muzzle, chin, bridge of the nose, and periorcular area. Occasionally, lesions may also appear on the feet, abdomen, thorax, vulva, prepuce, or anus. Lesions typically fistulate, drain, and crust. Affected eyelids are often painful but not pruritic. Approximately 50% of affected puppies are lethargic and depressed. Fever, anorexia, and sterile suppurative arthritis manifesting as joint pain are inconsistent findings. Leukocytosis with neutrophilia and normocytic, normochromic anemia may also be seen [44].

Canine juvenile cellulitis may be diagnosed primarily on a clinical basis, although a definitive diagnosis requires cytologic and histopathologic evaluations [46]. Even if the patient presents with only blepharitis, the diagnosis should be suspected because of the age of the dog and the bilateral eyelid involvement [6]. Cytologic examination of eyelid papulopustular lesions reveals pyogranulomatous inflammation with no microorganisms, and carefully performed cultures are negative. Biopsies of early eyelid lesions reveal multiple discrete or confluent granulomas and pyogranulomas consisting of clusters of large epitheloid macrophages with variably sized cores of neutrophils [44].

The cause of canine juvenile cellulitis is unknown, but a bacterial hypersensitivity has been postulated to explain the response to corticosteroids and the

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**Fig. 4.** Dermatologic signs in a 4-month-old English cocker spaniel affected by juvenile cellulitis. The animal has been treated with topical diluted chlorhexidine. (Courtesy of Mar Bardagi, Barcelona, Spain.)
explosive course of the disease [6,46]. Early and systemic aggressive therapy is indicated; otherwise, eyelid scarring may be severe. Immunosuppressive doses of systemic corticosteroids, tapered following 3 to 4 weeks after resolution of clinical signs, are recommended [6,45]. If cytologic or clinical evidence of secondary bacterial infection exists, systemic bactericidal antibiotics such as cephalexin, cefadroxil, and amoxicillin clavulanate should be prescribed [45]. Nursing care consisting of gentle cleansing or soaking of the skin lesions may also be attempted. With appropriate treatment, the prognosis is excellent.

Acute Allergic Blepharitis and Conjunctivitis

Acute allergic blepharitis and conjunctivitis can occur at any age and in atopic or non-atopic dogs. It is considered a hypersensitivity reaction in which allergens (e.g., plant pollen, topical drops, insect bites) are inoculated into the eyelid or the conjunctival surface. It causes intense itching, eye redness, and dramatic and immediate swelling of the eyelids and conjunctiva which may be so severe that the eye closes. Several breeds are more affected; the West Highland white terrier demonstrates an especially high incidence [7]. It is of relevant importance to compile a completed history taking into consideration environmental aspects such as recent exposition to cut grass, plant pollen allergens in the surroundings, cleaning products, and so on. This condition is self-limiting and normally requires no treatment, although an intensive wash out of the conjunctival fornix is recommended [51,52]. If the allergen is identified, it may be needed to be avoided. If the inflammation is severe, it is important to protect the eye from self-trauma and to give some topical or systemic corticosteroids depending on the severity of the clinical signs. In humans, if the condition becomes recurrent, it may be helpful to protect patients from allergic challenges with mast cell inhibitors such as sodium cromoglycate or nedocromil sodium [53]. The effectiveness of these medications has not been proven in dogs, although anecdotal evidence suggests that antihistamines such as levocabastine and sodium cromoglycate can be valuable when given topically.

Contact hypersensitivity has also been described in the eyelids and conjunctiva [7,52]. This condition is related to the use of topical ophthalmic medication. The reaction can be induced by the active ingredient or by the excipients. Some reported drugs are benzalkonium chloride, neomycin, pilocarpine [53], thimerosal [52], 2% dorzolamide [54], and prostaglandin analogues [55]. The allergic reaction can be acute, with immediate chemosis and discomfort, or more chronic, with conjunctival redness, serous discharge, and swollen medial canthus blepharitis [56]. In chronic cases, affected animals have a history of non-responsive conjunctivitis. Diagnosis and treatment include cessation of all topical medication for a week [52]. It is easier to diagnose and identify the allergen in acute cases. In the authors’ opinion, some cases could be misinterpreted as a treatment failure, more so when the allergen is the active ingredient. For example, an antibiotic could be replaced by another on the basis of a lack of sensibility rather than contact hypersensitivity. Reactions to excipients can be difficult to evidence. In human ophthalmology, allergic reactions to excipients are
a frequent disorder; therefore, excipient-free ophthalmic drugs are increasing in the market [57].

Another type of acute blepharoconjunctival allergy involves the urticarial lesions of acute angioneurotic edema. Dogs may develop urticarial lesions of the head in the skin involving the ears, muzzle, and periorbital areas [6,51]. Lesions are characterized by the acute onset of skin edema, chemosis, and edema of the subcutaneous connective tissue of these areas. Swelling around the eyes may be severe enough to close the palpebral fissures and prevent the animal from seeing. The cause of urticarial eye disease is usually associated with the stings of insects, with ingestion of spoiled protein material in foods, and with the administration of systemic drugs. Treatment of angioneurotic edema depends on the severity of the clinical signs and includes the following:

- Identify and remove the irritating substance if possible. Wash the eye to eliminate any chemical residues. Stop any ongoing systemic medication.
- Administer high doses of a rapidly acting corticosteroid such as hydrocortisone hemisuccinate intravenously (10 to 20 mg/kg). Administer adrenalin only if angioneurotic edema is severe and swelling of the face and neck may interfere with normal breathing (1:10,000 epinephrine, 0.5 to 1.0 mL intravenously) [51].

Necrotizing Marginal Blepharitis
Marginal blepharitis or meibomitis is the term used to describe inflammation of the lids that involves the meibomian glands. Necrotizing marginal blepharitis is a meibomitis secondary to the necrotizing direct effect of *Staphylococcus* toxin [58], although an immune-mediated response to *Staphylococcus* toxin should not be excluded.

*Staphylococcus* spp are distributed everywhere in the nature; therefore, exposure of the eye is unavoidable. With such widespread occurrence of *Staphylococcus* spp, animals would normally carry these organisms in their eyes as potential commensals or pathogens. In affected animals, the lid margins become swollen, red, inflamed, and pruritic [7,59,60]. In severe cases, crusts of fibrin may develop on the lid margins, and tear film abnormalities can be present.

The pathogenic mechanism is related to the bacterial presence and the immune-mediated reaction induced by the toxin. For that reason, a combined treatment based on topical and systemic antibiotics and corticosteroids is indicated in the majority of cases. Autogenous vaccine can be effective in chronic and seemingly resistant staphylococcal infections [58]. The prognosis is good if the disease is diagnosed and treated early.

**CHRONIC ALLERGIC BLEPHARITIS AND CONJUNCTIVITIS**

**Canine Atopic Disease**
The eyelids and conjunctiva are exposed structures that come into contact with a huge number and variety of airborne particles. Chronic ocular allergic diseases also occur in humans and can be concomitant with systemic atopic clinical signs [61]. The term *atopy* was introduced to describe the ability to produce
a hypersensitivity reaction against common environmental allergens, a response that has been identified to be mediated by IgE. An exaggerated IgE response produces tissue damage as a type I hypersensitivity reaction [62]. The pathophysiology of the disease is still under study in humans. A cascade starts by the activation of mast cells, which release histamine, tryptase, or leukotriene C4 in tears, mediators that promote eosinophil adhesion and degranulation. Mast cell proteases also activate the matrix metalloproteinases MMP-2 and MMP-9 [63]. Several cytokines are involved in the recruitment and activation of inflammatory cells, many of them produced by conjunctival fibroblasts. Although cytokine levels in tears can be used to diagnose ocular allergic diseases in humans, they have not been characterized in dogs [64].

Chronic atopic blepharitis and conjunctivitis is characterized by redness, blepharospasm, erythema, and crusting extending from the eyelid margin upward for 8 to 10 mm accompanied by excoriation and ulceration. In chronic situations with persistent eye rubbing it may lead to secondary bacterial marginal blepharitis, corneal involvement, and secondary visual impairment. Chronic meibomian gland inflammation can induce production of a more polar lipid secretion and can induce surface corneal disease due to early preocular tear film evaporation (Fig. 5) [65]. Atopic keratoconjunctivitis is the human counterpart of the disease. The presence of conjunctival giant papilla is one of the most common clinical signs. Matrix metalloproteases (MMP-2 and MMP-9) have been proposed to be the vehicle for the corneal involvement [63].

The diagnosis of atopic eye disorders is based on history, physical examination, and the use of intradermal and ocular allergy testing. Physical examination is important to evaluate other dermatologic conditions and to rule out other causes of pruritus and periocular excoriation. A commercially available ocular allergy test in humans is the rapid assay for total IgE determination in tears (Lacrytest, ADIATEC S.A. Diagnostic and Biotechnologies, Nantes, France) [66]. There are no reports of the use of this test in dogs.

Fig. 5. Atopic blepharoconjunctivitis in a poodle. Note the alopecic, erythematous, and red eyelids.
Treatment of chronic atopic blepharitis and conjunctivitis follows a regimen similar to that described for the skin and involves avoidance of the offending allergen, pharmacologic modification of the clinical signs, and hyposensitization of the offending allergens. The most important diagnostic problem is that the offending allergen cannot be identified as easily as in skin diseases. In cases in which important dermatologic problems are associated, allergy skin tests can be performed to identify the antigen. Once identified, if the allergen cannot be removed, the animal may need a change in environment. For the control of clinical signs, a variety of pharmacologic and supportive measures are available. Cold compresses can bring relief to the ocular pruritus. In general, all ocular medications when refrigerated provide additional subjective relief when applied immediately in a cold state. A deficient tear film may be rectified by giving tear supplement drops. In more severe cases, topical or systemic glucocorticoids and antibiotics may be needed to treat lid margin blepharitis, as well as an Elizabethan collar to avoid self-trauma. In the authors’ opinion, dexamethasone and prednisone ointments are the most helpful topical glucocorticoids in these cases. Systemic and topical antihistamine drugs have been used with benefit in mild human ocular allergies [57]. Although topical application has been recommended in veterinary ophthalmology, there are no reports on its effectiveness. New therapeutic modalities in humans such as chemokine antagonists have been proposed to treat chronic allergic disease. One relevant and attractive approach is to employ CCR3 (chemokine receptor type 3) antagonism. Conjunctival mast cells express CCR3, which is essential for their maintenance and differentiation. The inhibition of CCR3 has been proven to diminish the immune-mediated ocular response [63]. Several pharmaceutical approaches have been described, including amino terminus modification of natural chemokines, a development of peptide-based and nonpeptide-based antagonists, and monoclonal antibody generation. Nevertheless, these drugs have been described to be species specific and to have tissue-specific effects. It would be necessary to improve research before using these drugs in veterinary ophthalmology [63].

Canine Food Hypersensitivity

Canine food hypersensitivity is a nonseasonal pruritic skin disorder of dogs associated with the ingestion of allergens found in the diet. Presumably, it is a hypersensitivity reaction to an antigenic ingredient. Although the pathomechanism of food hypersensitivity is unclear, type I hypersensitivity reactions are well documented as the most common type of hypersensitivity reactions in humans. Why the skin is a frequent target of food-induced hypersensitivity is not well known, although it has been recognized in humans that cutaneous lymphocyte antigen is induced on T cells when cutaneous disease is present [62].

Pruritus with or without a primary eruption is the only consistent finding. No classic set of cutaneous signs is pathognomonic for food hypersensitivity in the dog. A variety of primary and secondary skin lesions are noted and can affect the eyelids. These lesions include papules, plaques, pustules, wheals,
angioedema, erythema, ulcers, excoriation, lichenification, pigment changes, alopecia, scales, crusts, and moist erosions (Fig. 6).

Currently, the definitive diagnosis of food hypersensitivity in dogs is attainable only on the basis of elimination diets and provocative exposure testing. Routine laboratory tests are not useful in diagnosing canine food hypersensitivity [62].

Treatment consists of allergen detection and elimination. In the meantime, eye topical treatment is needed to reduce ocular discomfort and pruritus that can induce secondary corneal problems. The topical treatment is individual, depending on ocular discharge, secondary bacterial infection, and conjunctival involvement. The most used therapy is a topical combination of antibiotics and glucocorticoids. The ocular signs will disappear as soon as the allergen is detected and eliminated.

Allergic Conjunctivitis without Systemic Clinical Signs
Seasonal and perennial allergic conjunctivitis have been well reported in human ophthalmology as non–sight-threatening ocular allergies [67]. Several cytokines have been found in the tears of patients sustaining allergic conjunctivitis. In patients who have seasonal and vernal keratoconjunctivitis, the most frequently found are interleukin-4 (IL-4), IL-10, and interferon-\(\gamma\) (IFN-\(\gamma\)) [64]. In most reports, allergic conjunctivitis in dogs is associated with allergic systemic signs. Nevertheless, conjunctival signs can also be present alone. The affected animals present with chronic epiphora and ocular redness without any other ophthalmic clinical signs. Diagnosis can be challenging. Conjunctival biopsy shows a mild lymphoplasmacytic infiltrate with variable amounts of eosinophils, vascular congestion, and dilation. IgE determination in tears is actually used in human medicine to diagnose ocular allergies [66]. There are no reports of the use of this test in dogs.

The response to topical corticosteroids or non-steroidal anti-inflammatory drugs is poor. Other therapeutic options include vasoconstrictors such as

Fig. 6. Food hypersensitivity in a golden retriever. Note the periocular alopecia and hyperpigmentation. (Courtesy of Mar Bardagi, Barcelona, Spain.)
phenylephrine or tetrahydrozoline. These drugs are sympathomimetic agents that decrease vascular congestion and eyelid edema via \( \alpha \)-adrenoceptor stimulation but have no effect in diminishing the allergic response. Topical antihistamines are useful in human ophthalmology, but there are no studies showing their efficacy in veterinary ophthalmology [57].

**Follicular Conjunctivitis**

Follicular conjunctivitis consists of a macroscopic proliferation of the conjunctival-associated lymphoid tissue of the palpebral or bulbar conjunctiva. Follicles appear primarily on the bulbar surface of the nictitating membrane, being outnumbered and larger than those normally seen. In more severe cases, the follicles can involve palpebral and bulbar conjunctiva. Concurrent mucous or serous ocular discharge and redness are present (Fig. 7) [52]. This condition occurs most frequently in dogs younger than 18 months of age, although older animals can also be affected. It develops secondary to chronic antigenic stimulation. Vernal keratoconjunctivitis is a clinically similar entity present in humans [64]. Although there is a histologic and pathogenetic difference between follicular conjunctivitis and vernal keratoconjunctivitis, the human disease is also more frequently diagnosed in children and usually resolves without treatment. Clinical signs include the presence of conjunctival giant papillae; in severe cases, corneal inflammation can also be present [67]. IFN-\( \gamma \) levels in tears have been correlated with disease severity and have been suggested to have a role in the inflammatory phase of chronic eye allergy [68].

The diagnosis is made by clinical signs and conjunctival cytology. Cytologic results of conjunctival scraping demonstrate the presence of lymphocytes. Most cases respond to treatment with saline irrigation and topical corticosteroids. Some authorities describe that nonresponsive cases can be treated by mechanically debriding the follicles. The debridement should be performed after

**Fig. 7.** Follicular conjunctivitis involving the palpebral conjunctiva in an 8-month-old dog.
instillation of ophthalmic topical anesthetic with a dry cotton-tipped applicator. In the authors’ experience, follicle debridement can sometimes worsen the situation, increasing local inflammation and predisposing to chronic conjunctivitis.

The conjunctiva is the most immunologically active tissue of the external eye and undergoes lymphoid hyperplasia in response to stimuli. The conjunctival-associated lymphoid tissue is mainly located in the conjunctival superficial layers and in normal situations is CD8 dominated. The purpose of conjunctival-associated lymphoid tissue is to receive antigen and to present it to the circulating mononuclear cells, acting as the first line of the ocular defense system [52]. In the authors’ opinion, the lymphoid tissue is critical to conjunctival immunity. It is important to maintain its integrity as much as possible, trying not to eliminate the conjunctival follicles. Dogs with chronic nonresponsive conjunctivitis should be reevaluated for previous follicle debridement.

Acknowledgments

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References


Canine Infected Corneal Ulcers - The Latest in Aggressive Medical Therapy

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INTRODUCTION
The diagnosis of a corneal ulcer is often relatively straightforward with evidence of positive fluorescein stain uptake as a confirmation of the suspected lesion. Most recommendations for treatment involve using a broad spectrum antibiotic q6-8hrs with or without atropine to dilate the pupil. This approach works for many patients. However, there are certain breeds as well as patients with underlying ocular and systemic medical conditions that warrant a more fine-tuned aggressive approach.

ETIOLOGY
There are many causes of corneal ulceration including infection, trauma, poor tear film, mechanical irritation (i.e. foreign body, ectopic cilia), loss of corneal sensation, chemical irritant, insect venom, immunologic, and dystrophy. Almost all ulcers that are rapidly progressive leading to melting or perforation are infected with bacteria with the exception of some immune-related conditions. Patients with infected ulcers often have underlying conditions that potentiate the pathogenicity of normal ocular surface bacteria.

PATIENTS AT HIGHER RISK FOR MELTING ULCERS
1. Brachycephalic breeds are commonly (Shih tzu, Pug, Pekingese, Boston terrier, English bulldog) seen on referral by veterinary ophthalmologists for melting ulcers and perforation. They have factors that predispose them to develop severely infected melting ulcers that go on to perforation within 24 to 48 hours of the first sign of stromal loss. Decreased corneal sensitivity, trichiasis/distichiasis/ectopic cilia common, corneal exposure and tendency to have hair from the face in or near eyes increases bacterial contamination of the cornea in the long-haired breeds.

2. Keratoconjunctivitis sicca (KCS) causes the most problems when acute and severe (Schirmer Tear Test <5mm/min). With uncontrolled KCS, thinning of the epithelium occurs and ulcers can occur spontaneously or secondary to self-trauma from intense discomfort of dryness. Chronic, uncontrolled KCS leads to thickening of the epithelium and keratinization of the cornea. Ulcers frequently go unnoticed initially as they are masked by existing clinical signs of KCS.

3. Diabetic or immunocompromised patients are predisposed to developing KCS/ocular surface abnormalities. In dogs with Cushing’s syndrome, corneal MMPs (collagenase) may be activated by high endogenous steroid levels resulting in rapid development of corneal malacia. This group of patients has a decreased ability to fight infection and exhibits delayed wound healing. Much desired corneal vascular in-growth to bolster defects caused by infection and stromal loss is often severely delayed or non-exsistent.

4. Geriatric dogs are similar to immunocompromised patients. They often have central corneal deposits (mineral mostly, rarely does lipid causes a problem) related to corneal degeneration that spontaneously slough leaving minute epithelial defects prone to infection. The pinpoint areas of stain uptake can result in major pain for the dog. Or alternatively, the small fluorescein positive areas can be present for months with no pain. These spots go unnoticed and can develop serious eye-threatening infections.
5. **Cats with chronic corneal sequestrum** that are not on antibiotic therapy can present with deep painful ulcers formed around the sequestrum rim and underneath the necrotic mass. Cats on chronic low level antibiotic therapy can develop bacterial resistance. Although flare-ups of corneal disease can be associated with FHV-1 recrudescence, any lesion with stromal loss is considered infected with bacteria and must be treated appropriately.

6. **Facial dermatitis** predisposes dogs to self-trauma and repeated corneal ulcerations. The ulcers are at higher risk of infection due to the high number of bacteria on the periocular skin as well as on the limbs used to rub the eye. Facial pruritus must be controlled to break the self-trauma cycle. Often these dogs are given Elizabethan collars to prevent self-trauma. The increase in humidity and bacterial/fungal growth within the collar can worsen their facial dermatitis, exacerbate otitis externa and increase problems for the owner and pet.

**CLINICAL SIGNS**

Most of the patients with these risk factors will exhibit the classic signs of an infected, progressive corneal ulcer: blepharospasm, mucopurulent discharge, conjunctival hyperemia, corneal edema, corneal neovascularization, +/- corneal infiltrate (yellow usually), corneal defect, +/- gelatinous (melting) stroma. **Brachycephalic breeds typically fail to show the expected level of pain** equivalent to the level of severity of the ulcer. Any lesion in brachycephalic patients especially should be regarded as potentially eye-threatening and treated with extra attention.

**DIAGNOSTIC TESTS**

1. Cytology – topical proparacaine, cytobrush/blunt end of scalpel blade/mini cotton swab for very small lesions; DO NOT PERFORM IF MAY RUPTURE; Dif-Quik or Gram Stain

2. Culture and sensitivity – Antech Diagnostic Lab has special “Corneal panel” with all ophthalmic drugs – must make note on form to use this panel

**TREATMENT**

Traditionally melting ulcers have been associated with Pseudomonas infection. We are seeing more cases with Streptococcus and Staphylococcus spp. causing severe ulcers progressing to perforation. Cytology is extremely helpful in guiding initial therapy as the battle is typically won or lost in the first 24-28 hours of therapy before culture results have returned. The culture and sensitivity results are important to guide therapy if improvement is noted initially but stalls shortly thereafter. The most important element regarding treatment is antibiotic drug selection and frequency of administration. All other medications are aimed at speeding wound healing, improving corneal health and providing comfort.

1. **Antibiotics**

   a. Frequency – no less than q4-6hr if in any of these patients with underlying risk factor; q 1-2hr if stromal loss or melting noted

   b. Drug choices – combine for max effect

      i. Gram positive – **Cefazolin 5.5% suspension**, neopolygram (drops better than ointment if high frequency), neopolybac, erythromycin, oxytetracycline

      ii. Gram negative – tobramycin (will cover resistant Gram neg), **fluoroquinolones** (ciprofloxacin – cheaper, less Gram + coverage; ofloxacin – higher cost but better against Gram positive)

2. **Atropine**

   a. Ointment (cats) or drops

   b. Frequency – to effect for dilation

   c. Decrease risk of synechia and relieve pain by relaxing ciliary muscle
3. Anti-collagenases
   a. Serum – can use from patient, other animal of same species, or another animal of different species; can freeze for later use
   b. Acetylcysteine in artificial tears
   c. Oral doxycycline, topical oxytetracycline (Terramycin)

4. Lubricants - Optixcare eye gel, Hyaluronic acid (i-drop by i-Med), Genteal gel, Refresh liquigel

5. Sedation and pain medication

6. Elizabethan collar

**MONITORING**

Patients should be rechecked within 1 – 2 days if melting/progressive ulcer. If you think the defect is >50% deep and is progressing at the time you examine the patient, may want to consider a phone call to specialist or referral over for evaluation and possible conjunctival graft. In general, if an area of yellow infiltrate is noted, much of this tissue will likely slough during treatment before the patient improves. The art of guessing whether or not the amount of tissue loss will result in a defect which will leave the patient at risk of rupture improves with experience. Conjunctival grafting has a very high rate of success if the eye has not perforated and the defect is less than 7-8mm or so. If the defect is larger, or has already perforated, prognosis is guarded. Consider re-checking the eye in 2-3 days if there is a small or very shallow defect present. Referral for surgery to repair the cornea should be offered if descemetocele or perforation is evident.

**PREVENTION**

These patients at higher risk for severe corneal ulcers are also at high risk for recurrences due to persistence of the underlying conditions. Prevention involves addressing the underlying condition with long term topical/systemic therapy, providing excellent client education, and scheduling regular visits to monitor the patient’s status.
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MANAGEMENT OF COMMON CANINE OCULAR EMERGENCIES

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Ocular emergencies in the dog are common in small animal practice. A thorough understanding of the eye and the clinical manifestations of different disease processes of the eye are important to proper diagnosis and treatment. Recognition and appropriate treatment of ocular emergencies may mean the difference between retention or loss of vision, and retention or loss of the eye. Below are some of the more common ocular emergencies likely to be encountered in the dog.

GLAUCOMA

Glucoma, or an increase in intraocular pressure that affects function of the eye, can result from either primary or secondary causes. Primary glaucoma is especially common in the dog, particularly as an inherited trait in certain breeds. Primary glaucoma occurs when the iridocorneal angle and ciliary cleft are abnormal and aqueous humor can no longer egress from the eye adequately. While this can occur in mixed breed dogs as well, it is often noted in cocker spaniels, Bassett hounds, arctic breeds, chow chows, shar peis, and some terriers. Secondary glaucoma may occur with anterior uveitis, lens luxation, hyphema, and intraocular tumors.

Clinical Signs of Acute Glaucoma

Pain as evidenced by blepharospasm, tearing, elevated third eyelid, rubbing at eye, resentment of touch around the affected eye; conjunctival and episcleral hyperemia; corneal edema, dilated pupil with no pupillary light response, loss of vision in affected eye (negative menace response). In acute glaucoma the globe will be normal sized. When the eye becomes buphthalmic (enlarges) this is a sign of chronic glaucoma. Dogs also tend to be less demonstrative of pain when glaucoma becomes chronic than when it is acute, although their pain should not be discounted. Most dogs are irreversibly blind with chronic glaucoma.

Diagnosis of Glaucoma

Measurement of intraocular pressure (IOP) is imperative. Normal IOP in the dog is typically between 12 and 20 mmHg. In veterinary medicine the applanation (TonoPen) and rebound (TonoVet) tonometers are recommended.

Treatment of Acute Glaucoma

Reducing IOP as quickly as possible should be the goal of treatment. A variety of topical glaucoma drugs are available, some very good at reducing IOP. Drugs working by different mechanisms can be administered together, waiting approximately 10 minutes between drops.

Prostaglandin Analogs (PA): These are the newest miotic agents. Constriction of the pupil usually occurs within 1 hour of administration and dramatic decreases in IOP can be seen in some dogs within the first 1 to 2 hours. In addition to physically opening the iridocorneal angle through their miotic effect, prostaglandin analogs are thought to increase uveo-scleral outflow of aqueous humor, an alternative pathway. Examples include latanoprost (Xalatan), travoprost (Travatan), and bimatoprost (Lumigan). These agents can be used every 12 to 24 hours depending on the severity of the glaucoma. If the pupil does not move, as for example with synechia or chronic glaucoma in which the sphincter muscle is damaged, PAs may not significantly reduce IOP.

Carbonic Anhydrase Inhibitors (CAI): These drugs decrease aqueous humor production. The most common drug in this category used in dogs is dorzolamide (Trusopt). Brinzolamide (Azopt) is a similar drug. CAIs inhibit aqueous humor production and have their onset of action within a few hours. These agents should be used every 8 hours.

Beta Blocking Agents: These agents decrease aqueous humor production. The most common one used in the dog is 0.5% timolol maleate (available generically) and is recommended not as a sole agent but for use with other types of drugs (above). Timolol should be administered every 12 hours. At this frequency heart rates are not typically affected in the dog. Other beta blockers available are betaxolol (Betoptic) and levobunolol (Betagan). These latter two have not been well studied in the dog.

Hyperosmotic Agents: The use of prostaglandin analogs in dogs with acute glaucoma has lessened the need for hyperosmotic therapy and they should be employed first. If combinations of the above topically applied agents are unsuccessful at reducing IOP within 2 to 4 hours, mannitol can be administered. The dose is 1 to 2 g/kg given intravenously, over about 30 to 45 minutes. Water should be withheld for about 6 hours. Mannitol will create an osmotic gradient between the eye (primarily the vitreous body) and the vasculature, drawing fluid from the eye and reducing IOP. Effects can often be seen within 1 to 2 hours with a maximal effect seen at about 6 hours. Topical glaucoma drugs should be continued as the effects of mannitol will last no longer than 24 hours.

Other Agents: Older topical drugs such as pilocarpine, epinephrine, and demecarium bromide are used less often today with the advent of newer and more efficacious therapies. Oral CAI (acetazolamide, methazolamide, dichlorphenamide) have a wide variety of systemic side effects and have largely fallen out of use for this reason. The topical CAIs have no systemic side effects.

LENS LUXATION

The lens is free to move within the eye when the zonules which normally attach it to the ciliary body are broken. The most common reasons for canine lens luxation are primary (abnormal zonules, seen in terrier breeds) and secondary to hypermature cataracts. If the lens falls posteriorly into the vitreous cavity, there may
be no immediate emergency. However, when it moves into the anterior chamber, it may cause acute pain and/or glaucoma.

Clinical Signs of Anterior Lens Luxation
Clinical signs include pain as evidenced by blepharospasm, tearing, elevation of third eyelid, corneal edema, and glaucoma.

Diagnosis of Lens Luxation
Diagnosis is by visualization of the lens in the anterior chamber or the vitreous cavity. If the cornea is severely edematous an ocular ultrasound may be needed to diagnose an anterior lens luxation. Intraocular pressure should always be measured.

Treatment of Lens Luxation
Initial therapy for an anterior lens luxation should include topical agents for treating glaucoma and uveitis, both of which are commonly associated with this disorder. Systemically administered analgesic and anti-inflammatory agents (NSAIDs, tramadol) are also helpful. Even if the IOP is not elevated, prophylactic therapy with agents such as dorzolamide and timolol are indicated. The miotic agents such as prostaglandin analogs should be avoided so as not to trap the lens in front of a closed pupil. Topical anti-inflammatory therapy (see Uveitis section) should be instituted with prednisolone acetate or dexamethasone as long as no corneal ulceration exists. The only definitive therapy for a lens luxation is surgical, so referral to an ophthalmologist should be recommended as soon as possible.

ACUTE UVEITIS
Inflammation of the uvea may involve iris and ciliary body (anterior uveitis) or choroid (posterior uveitis) or both (panuveitis). Anterior uveitis is more common. Underlying causes of canine uveitis can sometimes be difficult to pinpoint. All dogs with uveitis should have a thorough physical examination. A complete blood count (CBC), chemistry panel, and infectious disease titers should be considered on each individual case and prevalence of infectious disease in the area.

Clinical Signs of Acute Anterior Uveitis
Clinical signs include pain, conjunctival and episcleral hyperemia, corneal edema, miosis, decreased intraocular pressure, aqueous flare, hyperemic iris, fibrin or blood (hyphema) or white blood cells (hypopyon) in the anterior chamber, and blindness in affected eye (especially if posterior uveitis is present as well).

Diagnosis of Acute Anterior Uveitis
Diagnosis is by visualization of some or all of the above clinical signs. Rule out glaucoma through measurement of IOP. Stain the cornea with fluorescein dye to check for ulceration.

Treatment of Acute Anterior Uveitis
Treatment should be very aggressive to manage ocular inflammation and pain. Topical corticosteroid therapy should be instituted (as long as no corneal ulceration is present) with either 1% prednisolone acetate (shake very well) or 0.1% dexamethasone, four to six times daily. Atropine for iridocyclopexia should be administered at twice daily as long as IOP is low. If IOP is normal in the face of uveitis, glaucoma may already be developing and atropine should be avoided. Systemic anti-inflammatory agents such as NSAIDs or in severe uveitis, oral prednisolone at 1 to 2 mg/kg/day, should also be started. If posterior uveitis exists, only systemically administered agents will reach these tissues and oral prednisolone becomes imperative. If pain is severe, oral narcotic agents such as tramadol should also be administered. Dogs with acute uveitis should be re-examined in about 2 to 3 days. Therapies should be only gradually decreased as improvement is seen. IOP should be measured at every visit.

DEEP CORNEAL ULCERS
Deep corneal ulcers in dogs should be assumed to be infected with bacteria regardless of appearance. Most corneal stromal ulcers will have a purulent cellular infiltrate and associated uveitis. Very aggressive medical therapy is required to treat deep corneal ulcers. Once ulcers become descemetoceles, or if they fail to respond to medical therapy within a couple of days, surgery with a conjunctival graft will be needed to prevent corneal perforation.

Clinical Signs of Deep Corneal Ulceration
Clinical signs include pain, tearing (unless dry eye is present), conjunctival hyperemia, corneal edema and yellowish cellular infiltrate around the ulcer, variable corneal vascularization arising from the limbus, and miosis due to associated uveitis.

Diagnosis of Deep Corneal Ulceration
If profuse tearing is not evident check tear production with a Schirmer Tear Test (normal ≥ 15 mm/min) before administering any fluids to the eye. Visualization of above clinical signs; fluorescein staining (a stromal ulcer will take up fluorescein dye; a desmetocele will not absorb the dye on Descemet’s membrane). If possible, a culture of the ulcer should be taken prior to treatment, although one cannot await results of a culture for treatment choices. Following proparacaine, the edge of the ulcer can be scraped gently and a cytologic preparation made to look for bacteria. Gram-positive cocci are the most common organisms infecting the canine cornea.

Treatment of Deep Corneal Ulcers
Two different broad spectrum antibiotic solutions should be chosen and alternated every hour for as much of the day as possible (see below for combinations); atropine (if dry eye not present) two to three times daily, oral NSAID therapy +/- tramadol for pain. If dry eye is present, cyclosporine ointment should be administered twice daily. Autogenous serum handled steriley can also be helpful to arrest corneal melting – apply four to six times daily. A 1% to 2% compounded EDTA solution can
also be used for corneal melting. Ointments should be avoided due to difficulty of administration and limited spectrum of choices.

- Antibiotic combinations recommended:
  - Fluoroquinolone (ofloxacin or ciprofloxacin) + tobramycin
  - Fluoroquinolone + neomycin-polymixin B-gramicidin
  - Fluoroquinolone + cefazolin (made from lyophilized powder for injection: 100 mg/mL)

If therapy is effective the ulcer will stabilize and not look worse for the first 24 to 48 hours. After that gradual clearing of the purulent infiltrate and edema will be seen. Frequency of therapy should not be decreased too soon; although once it is clear the ulcer is healing antibiotic frequencies can be reduced to four times daily with each antibiotic. If the ulcer continues to worsen despite aggressive management, referral for surgery should be considered.

**GLOBE PROPTOSIS**

Proptosis of the globe is common in brachycephalic breeds with often surprisingly little trauma causing the event. Non-brachycephalic breeds with a proptosis have generally suffered severe head trauma. Unless the globe is badly damaged, repositioning of the eye should be attempted as enucleation can be performed later if warranted. Clients should be warned that dogs are usually blind in the proptosed eye (from optic nerve stretching) and that lateral strabismus (from a torn medial rectus muscle) is common.

**Procedure for Repositioning Proptosed Globe**

With dog under general anesthesia, gently clip periocular hair and cleanse skin with dilute betadine solution (not scrub) as well as the globe. Rinse well with sterile saline. Perform a lateral canthotomy to improve globe access. Place a sterile lubricant on the eye (such as KY) to protect cornea. Using forceps (such as Allis tissue) grasp upper and lower lids – have an assistant place gentle traction on the eyelids. Use a flat instrument such as a scalpel handle horizontally across the cornea. Apply gentle pressure against the cornea to move globe posteriorly as the assistant pulls the eyelids cranially in front of globe. The globe will often not fully reduce due to swelling and hemorrhage of retrobulbar tissues. Close lateral canthotomy. Place two horizontal mattress sutures (temporary tarsorrhaphy) half depth through the eyelids (so as not to have suture on the conjunctival surface rubbing cornea). Be sure to use stints (cut pieces of IV tubing work well) on the suture so it doesn’t cut into eyelids. Leave enough space at the medial canthus for topical medications to be used.

**Postoperative Care**

Postoperative care may include use of an E collar; topical antibiotic solution (neopolygram; tobramycin) three times daily; oral NSAID; oral antibiotic such as amoxicillin or cephalixin. Recheck in 5 days to assess tarsorrhaphy sutures and any ocular discharge – if doing well, leave sutures in place for 2 weeks.

**HYPHEMA**

Blood in the anterior chamber may occur from trauma, uveitis, retinal detachment, intraocular tumor, or a bleeding disorder. A thorough physical examination should be performed to look for other signs of bleeding. An ocular ultrasound may be necessary to look for a retinal detachment if this history is not known. Intraocular pressure should always be measured in eyes with hyphema. Fluorescein staining of the cornea should be performed to check for ulceration.

**Treatment of Hyphema**

Topical corticosteroids (if no ulcer) are used as above for uveitis; and topical tropicamide 2X daily to move pupil; the use of atropine may increase chances of glaucoma. A systemic NSAID is used for pain and inflammation of the eye. Recheck in about 3 to 4 days, measuring IOP again. An eye that continues to have fresh blood has an ongoing bleed and this carries a poor prognosis. Bleeding from trauma will have clotted. Depending on how much fibrin is present, an intraocular injection of tissue plasminogen activator may be needed to dissolve fibrin. Contact an ophthalmologist as the window of opportunity only exists for approximately one week.
A large variety of antiviral agents exists for oral or topical (ophthalmic) treatment of cats infected with feline herpesvirus type 1 (FHV-1). However, some general comments regarding these agents are possible. Knowledge of these general principles can be used to better understand antiviral pharmacology and thereby guide therapy for cats with herpetic disease.

- No antiviral agent has been developed specifically for FHV-1, although many have been tested for efficacy against this virus. Agents highly effective against closely related human herpesviruses (for which they were developed) are not necessarily or predictably effective against FHV-1 and all should be tested in vitro before they are administered to cats. In vitro potency is described as the drug concentration at which viral replication is suppressed by 50% (or IC50). Therefore, a more potent drug will have a lower IC50. Table 1 summarizes the relative antiviral efficacy against FHV-1 and human herpes simplex virus type 1 (HSV-1) for a number of antiviral drugs.

- No antiviral agent has been developed specifically for cats; although some have been tested for safety in this species. Agents with a reasonable safety profile in humans are not always or predictably nontoxic when administered to cats and all require safety and efficacy testing in vivo.

- Many systemically and topically administered antiviral agents require host and or viral metabolism before achieving their active form. These agents are not reliably or predictably metabolized by cats or FHV-1 and pharmacokinetic studies in cats and in vitro efficacy testing are required.

KEYWORDS
- Herpesvirus
- Feline
- Virology
- Antiviral therapy
- Pharmacology
Antiviral agents tend to be more toxic than do antibacterial agents because viruses are obligate intracellular organisms and co-opt or have close analogs of the host’s cellular “machinery.” This limits many antiviral agents to topical (ophthalmic) rather than systemic use. For those which can be administered systemically, a relatively narrow safety margin often exists and special considerations should always be given to patients with reduced hepatic or renal function.

All antiviral agents currently used for cats infected with FHV-1 are virostatic. Therefore, they typically require frequent administration to be effective and must be understood to merely retard viral growth while the host immune response clears the virus.

The following antiviral agents have been studied to varying degrees for their efficacy against FHV-1, their pharmacokinetics in cats, or their safety and efficacy in treating cats infected with FHV-1.

**IDOXURIDINE**

Idoxuridine is a thymidine analog originally developed for treatment of humans infected with HSV-1. Following intracellular phosphorylation, it competes with thymidine for incorporation into viral DNA, rendering the resultant virus incapable of replication. However, it apparently does this less effectively in FHV-1 than in HSV-1 (see Table 1). In addition, idoxuridine is a nonspecific inhibitor of DNA synthesis, affecting any process requiring thymidine. Therefore, host cells are similarly affected, systemic therapy is not possible, and corneal toxicity can occur. It has historically been commercially available as an ophthalmic 0.1% solution or 0.5% ointment, but is no longer commercially available in the United States. It can be obtained from a compounding pharmacist in these forms and is well tolerated by most cats and seems efficacious in many. It should be applied to the affected eye five to six times daily.

**VIDARABINE**

Vidarabine is an adenosine analog that, following triphosphorylation, appears to affect viral DNA synthesis by interfering with DNA polymerase. However, like idoxuridine, vidarabine is nonselective in its effect and so is associated with notable host toxicity if administered systemically. Because it affects a viral replication step different from that targeted by idoxuridine, vidarabine may be effective in patients whose disease seems resistant to idoxuridine. Where it is not available commercially, it can be obtained from a compounding pharmacist as a 3% ophthalmic ointment. Anecdotal reports suggest that vidarabine may be better tolerated by cats than many of the antiviral solutions. Like idoxuridine, it should be applied to the affected eye five to six times daily.

### Table 1

<table>
<thead>
<tr>
<th>IC₅₀ (µM)</th>
<th>TFU</th>
<th>GCV</th>
<th>IDU</th>
<th>CDV</th>
<th>PCV</th>
<th>VDB</th>
<th>ACV</th>
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<td>1.7</td>
<td>0.8</td>
<td>1</td>
<td>9</td>
<td>2</td>
<td>4</td>
<td>1</td>
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<td>0.8</td>
<td>1</td>
<td>9</td>
<td>2</td>
<td>4</td>
<td>1</td>
<td>74</td>
</tr>
</tbody>
</table>

**Abbreviations:** ACV, acyclovir; CDV, cidofovir; GCV, ganciclovir; IDU, idoxuridine; µM, micromolar; PCV, penciclovir; TFU, trifluridine; VDB, vidarabine.
TRIFLURIDINE

Like idoxuridine, trifluridine is a nucleoside analog of thymidine. However, it is believed to have a somewhat different mode of action. Following intracellular phosphorylation it is presumed to reduce DNA synthesis via inhibition of thymidylate synthase. It is too toxic to be administered systemically but topically administered trifluridine is considered one of the most effective drugs for treating HSV-1 keratitis. This is in part due to its superior corneal epithelial penetration. It is also one of the more potent antiviral drugs for FHV-1 (see Table 1). It is commercially available in the United States as a 1% ophthalmic solution that should be applied to the affected eye five to six times daily. Unfortunately, it is expensive and is often not well tolerated by cats, presumably due to a stinging reaction reported in humans.

ACYCLOVIR

Acyclovir is the prototype of a group of antiviral drugs known as acyclic nucleoside analogs. Members of this group of antiviral agents all require three phosphorylation steps for activation. The first of these steps must be catalyzed by a viral enzyme, thymidine kinase. This fact increases their safety and permits them to be systemically administered to humans. However, the activity of this enzyme in FHV-1 is not equivalent to that in HSV-1. The second and third phosphorylation steps must be performed by host enzymes, which may not be present in cats or may not be as effective in cats as they are in humans. This knowledge helps explain why the acyclic nucleoside antiviral agents developed for humans infected with HSV-1 are not predictably safe or effective when administered to cats infected with FHV-1 and why pharmacokinetic studies are always needed to establish appropriate dosing in cats. In addition to relatively low antiviral potency against FHV-1, acyclovir has poor bioavailability in cats and is potentially toxic when systemically administered. Oral administration of 50 mg/kg acyclovir to cats was associated with peak plasma levels of approximately only one-third the IC50 for this virus (33 μM). Common signs of toxicity are referable to bone marrow suppression. In some countries, acyclovir is also available as a 3% ophthalmic ointment. In one study in which a 0.5% ointment was used five times daily, the median time to resolution of clinical signs was 10 days. Cats treated only three times daily took approximately twice as long to resolve and did so only once therapy was increased to five times daily. Taken together, these data suggest that very frequent topical application of acyclovir may produce concentrations at the corneal surface that do exceed the reported IC50 for this virus but are not associated with toxicity. There are also in vitro data suggesting that interferon exerts a synergistic effect with acyclovir that could permit an approximately eightfold reduction in acyclovir dose. In vivo investigation and validation of these data are needed.

VALACYCLOVIR

Valacyclovir is an acyclic nucleoside analog and a prodrug of acyclovir that, in humans and cats, is more efficiently absorbed from the gastrointestinal tract compared with acyclovir and is converted to acyclovir by a hepatic hydrolase. Its safety and efficacy have been studied in cats. Plasma concentrations of acyclovir that surpass the IC50 for FHV-1 can be achieved after oral administration of valacyclovir. However, in cats experimentally infected with FHV-1, valacyclovir induced fatal hepatic and renal necrosis, along with bone marrow suppression, and did not reduce viral shedding or clinical disease severity. Therefore, despite its superior pharmacokinetics, valacyclovir should never be used in cats.
GANCICLOVIR

Ganciclovir is another acyclic nucleoside analog that also requires triphosphorylation to achieve its active form. Like acyclovir, the first phosphorylation step is mediated by viral thymidine kinase. Despite these similarities, it appears to be at least 10-fold more effective than is acyclovir against FHV-1 suggesting a relative difference in cellular drug uptake, rate, or efficacy of host or viral phosphorylation. Ganciclovir is available for systemic (intravenous or by mouth) and intravitreal administration in humans, where it is associated with greater toxicity than acyclovir. Toxicity is typically evident as bone marrow suppression. Very recently, a 0.15% ophthalmic gel formulation of ganciclovir has become available for humans infected with HSV-1. Ganciclovir holds promise for feline herpetic disease and currently available formulations warrant safety and efficacy studies in cats.

PENCICLOVIR

Penciclovir is a nucleoside deoxyguanosine analog with a similar mechanism of action as acyclovir and potent antiviral activity for a number of human herpesviruses. It too requires viral and cellular phosphorylation and yet has relatively high antiviral efficacy against FHV-1, due at least in part to the efficiency with which this drug is phosphorylated by FHV-1 thymidine kinase. It is available as a dermatologic cream for humans that should not be applied to the eye. We have some preliminary data in which we administered PCV intravenously to cats, but this was done largely to assist with our ongoing investigations of the penciclovir prodrug, famciclovir (Thomasy SM and colleagues, unpublished data, 2008). In vivo studies of the safety or efficacy of penciclovir in cats are otherwise lacking and, at this time, its use in cats cannot be recommended.

FAMCICLOVIR

Famciclovir is a prodrug of penciclovir; however, metabolism of famciclovir to penciclovir is complex and requires di-deacetylation, predominantly in the blood, and subsequent oxidation to penciclovir by a hepatic aldehyde oxidase. Unfortunately, the activity of this hepatic aldehyde oxidase is negligible in cats. This necessitates cautious extrapolation to cats of data generated in humans. Data to date in normal and experimentally infected cats suggest that the pharmacokinetics of this drug are extremely complex and likely result from nonlinear famciclovir absorption, metabolism, excretion, or an combination of these three factors. In spite this, there is mounting evidence that suggests famciclovir is very effective in some cats with experimentally induced or suspected spontaneous herpetic disease. Further studies of this drug’s pharmacokinetics, safety, and efficacy are required before dose rates and frequency can be recommended.

CIDOFOVIR

Cidofovir is a relatively new cytosine analog that requires the typical two host-mediated phosphorylation steps without virally mediated phosphorylation. Its safety arises from its relatively high affinity for HSV DNA polymerase compared with human DNA polymerase. It is commercially available only in injectable form in the United States, but has been studied as a 0.5% solution applied topically twice daily to cats experimentally infected with FHV-1. Its use in these cats was associated with reduced viral shedding and clinical disease. Its efficacy at only twice daily (despite being virostatic) is believed to be due to the long tissue half-lives of the metabolites of this
drug. There are reports of its experimental topical use in humans and rabbits being associated with stenosis of the nasolacrimal drainage system components and, as yet, it is not commercially available as an ophthalmic agent in humans. Therefore, although extremely effective in cats, at this stage there are insufficient data to support its long term safety as a topical agent.

LYSINE

There is an expanding amount of literature regarding use of lysine as a therapy for cats with herpetic disease. Although the safety of this approach has not been questioned, there are some variable efficacy data.

IN VITRO EFFICACY AGAINST FHV-1

Lysine limits the in vitro replication of many viruses, including FHV-1. The antiviral mechanism is unknown; however, many investigators have demonstrated that concurrent depletion of arginine is essential for lysine supplementation to be effective. This finding suggests that lysine exerts its antiviral effect by antagonism of arginine. This is also true for FHV-1 where arginine is an essential amino acid for viral replication but, in the presence of small amounts of arginine, lysine supplementation reduces viral replication by about 50%. However, this effect was not seen in media containing higher arginine concentrations, suggesting that a high lysine/arginine ratio is critical for efficacy.

IN VIVO EFFICACY IN CATS

Results of two early independent in vivo studies supported the clinical use of lysine in cats. In the first of these studies, eight FHV-1–naive cats were administered 500 mg of lysine orally every 12 hours beginning 6 hours before, and continuing for 3 weeks after, experimental inoculation with FHV-1. Lysine-treated cats had significantly less severe conjunctivitis than cats that received placebo. In the second study, 14 cats latently infected with FHV-1 received 400 mg of lysine per os every 24 hours. Viral shedding was monitored for 30 days. Lysine administration in these cats was associated with a statistically significant reduction in basal viral shedding compared with cats that received placebo. Since these cats were normal, latently infected carrier cats, little or no clinical disease was seen during the month-long study in the placebo or lysine group. In both studies, plasma arginine concentrations remained in the normal range, and no signs of toxicity were observed, despite notably elevated plasma lysine concentrations in treated cats. Both of these studies used experimentally infected line-bred cats. Therefore, the applicability of these data in naturally infected, genetically diverse cats required investigation.

A subsequent study examined the effects of lysine in 144 cats residing in a humane shelter. Cats received oral boluses of 250 mg (kittens) or 500 mg (adult cats) of lysine once daily for the duration of their stay at the shelter and outcomes were compared with those of an untreated control group. No significant treatment effect was detected on the incidence of infectious upper respiratory disease (IURD), the need for antimicrobial treatment for IURD, or the interval from admission to onset of IURD. However it was not determined if and to what extent these cats were shedding or infected with FHV-1 or other pathogens. This study also highlights the concern that daily handling of cats for bolus administration of lysine may not only be ineffective but actually stimulate further viral reactivation through stress or cause transfer of pathogens between cats by shelter workers administering the lysine. Therefore studies examining the safety and efficacy of lysine incorporated into cat food were conducted. An initial
safety trial revealed that cats fed a diet supplemented with up to 8.6% achieved plasma lysine concentrations similar to those achieved with bolus administration, showed no signs of toxicity, and had normal plasma arginine concentrations. In a subsequent study, 50 cats with enzootic IURD were fed a basal diet (~1% lysine) or a diet supplemented to approximately 5% lysine for 52 days while subjected to rehousing stress, which is known to cause viral reactivation. Perhaps not unexpectedly, food (and, therefore, lysine) intake decreased coincident with peak disease and viral presence. As a result, cats did not receive additional lysine at the very time they needed it most. Analysis of the data revealed that disease in cats fed the supplemented ration was more severe than that in cats fed the basal diet. In addition, viral shedding was more frequent in cats receiving the supplemented diet.

To further elucidate the efficacy of dietary lysine supplementation, we performed a similarly designed experiment in a local humane shelter with a more consistent “background” level of stress and with greater numbers enrolled compared with the initial rehousing study. We enrolled 261 cats; each for 4 weeks. Despite plasma lysine concentration in treated cats being greater than that in control cats, more treated cats than control cats developed moderate to severe disease and shed FHV-1 DNA at certain points throughout the study.

Unfortunately, there is considerable variability among all of these studies of lysine safety and efficacy, especially with respect to methodology, study population, and dose and method of lysine administration. Taken together, data from these studies seem to suggest that lysine is safe when orally administered to cats and, when administered as a bolus, may reduce viral shedding in latently infected cats and clinical signs in cats undergoing primary exposure to the virus. However, the stress of bolus administration in shelter situations may well negate its effects and data do not support dietary supplementation. Unfortunately, no studies to date have been conducted on client-owned cats although anecdotal evidence suggests that there is a benefit from administration of lysine. Although each clinical presentation needs to be assessed individually, I recommend that lysine be administered to client-owned cats as a twice daily (500 mg) bolus and not added to food. Owners should be made aware that this is usually only an adjunctive or palliative therapy and that administration of antiviral drugs may also be necessary to gain better control of signs. Unlike the protocol for HSV-1-infected humans, owners of cats receiving lysine for FHV-1 should not be advised to restrict their cat’s arginine intake.

SUMMARY

Data generated in recent in vitro and in vivo studies have provided much support for the use of antiviral drugs as well as the amino acid lysine. Although these populations provide numerous advantages for initial studies of drug safety and efficacy, it is important to interpret these data in light of the populations in which they were generated. It is likely that data gained from treating laboratory-bred, experimentally-infected animals need not always apply directly to more genetically diverse naturally infected cats. It is to be hoped that well designed, placebo-controlled, double-masked studies in client owned animals will be forthcoming.

REFERENCES


Hyphema. Part I. Pathophysiologic Considerations

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ABSTRACT: Hemorrhage in the anterior chamber of the eye, or hyphema, results from a breakdown of the blood-ocular barrier (BOB) and is frequently associated with inflammation of the iris, ciliary body, or retina. Hyphema can also occur by retrograde blood flow into the anterior chamber via the aqueous humor drainage pathways without BOB breakdown. Hyphema attributable to blunt or perforating ocular trauma is more common than that resulting from endogenous causes. When trauma has been eliminated as a possible cause, it is prudent to assume that every animal with hyphema has a serious systemic disease until proven otherwise.

Hyphema is defined as hemorrhage within the anterior chamber of the eye (Figure 1). In contrast, the accumulation of leukocytes in the anterior chamber is termed hypopyon. The etiopathogenesis of hyphema is multifactorial, but ultimately the final common pathway is breakdown of the blood-ocular barrier (BOB) and subsequent intraocular hemorrhage that is often associated with inflammation. Many of the mechanisms that cause intraocular hemorrhage may also result in hemorrhage in other parts of the body. This article focuses on hyphema as a “red flag” for sight-threatening ocular or life-threatening systemic hemorrhagic disease.

When hyphema is present, a thorough diagnostic evaluation similar to that indicated for any third-compartment hemorrhage (e.g., hemoabdomen, hemothorax) should be initiated. Attentive clinicians will recognize the importance of a thorough diagnostic workup before or during the initial treatment of hyphema. Death attributable to systemic or vital organ hemorrhage may occur if the diagnostic workup is incomplete. Part I of this two-part presentation focuses on the many pathophysiologic mechanisms that most frequently result in hyphema, each of which is considered a separate entity in this article. However, concurrent involvement of more than one mechanism is common. Part II will cover diagnosis and treatment of hyphema.

BLOOD–OCULAR BARRIER

The BOB, which consists of the blood–aqueous and blood–retinal barriers, prevents erythrocytes and leukocytes and inhibits tissue fluids and proteins from entering nonvascular ocular tissues and compartments. The BOB consists of endothelial
and epithelial tight junctions with variations in their degree of permeability. Dysfunction of the blood-aqueous barrier frequently results in hyphema; breakdown of the blood-retinal barrier generally causes retinal, subretinal, and choroidal hemorrhage but infrequently results in hyphema. The posterior lens capsule and zonules limit but do not completely prevent movement of blood from the anterior chamber to the vitreous and vice versa.

Because the intraocular pressure (IOP) is normally higher than the pressure in the aqueous humor drainage pathways (the scleral venous plexus), retrograde blood flow into the anterior chamber is prevented. IOP lower than the pressure in the scleral venous plexus may predispose to hyphema via retrograde blood flow into the anterior chamber.

**PATHOPHYSIOLOGIC APPROACH**

With the exception of severe intraocular disease, the diagnostic differentials for hyphema do not differ substantially from those for hemorrhage in other areas of the body (e.g., hemotorax, hemoadenoma); therefore, the diagnostic approach to determine the underlying cause of hyphema is similar. In addition to systemic causes, ocular disorders should be considered. Clinicians must develop a sound understanding of the potential causes of hyphema so they are able to construct a list of differential considerations for each mechanism. The most common mechanisms of hemorrhage that may result in hyphema follow.

**Iridocyclitis**

Iridocyclitis (anterior uveitis) is the most common ocular disease associated with a breakdown of the blood-aqueous barrier. Disruption of the blood-aqueous barrier may lead to aqueous flare (predominantly proteins), hypopyon, and/or hyphema, depending on the inciting stimulus and duration of the disease. Most of the pathophysiologic mechanisms of BOB breakdown discussed in the remainder of this article are also possible causes for iridocyclitis. Regardless of the cause, if left untreated, hyphema will eventually result in iridocyclitis when chemotactic triggers recruit inflammatory cells for cleanup.

**Trauma**

Hyphema attributable to exogenous causes (blunt or perforating trauma) is probably more common than that resulting from endogenous causes (see Causes of Hyphema). Blunt trauma to the head seldom results in hyphema because the eyeball is protected by anterior portions of the bony orbit and orbital soft tissues. However, severe blunt trauma to the anterior orbital rim or periorbital soft tissues and eyelid may result in hyphema. In this case, examination and palpation of the periocular area usually reveals clinical signs of trauma, such as swelling and bruising of the eyelids and conjunctiva, fracture of the bony orbit, or orbital hemorrhage and resultant orbital mass effect. Bilateral hyphema is seldom caused by mild trauma. When blunt ocular trauma occurs, the sudden rise in IOP associated with ocular indentation causes anterior chamber angle distortion and may result in rupture of iris stromal or ciliary body vessels and subsequent hyphema.

Perforating trauma (e.g., cat scratch, BB pellet) to the eyeball (cornea, sclera) with direct damage to intraocular vasculature is more likely to result in traumatic hyphema than is blunt trauma. Traumatic hyphema can also be associated with proposis of the globe and may be accompanied by structural damage to the eye, including lens subluxation and dislocation, vitreous hemorrhage, or retinal detachment. Head radiographs help to reveal fractures of the orbit or skull in trauma cases. When exogenous sources of hyphema have been eliminated, the diagnostic approach is further directed by results of physical and ophthalmic examinations.

**Thrombocytopenia**

Lack of an adequate number of circulating platelets can result in hyphema and hemorrhage secondary to ongoing capillary microtrauma induced by normal activity or exogenous insult. Thrombocytopenia is typified clinically by petechial hemorrhage of mucosal and cutaneous surfaces. Hyphema and concurrent petechial hemorrhages should prompt clinicians to consider thrombocytopenia as a likely mechanism of disease. Thrombocytopenia may be induced by immune-mediated destruction of platelets, infectious agents (e.g., *Ehrlichia canis, plasmodium vivax, Leguizmo species*, *Rickettsia rickettsii*), sepsis, splenomegaly, neoplasia, or disseminated intravascular coagulation.
Causes of Hyphema

**Trauma**
- Blunt
- Penetrating (with or without foreign body)

**Thrombocytopenia**
- Decreased platelet production in the bone marrow
  - Drug or chemical toxicity–induced bone marrow hypoplasia (e.g., estrogens, antiinflammatory agents, antibiotics, tranquilizing agents, diuretic agents, dapsone, myelosuppressive chemotherapy)
  - Toxic doses of irradiation
  - Chronic infections (e.g., feline leukemia virus [FeLV], *Ehrichia canis*, *Ehrichia platys*, canine distemper, parvovirus, heartworm disease)
  - Myeloproliferative disorders (e.g., FeLV, feline immunodeficiency virus [FIV], lymphoma, tumor metastasis)
  - Estrogen-secreting tumors (e.g., Sertoli cell tumor)
  - Myelofibrosis
  - Immune-mediated megakaryocytic hypoplasia or aplasia
  - Chronic renal disease

**Reduced circulating platelet life span**
- Sequestration (e.g., splenomegaly)
- Immune-mediated platelet destruction
- Nonimmunologic platelet destruction
  - Microangiopathic thrombocytopenia (e.g., disseminated intravascular coagulation [DIC], tumor microvasculature [hemangiosarcoma, hepatic tumors])
  - Microangiopathic hemolytic anemia
  - Severe vascular injury and vasculitis (see Vasculitis and uveitis)
  - Drug-induced (e.g., heparin)
  - Platelet loss via hemorrhage (usually mild thrombocytopenia)
  - Infectious agents (e.g., *E. canis*, *Rickettsia rickettsii*, *Dirofilaria*)

**Thrombocytopenia** (defects in platelet adhesion, aggregation, or release reactions)
- Inherited von Willebrand’s disease and other hereditary thrombopathias, including breed-specific thrombopathias
- Systemic illness: Uremia, collagen deficiency disease, hepatic disease, pancreatitis, ehrlichiosis (*E. canis*, *E. platys*), FeLV, dysproteinemia, gammopathies, myeloproliferative myelodysplastic disorders, DIC, lymphoproliferative disorders, multiple myeloma
- Drug-induced: NSAIDs, corticosteroids, diuretic agents, tranquilizers, synthetic colloid solutions (e.g., dextran), α- and β-blockers and stimulators, hormonal agents (e.g., progestin, estrogen), vinca alkaloids, antibiotics and antiparasitic agents, heparin
- Antibody-mediated platelet dysfunction: Immune-mediated thrombocytopenia, systemic lupus erythematosus

**Coagulopathy**
- Inherited
- Acquired

**Vasculitis and uveitis**
- Infectious: Rocky Mountain spotted fever, ehrlichiosis, leptospirosis, brucellosis, piroplasmosis, leishmaniasis, onchocerciasis interna, ocular filariasis (*Dirofilaria immitis*), tuberculosis, geotrichosis, protothecosis, toxoplasmosis (*Toxoplasma gondii*), FIV, FeLV, feline infectious peritonitis (FIP), canine adenovirus 1, cryptococcosis, blastomycosis, coccidioidomycosis, candidiasis
- Immune-mediated (e.g., uveodermatologic syndrome)
- Neoplasia (e.g., lymphosarcoma, ocular sarcoma, metastatic tumors)
- Lens-induced uveitis
- Episcleritis
- Systemic inflammatory response syndrome: Sepsis, endotoxemia (e.g., pyometra)
- Secondary to keratitis or trauma
- Idiopathic

**Noninflammatory vascular disorders**
- Hyperadrenocorticism
- Ehlers-Danlos syndrome
# Causes of Hyphema (continued)

**Hyperviscosity Syndrome**<sup>6,10-17</sup>
- Mono- or polyclonal gammopathies: Multiple myeloma, lymphoma, leukemia, chronic inflammation, antigenic stimulation (e.g., dirofilariasis), FIV, FIP, ehrlichiosis (<i>E. canis</i>, <i>E. phaeocyrtis</i>)
- Severe erythrocytosis: Hemorrhagic gastroenteritis, polycythemia vera, erythropoietin-secreting neoplasms

**Systemic Hypertension**<sup>29-30</sup>

**Neovascularization of Uveal and Retinal Tissues**
- Retinal detachment<sup>14,15,27-33</sup>
  - Primary
  - Secondary: Lenticular disease, infective diseases (see Vasculitis and uveitis), nonseptic inflammation (see Vasculitis and uveitis), trauma (see Trauma), intraocular neoplasia (see Neoplasia), systemic neoplasia (<i>e.g.</i>, multiple myeloma), systemic hypertension (<i>i.e.</i>, hypertensive retinopathy; see Systolic Hypertension section in text), congenital abnormalities (<i>e.g.</i>, retinal dysplasia), senile degenerative changes
  - Chronic glaucoma<sup>14</sup>
  - Intraocular neoplasia<sup>24</sup>
    - Primary: Lymphosarcoma, adenoma and adenocarcinoma, melanoma, posttraumatic uveal sarcoma in cats
    - Secondary: Adenocarcinoma, transitional cell carcinoma, lymphoma, multiple myeloma

**Congenital Anomalies**<sup>34,35</sup>
- Colle eye anomaly
- Vitreal detachment (<i>e.g.</i>, in Bedlington terriers, Sealyham terriers, Labrador retrievers)
- Persistent hyaloid artery (<i>e.g.</i>, with persistent hyperplastic primary vitreous in Doberman pinschers)

**Coagulopathy**

Abnormalities of the intrinsic, extrinsic, or common pathways of the clotting cascade may result in clotting abnormalities and subsequent hemorrhage and hyphema. Coagulopathies are typified clinically by large third-compartment or major organ hemorrhages (<i>e.g.</i>, body cavity, pulmonary, muscle/deep tissue) and may be inherited or acquired. Although echymotic hemorrhages are classically described in coagulopathies, cutaneous hemorrhages are less common in animals with coagulopathies than are thrombocytopenias and thrombocytopenias. Clinical presentation is extremely variable depending on the site of hemorrhage. Secondary signs of anemia (weakness, pallor) are often noted by owners of animals with a coagulopathy.

**Thrombocytopenia**

Defects in platelet adhesion, aggregation, or release can result in ineffectual platelet function.<sup>44</sup> These defects may be inherited (<i>e.g.</i>, von Willebrand's disease); be induced by systemic disorders, or, as in most acquired cases, occur as an idiosyncratic reaction to certain drugs (see Causes of Hyphema). Thrombocytopenia should be suspected in patients with hemorrhagic tendency, prolonged bleeding time, appropriate platelet count, and normal tests of secondary hemorrhage.

**Vasculitis**

Vascular endothelial cell abnormalities may result in transmural extravasation of blood from vascular channels in the iris and ciliary body, resulting in breakdown of the blood–aqueous barrier and hyphema. Vasculitis may result from primary or secondary immune-mediated destruction of endothelial cells (<i>e.g.</i>, immune-mediated vasculitis, toxoplasmosis), infectious diseases (<i>e.g.</i>, leptospirosis, Rocky Mountain spotted fever, feline infectious peritonitis), neoplasia, or systemic inflammatory response syndrome (<i>e.g.</i>, sepsis). Noninflammatory vascular disorders, including hyperadrenocorticism and Ehler-Danlos syndrome, can also result in hemorrhage.

**Hyperviscosity Syndrome**

Diseases that produce excessive globulins or other plasma proteins may result in hyphema because of (1) vascular endothelial cell compromise caused by intravascular sludging of blood with vessel wall necrosis, (2) infiltration of proteins into the vessel wall, (3) inhibition of hemoesis secondary to reduction in clotting factors, and/or (4) coating of platelets by abnormal paraproteins resulting in abnormal platelet aggregation.<sup>23</sup> Funduscopic examination of the contralateral eye may reveal engorged retinal vasculature and retinal hemorrhages. Common causes of hyperviscosity include plasma cell myeloma,
lymphoma, ehrlichiosis and chronic inflammatory disease. Serum total solids will generally be excessively elevated because of hyperglobulinaemia. Hyperviscosity syndrome can also be induced by severe erythrocytosis, such as hemorrhagic gastroenteritis, polycythemia vera, and erythropoietin-secreting neoplasms.

Systemic Hypertension

Hyphema attributable to systemic hypertension is most common in old cats and dogs and is often caused by chronic renal insufficiency. Systemic hypertension affects only the arterial vascular system. Chronic high arterial pressure may result in arteriosclerosis and autoregulatory arteriolar vasospasm. Arteriolar disease causes ischemia and capillary permeability changes (with leakage of plasma proteins) and eventually hemorrhage. In our experience, most cases of hyphema from vascular hypertension are attributable to retinal detachment (see Neovascularization of Uveal and Retinal Tissues section) and most likely occur in response to choroidal vascular hypertension. Hyphema may be less commonly caused by tearing of retinal vasculature that occurs during retinal detachment. Other common causes of vascular hypertension include hyperviscosity, hyperadrenocorticism, hyperaldosteronism, and pheochromocytoma.

Neovascularization of Uveal and Retinal Tissues

Although the presence of blood vessels is necessary in most tissues, neovascularization or angiogenesis of tissues can cause severe disease. The surfaces of the retina and iris are vulnerable to symptomatic neovascularization. Possible causes for neovascularization are ischemia (including long-standing retinal detachment), intraocular neoplasia, and inflammation. Vascular proliferation on the anterior iris surface (tuberculosis iridis) leads to the formation of a pre-iridal fibrovascular membrane, which can involve the peripheral iris and iridocorneal drainage angle and result in obstruction of aqueous humor outflow. Angiogenesis, a complex process that includes degradation of extracellular matrix and endothelial cell proliferation, is stringently regulated by numerous proangiogenic and antiangiogenic factors. Examples of growth factors that stimulate endothelial cell proliferation include fibroblast growth factors, insulintlike growth factors, transforming growth factor-β (TGF-β), and vascular endothelial growth factor (VEGF). The newly grown vessels are exceedingly fragile, leak readily, and can potentially result in hemorrhage and hyphema.

Retinal Detachment

Long-standing retinal detachment stimulates production of growth factors that induce vascular endothelial cell and fibroblast proliferation and subsequent fibrovascular membrane formation. The most frequent site of fibrovascular membrane formation in eyes with chronic retinal detachment is overlying the anterior iris surface (pre-iridal fibrovascular membrane). Acute hyphema may occur if the retinal vasculature tears when the neurosensory retina detaches from the underlying retinal pigment epithelial cells. Clinicians must determine the cause of the retinal detachment because life-threatening systemic disease may be the underlying abnormality (see Causes of Hyphema). In our experience, spontaneous (idiopathic) retinal detachment is rare in dogs and cats and an underlying cause is usually present.

Chronic Glaucoma

Pre-iridal fibrovascular membranes are also frequently detected in eyes with chronic (end-stage) glaucoma. It is likely that hyphema attributable to chronic glaucoma occurs secondary to tearing and leakage of the fragile pre-iridal microvasculature.

Intraocular Neoplasia

Growth of a neoplasm larger than 2 to 3 mm³ requires development of a microvascular network to facilitate delivery of nutrients and oxygen and removal of catabolites. Primary and metastatic intraocular neoplasms of the anterior uveal tissues are highly vascular. These neoplasms secrete vascular growth factors (e.g., VEGF, TGF-β) that stimulate formation and rapid growth of vessels to support and sustain tumor growth. Newly developed capillaries of neoplasms are prone to hemorrhage because they have incomplete basement membranes, are leaky, and
often fracture. Animals with hyphema attributable to intraocular neoplasia are usually in late middle age or older, however, we have diagnosed ciliary body hemangioendotheliomas and iris melanomas in dogs as young as 7 months of age. Most primary intraocular neoplasms are unilateral, and thus hyphema attributable to primary intraocular neoplasia is unilateral. Bilateral primary intraocular neoplasms are reported infrequently. Second- or tertiary intraocular neoplasia (e.g., lymphoma) may affect one or both eyes and may therefore result in unilateral or bilateral hyphema.

**Congenital Ocular Anomalies**

Hyphema in young animals should prompt clinicians to consider congenital ocular malformation as a likely cause. Collie eye anomaly, which is recessively inherited, is characterized by defects of the choroid and sclera attributable to abnormal mesodermal differentiation. In severe cases of vitreoretinal dysplasia (e.g., in Bedlington terriers, Sealyham terriers, Labrador retrievers, or springer spaniels), retinal folding is sufficient to permit complete retinal detachment. Retinal detachment and subsequent hyphema may occur with collie eye anomaly and vitreoretinal dysplasia. Persistent hyaloid artery occurs sporadically in dogs and is caused by failure of the fetal hyaloid vasculature to regress. Rupture of a persistent hyaloid artery leads to hemorrhage into the vitreous body, with blood passing into the anterior chamber.

**Anemia**

According to our experience and a previous report, severe acute anemia (e.g., severe tick or flea infestation) can cause hyphema when hemoglobin rapidly drops below 5 mg/dl. Insufficient oxygen supply may cause endothelial cells to die, which leads to leaking of blood vessels.

**REFERENCES**


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Topics covered

• Retrobulbar disease
• Glaucoma
• Proptosed globe
• Melting cornea
• Deep cornea
• Blood in the eye
• Viral keratitis
Retrobulbar disease

- Disease process is behind the eye
- The eye itself is usually normal
- Commonly mistaken for glaucoma

Retrobulbar disease

Clinical signs

- Vision is usually present
- PLR is usually present
- NOT BREED PREDISPOSED
Retrobulbar disease

Clinical signs
- Eye is prominent – look from above
- Globe may be deviated
- Reduced retropulsion – feel both eyes at the same time
- Cornea may be cloudy due to “exposure” = “ulceration”

Retrobulbar disease

Clinical signs
- Perilimbal hyperaemia “red eye”
- Conjunctival swelling “chemosis”
- Third eyelid prominent
Retrobulbar disease

Clinical signs

- Painful on opening the mouth
- Severe halitosis
- Whole head can be swollen
- High temperature
How do you approach a prominent eye?
Approach to a prominent eye?

Signalment

• Breed Predisposition
  – Brachycephalics → globe prolapse
  – German Shepherds → eosinophilic myositis
  – Golden Retrievers → extraocular myositis
  – Bassets, Cockers, Maltese → glaucoma

• Cats
  – Immune suppressed cats may have fungal infection

Approach to a prominent eye?

• Age
  • Young dogs → orbital cellulitis
  • Old dogs → orbital neoplasia

• Open the mouth
  • Pain retrobulbar abscess, orbital cellulitis

• Focal Light examination
  • Check the PLR – abnormal PLR eg dilated and non responsive pupil indicates glaucoma
  • Check depth of the anterior chamber and lens position
Approach to a prominent eye?

• Palpation
  – Retropulsion – push the eye back into the eye socket
  – Around the eye
    • Pain could suggest eosinophilic myositis or extraocular myositis

• Open the mouth
  – Pain on opening the jaw is suggestive of retrobulbar abscess

Approach to a prominent eye?

• Tonometry – measure the IOP

• Ultrasonography
  • Cystic structures show up well
  • US guided FNA or TruCut biopsy

• Radiology
  • Bone changes suggest neoplasia

• CT/MRI scans
  • Are the best way to image the orbit
Diseases commonly confused with retrobulbar disease

- Glaucoma – buphthalmic
- Uveitis
- Keratitis
- Episcleritis
- Conjunctivitis
- Extrocular myositis
- Eosinophilic myositis
- Orbital mucoceles

What do we do next?

- If the patient is pyrexic – broad spectrum antibiotics
  - Amoxycillin – clavunoic acid + metronidazole
  - Clindamycin
- Revisit in seven days
Pain - management

- NSAIDs
  - Carprofen
  - Meloxicam

Protect the CORNEA!!!

- Cornea can become ulcerated – lubricate topical antibiotic ointment or viscotears
- Light general anesthetic
- 2-3 temporary tarsoraphies – until the cornea is no longer at risk
- 4/0 Monofilament suture
Glaucoma

- Normal Intraocular pressure (IOP) is 10 to 25 mmHg
- Glaucoma is defined as increased IOP to above 30 mmHg
Be suspicious of glaucoma if…..

• Red eye unresponsive to treatment
• Breed predisposed
• One eye already been removed
• Dog depressed or in pain
Glaucoma

- Deep red eye (PLH)
- Blue eye - corneal oedema
- Mid-dilated non-responsive pupil
- Pain – depressed

NOTE - DON’T ALWAYS PRESENT LIKE THIS
Signs also seen with chronic glaucoma

- Globe enlargement = buphthalmos
- Lens luxation
- Vision loss - retinal and optic nerve atrophy
- Descemets streaks
Why worry about the IOP?

- Vision can be lost within 48 to 72 hours
- Once the eye is enlarged the eye is blind!
- Increased IOP is usually associated with discomfort, humans describe the pain is like having a headache, you can function but not happily

Diseases commonly confused with glaucoma

- Uveitis, especially LIU – lens induced uveitis
- Keratitis
- Dry Eye
- Retrobulbar Disease
- Episcleritis
- Conjunctivitis
Breed Predisposition

Breeds seen with glaucoma

- Basset
- Cocker Spaniel
- Fox Terrier/JRT
- Golden Retriever
- Labrador
- Maltese
- Poodle
- Springer Spaniel
- Samoyed
- Terriers
## Causes of Glaucoma

**PRIMARY**
- Malformation of the iridocorneal drainage angle
- Both eyes affected
- Breed
- Breed
- Breed

**SECONDARY**
- Lens luxation
- Uveitis
- Intraocular neoplasia
- Hyphaema
- Retinal detachment
- Fibrin

## Secondary Glaucoma - Causes

- Lens luxation
- Uveitis
- Intraocular neoplasia
- Hyphaema
Passage of Aqueous

- Produced in ciliary body
- Passes through the pupil
- Into the iridocorneal angle
- Through the pectinate ligaments
- Through the ciliary cleft
- Into the scleral venous plexus and bloodstream
Diagnosis of Glaucoma

• Clinical signs
  – Red eye
  – Blue eye
  – Pupil – dilated and non responsive

• Breed

• Measurement of IOP

Management of Glaucoma

• Refer if concerned re glaucoma and the owner is willing

• Early referral is required to save vision (under 72 hours of initial signs)

• Glaucoma is the most difficult condition that we treat
  – Many end up blind despite all that we do!
Aims of glaucoma therapy

- Relieve pain
- Save useful vision
- Prophylaxis in the fellow eye

Emergency Treatment

- Potential for vision

- No point in treating the glaucoma once the eye is enlarged
  - Enlarged eyes are BLIND!
  - Either eye removal or an ISP –intrascleral prosthesis
Emergency treatment

- Xalatan/Travatan
  - Expensive
  - Very effective
  - For 4 weeks

- Norvasc – protect the optic nerve

- Cortisone IV

Emergency Treatment

- If the IOP is slightly increased eg with a secondary glaucoma, or with hyphaema – blood in the eye

- Use Trusopt - a topical carbonic anhydrase inhibitor
Old emergency treatment

• Mannitol or Oral glycerin

• Carbonic hydrase inhibitors
  – Daranide
  – Neptazane
  – Diamox

• No longer used at our practice

Surgery for Glaucoma – potential for vision

• Diode laser surgery

• Cyclocryotherapy- freezing

• Drainage implants

• Endolaser (cataract surgery followed by laser + shunt)
Acute Glaucoma - Treatment

• Potentially sighted eyes – refer

• Primary glaucoma - diode laser transcleral cyclophotocoagulation

• Adjunctive therapy ie glaucoma drops may be required

Results of diode laser treatment

• Maintains the IOP within the normal range in 92% of cases after 1 treatment

• Useful vision in 50% of cases that were considered potentially sighted

• Follow up range 10-22 months
Secondary Glaucoma - Treatment

- Uveitis - medical therapy, laser, tissue plasminogen activator to remove clots of fibrin
- Lens luxation - lens removal
- Intraocular neoplasia - eye removal, pathology
Chronic Glaucoma - Treatment

• The eye is often blind, enlarged and painful

• Eye removal

• Intrascleral prosthesis

• Intraocular gentamicin

Intrascleral Prosthesis ISP

• Alternative to eye removal
Why do an ISP?

- This is an alternative to eye removal
- We save the “eye”
- Produces a more cosmetic look
- No pain
What happens?

• Under general anaesthetic

• All the unhealthy contents of the eye are removed

• A solid implant is injected into the eye

• A temporary stitch is then placed

Care after ISP

• Tricin Antibiotic Ointment TID for 10 days

• Rimadyl anti-inflammatory tablets for 10 to 14 days

• The temporary eyelid stitch is left in place for 3 to 4 weeks
Care after ISP

• Most dogs are more comfortable than before surgery within 2 days

• Revisits are required 10 to 14 days after surgery, then 3 to 4 weeks after surgery

• Some dogs may require drops to reduce excess healing reaction on the cornea

A cosmetic looking eye!
Complications

• Generally rare

• Some corneas take on a blue appearance

• Some dogs can develop corneal ulcers after surgery, which may take some time to heal, usually with scar tissue

This cornea has gone cloudy
Glaucoma

• Whenever you make a diagnosis of glaucoma you should assume that the other eye is predisposed to glaucoma

• Warn the owner to the early signs of glaucoma

• Prophylactic therapy will reduce the risk of glaucoma developing

Prophylaxis

• Use 1 drop twice daily

• Pilocarpine OR

• Timolol

• Trusopt
Glaucoma in cats

• Rare

• Inherited in Burmese & Siamese

• Usually secondary to
  – Chronic Uveitis – lymphocytic & plasmoctytic
  – Intraocular neoplasia
Glaucoma in Cats

- Treat intensively with anti-inflammatory medications
  - Pred Forte or Maxidex eye drops
  - Oral Prednisolone
  - Topical CAIs – Trusoptic
  - Prostanoids eg Xalatan do not seem to work in cats at all

- Consider enucleation with pathology if response is poor (TAKE CARE)
Melting Cornea

A bowl of custard
Keratomalacia – melting cornea
Melting Cornea

- Rapidly progressing, ulcer deepens within hours
- Copious amounts of discharge
- Painful eye
- Red eye

Keratomalacia

- Cortisone on an ulcer is often in the history
- In house Cytology – is VERY HELPFUL
  - *Pseudomonas* - rods
  - *Streptococcus* - cocci
Management of a Melting Cornea

• Antibiotic
  – Gentamcin or ocuflox or ciprfloxac in with Conoptal

• NSAIDs
  – Systemic carprofen/meloxicam

• Surgery
  – conjunctival graft

Careful Antibiotics usage

• For simple superficial corneal ulceration

• DO NOT USE OCUFLOX !

• DO NOT USE FORTIFIED GENTAMICIN !

• DO NOT USE TOBRAMYCIN !
Careful Antibiotics usage

• Gentamicin or fortified gentamcin:
  – Fortified gentamcin = 1 ml of Gentam (50mg/ml injectable) into a Gentamicin bottle

• Effective particularly against Gram-negative bacteria (*Pseudomonas*)

Careful Antibiotics usage

• Ofloxacin
  – Effective against – Aerobic gram-positive
    • (*Staphylococcus and some Strep species*)
  – Effective against – Aerobic gram-negative

• Conoptal is often used in conjunction with oculfox against gram – positive *Staphylococcus* and Beta-haemolytic - *Streptococcus*
Systemic Antibiotics

- Doxycycline as monohydrate at 5mg /kg in twice daily
- Promotes epithelialisation
- Reduces the activity of MMP2 and MMP 9 activity

Antibiotics
Pain - management

- NSAIDs
  - prolonged therapy
  - usually systemic
    - Carprofen
    - Meloxicam

NO STEROIDS!!

Atropine

- Dilates the pupil
  - reduces risk of synechiae
- Reduces pain
- Reduces the increased vascular permeability
Atropine

- Cats Ointment
  - tend to salivate - warn the owner

- Dogs 0.5% to 1% drops or ointment

- Subconjunctival injections in severe cases

360 degree Conjunctival Graft
360 degree conjunctival graft

• Leave the graft up for 2-3 weeks

• Surgically remove the graft leaving the cornea

• There will always be a scar – but we are trying to save the globe!!

• The amount of vision depends upon the amount of damage!!
What do you see?

- Deep corneal ulcer
- Little to no neovascularisation
- Surrounding corneal oedema
- Can see the pupil, iris and lens
- Descemet’s membrane
- Whitish gritty refractile substance
Write yes if you think this is infected?

Do we need antibiotics?

- Yes – this cornea is exposed and at greater risk of developing an infection
- You don’t need fortified gentamicin or ofloxacin
- Choose a broad spectrum antibiotic
What diagnostic tests?

- Fluorescein dye – paper not drops
- STT – Schirmer tear test
- Can the dog blink?
- Magnification – look at the eyelids
  - Extra eyelashes
  - Eyelid position

Dry Eye – always do a STT
Can I treat this medically?

**NO**
Surgical Options

- Clear corneal-conjunctival sliding graft
- Conjunctival pedicle graft
- Acell plus a pedicle graft
- Autogenous corneal transplant
- 360 degree conjunctival graft

Deep ulcer
How do I stabilise my patient?

• Elizabethan collar – protect your surgery
• Systemic NSAIDS – reduce inflammation
• Systemic Doxycycline – promote healing
• Atropine eye drops/ointment – stabilise blood ocular barrier
• Topical antibiotics – protect against infection
• Sedation – protect the dog against itself
Antibiotics

• Doxycycline as monohydrate
  – Oral dosing gives very effective corneal and conjunctival concentration
  – Promotes healing
  – Reduces corneal inflammation
  – Inhibits MMP 2 and MMP9

Ulcers – anti-inflammatories

• Just assume all ulcers are inflamed
  – Oral Carprofen (Rimadyl, Norocarp)
  – Oral cortisone is OK, but not in a melting cornea
  – NO topical anti-inflammatories
    • NO TOPICAL CORTISONE !!!!
Ulcers - atropine

• Pupil can become miotic – small

• Atropine is needed to dilate the pupil
  – Atropine drops 0.5% small dogs
  – Atropine drops 1% larger dogs
  – Atropine eye Ointment – cats

Cyclosporin

• The most important drug in treating these dogs is...

• CYCLOSPORIN

• Stabilised tear film, promotes better quality of tears and can help thin out the corneal lipid safely
Hyphaema

• Blood inside the eye

• Anterior chamber

• Posterior chamber

Hyphaema - blood in the eye
Causes of hyphaema

- Trauma
- Intraocular neoplasia
- Systemic neoplasia (lymphoma)
- Hypertension and its causes
- Coagulopathy, Thrombocytopenia, Hyperproteinaemia
- Collie Eye Anomalie (retinal detachment)

Hyphaema

- Look for another causes
- Always look at the other eye
- Dilate the other eye
- Look at both retinas
- Bilateral hyphema look for systemic disease
Approach to hyphaema

- Focal light
- Examine anterior chamber for changes
- Dilate the pupil – examine the retina
- Ultrasound the eye
- Measure blood pressure
- Systemic profile
- Refer to medicine for HELP!

Hyphaema

- Small bleeds will resorb within 3-5 days
- Poor prognosis - continual bleeding and black ball
Hyphaema - treatment

- Depends upon the cause
- Rest
- Cortisone – topically and orally
- If inflamed eg low IOP use atropine
- Tissue plasminogen activator?
- If IOP increased use Trusopt

Vitreal Haemorrhages

- Trauma

- Hypertension
  - older cats
Hypertension in cats

- Underlying renal disease
- Underlying endocrine disease
- Treat with amlodipine besylate
- ¼ of a 5mg tablet once daily recheck in 2 weeks and increase if required
- Prefer amlodipine to fortekor in cats

Remember – always look further
Viral Keratitis

FHV-1

- Conjunctivitis
- Keratitis
- Scarring of the nasolacrimal ducts
- Facial dermatitis
- Uveitis
FHV-1 in kittens

• Kittens versus adults

• Kittens get a severe bilateral conjunctivitis with marked chemosis and hyperaemia

• Blocked nasolacrimal ducts that can permanently scar

• Symblepharon formation

FHV-1 in kittens

• Supportive treatment

• Lysine powder – safe in kittens

• 1/8 of a teaspoon twice daily = 250 mg BID

• Bathing the eyes with warm compresses
FHV-1

- Surgical treatment of flushing the ducts can be frustrating and if too aggressively done can lead to duct rupture
- Surgical resection of the symblepharon is unrewarding as the conjunctiva can reattach very quickly post surgery

FVH-1

- Adults usually get a keratitis
- Early dendritic ulceration
- Geographical ulceration
- Superficial ulceration
- Indolent in appearance
- Vascularisation is variable
- Painful
FHV-1 - treatment

- Medical treatment first
- Idoxuridine hourly for the first 24 hours and the 6-8 x daily – compounded by Richard Stenlake in Sydney
- Zovirax ophthalmic ointment – 6 times daily
- Interferon injections – painful but seem to have a better response - twice weekly subcutaneously
FHV-1 - treatment

• Famcyclovir large cats ½ a 125mg once daily

• Famcyclovir small cats ¼ of a 125mg once daily

Cidofovir

• New exciting drug with lots of promise

• Only need to use it twice daily into the eye

• Good patient and owner compliance

• So far good results at Animal Eye Care
FHV-1 - treatment

- Lysine 250 mg twice daily
- Mushai powder 1/8th of a teaspoon twice daily
- Interferon injections twice weekly subcutaneously (these are made up in the clinic using Beta interferon??)
- Doxycycline 50mg once daily

FHV-1

- Corneal sequestrum can follow FHV-1
- Eosinophilic keratitis can follow FHV-1
The Veteducation Web-Seminar Series 2011
Eye Emergencies made Easy

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