What the heck is adnexa, anyway?

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I. Definitions of Eyelid Diseases.

A. Entropion--A turning in of the eyelid.
B. Ectropion--A turning out of the eyelid.
C. Trichiasis--Distortion of normally positioned lashes or periocular hairs so they irritate the conjunctival or corneal surface.
D. Distichiasis--Condition in which a hair emerges from one or more meibomian gland openings.
E. Distichiasis--Condition in which more than one hair emerges from one or more meibomian gland openings. (not a very commonly used term).
F. Atypical distichia (ectopic cilia)—a cilia growing from the meibomian gland through the palpebral conjunctiva—very painful.
G. Blepharitis--Inflammation of the eyelids.
H. Meibomian cyst--Collection of oily secretion in meibomian glands and ducts.
I. Chalazion--Granulomatous reaction in and around meibomian glands.
J. Hordeolum--Inflammation of glands of Zeis or Moll--"STYE".
K. Ptosis (Blepharoptosis)--Drooping of upper lid due to levator paralysis, CN III dysfunction, or sympathetic disturbance.
L. Symblepharon--An adhesion of the conjunctiva to itself or another structure. May be congenital or secondary to trauma, inflammation. Usually surgically corrected.
M. Lagophthalmos--Inability to completely close the eyelids.

II. Anatomy

A. External Features

1. Palpebral or lid fissure--dogs--10-35 mm; horses--36-51 mm.
2. Medial and lateral canthus--the medial canthus is more less distinct than the lateral.
3. Tarsal plate--Dense connective tissue which gives rigidity to eyelids and serves as an insertion for levator and Muller's muscles. Poorly developed in animals.

5. Cilia--the dog has cilia on the upper lid only; the cat has no true eyelashes. In the equine there are roughly 100 cilia on the upper lid but very few cilia on the lower lid. Vibrissae in the horse and cat aid in protection of the globe.

6. Lid margin--these contain the openings of the meibomian or tarsal glands.

7. Lacrimal puncta--located in upper and lower lids 2-4 mm from medial canthal angle in the dog and cat and 5-8 mm away in the horse.

B. Muscles and Innervation

The orbicularis oculi is a flattened muscle completely surrounding the palpebral fissure. It attaches to the orbital wall by medial and lateral palpebral ligaments. It is innervated by the VII cranial nerve and functions to close the eyelids.

The levator palpebrae superioris arises dorsal to the optic canal between the dorsal rectus and dorsal oblique muscles. Insertion into the tarsal plate of the upper lid is by a wide flat tendon passing between fascicles of the orbicularis oculi. The innervation is by CN III and the function is to elevate the upper lid.

Muller's muscle originates among the fibers of the levator muscle and inserts on the tarsal plate with the levator muscle. The function of this muscle is to assist in elevation of the eyelid. It is innervated by sympathetic nerve fibers.

The superciliaris or corrugator supercilii muscle originates from the median line of the frontal bone, extends over the orbicularis oculi and into the medial half of the upper eyelid. Its function is to elevate the nasal portion of the upper lid. It is innervated by the auriculopalpebral branch of CN VII.

The retractor anguli oculi muscle, which is a division of the frontalis m., arises from the temporal fascia and extends horizontally to the lateral palpebral angle. The function of this muscle is to maintain the normal size of the palpebral aperture. Innervation is via the auriculopalpebral branch of CN VII.

The sensory nerve supply to the eyelids is the ophthalmic branch of CN V to the upper lid and maxillary branch of CN V to the lower lid.
C. Glands of the Eyelids

1. **Meibomian** or tarsal glands are long sebaceous glands whose openings form a row posterior to the cilia. The glands themselves are close to or within the tarsal plate. The secretion is oily and forms the outer layer of the precorneal tear film. These number 20 to 40 per lid in the dog.

2. Glands of Zeis are sebaceous glands associated with the cilia.

3. Glands of Moll are sweat glands associated with the cilia.

4. Accessory glands or glands of Krause and Wolfring lie subconjunctivally. These produce part of the precorneal tear film in man, but their presence and function are not firmly established in the domestic species.

D. Function of the Eyelids

1. Protection of the globe.

2. Production, distribution, and removal of tears.
   a. Tear production.
      (1) Outer oily layer produced by meibomian glands--prevents tear evaporation.
      (2) Middle aqueous layer--majority of precorneal tear film.
      (3) Inner mucoid layer produced by conjunctival goblet cells.
   b. Tear distribution--eyelid closure moves tear film from lateral-temporal to nasoinferior (puncta).
   c. Tear removal--pressure gradient within nasolacrimal duct caused by eyelid movement, "draws" tears into puncta.

III. Disease of the Eyelids

For purposes of this discussion of disease states, we will use three broad categories: functional, inflammatory, and neoplastic. It is important to remember that these categories overlap to a large extent.

A. Functional Abnormalities

These may be either congenital or acquired. In most cases treatment is similar regardless of the etiology.
1. **Atresia or agenesis of the eyelid**: Most commonly seen in cats, primarily Persians. The most commonly affected area is the dorsolateral upper lid. Correction is by use of one of many blepharoplastic procedures.

2. **Ankyloblepharon**, or adhesion of the eyelid edges to each other, is physiologic in dogs and cats up to 10-15 days of age. If the condition persists, gentle traction or incising with tiny blunt scissors may be required. Usually the edges will separate with gentle traction or the use of a blunt instrument. If there is an associated infection, (neonatal conjunctivitis or *ophthalmia neonatorum*), excess swelling and discharge at the medial canthus will be noted. The eyelid opening must be opened and the patient treated with antibiotics. Untreated neonatal conjunctivitis can lead to severe corneal scarring and even loss of the globe.

3. **Blepharophimosis** or narrow palpebral fissure. Usually this is incidental, but in some cases may be a contributing factor in entropion. Correction, if needed, is by a plastic surgical procedure depending on the cause, species and breed.

4. **Enlarged palpebral fissure or macroblepharon**. This is often a problem in brachycephalic breeds with a large eyelid opening, e.g., Pekingese; Pug; Shih Tzu. A simple technique of shortening the palpebral fissure can be used, but a **medial canthoplasty is usually more effective**. A medial canthoplasty protects from lagophthalmos, proptosis and from nasal folds rubbing on the cornea. It will also correct any lower lid nasal entropion often found in affected breeds. It will help prevent or correct pigmentary keratitis due to exposure and irritation in affected breeds.
5. Eyelash diseases

a. Distichiasis. Most common form of eyelash disease. Extra cilia (hairs) arise from meibomian gland openings. Both upper and lower lids can be affected. These cases must be evaluated carefully as only those causing a problem need to be corrected. Often Cocker Spaniels and Poodles have a few to many fine soft lashes which do not cause a problem. The clinical signs to look for are excessive tearing and blepharospasm. Secondary corneal damage may occur.

Correction
1) Manual epilation. Only good if few in number. The effect is only temporary but may aide in determining if the hairs are causing clinical disease.
2) Electrolysis. Many units are available. A low current must be used to avoid eyelid scarring. A fine needle is run parallel to the hairshaft to the root. Then the current is turned on. You may have to repeat this procedure several times in young dogs.
3) Cryotherapy for distichiasis has also been described. Therapy of choice for multiple distichia if they are causing a problem.
4) Laser: Be careful. Aggressive lasering can damage tarsal plate and result in significant eyelid abnormalities.

b. Trichiasis. A normal placement of cilium, but the direction of growth is aberrant. Treatment as for distichiasis or, in some cases, a very slight entropion procedure may be used to roll the hairs away from the cornea.

c. Ciliated caruncle. Occurs in many “hairy” breeds. The hairs will often “wick” tears from the puncta onto the face. If the animal has a light haircoat, the overflow of tears will cause tear staining. Generally only a cosmetic issue.

d. Ectopic cilia (atypical distichia). A hair or bundle of hairs growing through the conjunctival surface of the lid at about the base of the meibomian gland (but not necessarily associated with the meibomian gland). It is often near the center
of the lid and usually in the upper eyelid. Clinical signs are blepharospasm and lacrimation and occasionally ulcerative, vascular or pigmentary keratitis that is closely associated with the location of the ectopic cilia. Surgical correction is by partial-thickness excision and/or cryoablation.

6. Entropion. The rolling in of the eyelids may be congenital; e.g., Shar Pei, Chow, Bulldog, St. Bernard, Golden Retriever; or acquired (spastic entropion) due to corneal pain; or cicatricial due to eyelid damage. Entropion is most common in dogs and sheep but does occur occasionally in cats (Persians primarily) and horses.
   a. In puppies less than 4½-5 months of age—recommend temporary eyelid tacking procedure. Use enough tacking sutures to “roll out” the eyelid margins. Topical lubricating ointments can be used to protect the cornea if needed after tacking. Surgical glue between the skin ridges created by the tacking sutures will relieve tension on the eyelid skin from the tacking sutures.
   b. For primary entropion, a combination surgery of excision of skin parallel to the lid margin and full thickness eyelid resection may be necessary.
   c. Temporary eyelid tacking may be utilized in adult animals that have significant corneal disease. This allows for secondary blepharospasm to abate and reduces the chance of over correction in animals that have keratitis and entropion.

The amount of correction should be estimated prior to anesthesia. Minor correction may require only the excision of skin parallel to the lid margin. Closure is with interrupted 4-0 or 5-0 nonabsorbable sutures. The major error with this method is for the incision to be placed too far from the lid margin. The incision should be only 2-3 mm from the margin.

In some cases entropion may be accompanied by ectropion of a portion of the lid. This is typically seen in St. Bernards, Newfoundlands, Chows, and Bull Mastiffs, but can occur in any breed. While some ophthalmologist think that this condition is due primarily to a defect of the retractor anguli oculi muscle, it seems also to be related to excess lid tissue and poorly developed tarsal plates. Correction involves creation of new lateral canthus, removal of excess lid tissue and/or primary entropion repair.
There are numerous gradations of entropion and many procedures have been devised to correct these based on surgeon experience and preference.

7. **Ectropion.** Rolling out of the eyelid may be congenital, e.g., St. Bernards, Spaniels, and Hounds; cicatricial following injury; or paralytic following facial nerve damage. Careful evaluation of ectropion is required. **Correction should be undertaken only if it is causing corneal disease or excessive ocular discharge.** Once again, numerous surgical procedures have been devised. A "V to Y" correction is used for cicatricial ectropion. This frees skin overlying scar tissue and allows the lid margin to retract to a more normal position. For congenital or conformational ectropion, the eyelid margin may be shortened or various sliding skin graft techniques have been developed.

8. **Wounds.** Lid lacerations are most commonly due to bite wounds or automobile trauma (or, in horses, catching the lid on some sharp protrusion from the wall of a stall, i.e., a nail). Always evaluate the patient carefully; if only the eyelid is involved repair as soon as possible. Flush the nasolacrimal ducts to be certain they are not damaged. Careful primary repair must be undertaken to ensure adequate physiologic and cosmetic results. **The wound should be cleaned of all debris and prepped with Betadine. Debridement should be minimal.** If the wound is not fresh or is extremely swollen and edematous, a Furacin® pack bandage for 12 to 24 hours will provide dramatic improvement in the appearance of the wound. This works especially well in large animals. **The wound is sutured in two layers.** Five-0 or 6-0 absorbable suture is used for the subcutaneous layers, taking care to bury the knots in the tissue to avoid corneal damage. Simple interrupted sutures of 4-0 or 5-0 silk or nylon are used for the skin. **The first suture is placed at the edge of the eyelid to ensure accurate apposition in a figure-8 pattern.** The next suture is placed 1-2 mm from the appositional suture. This is a tension suture and should be deep enough to catch the tarsal plate. **Close the rest of the wound with simple interrupted sutures.** Aftercare consists of topical and systemic antibiotics for 7-10 days. If there is excessive swelling, a light pressure bandage or hot pack may be required for 1-2 days.

9. **Coloboma.** A congenital, usually 'notch-like', defect of part of the eyelid. If mild, no
therapy; but if severe, surgical excision of the notch or a blepharoplasty technique may be required.

10. **Excessive nasal folds.** Brachycephalic breeds with enlarged nasal folds may require surgical correction if the folds are causing a secondary keratitis. Treatment may be conservative (keep fold clean and dry) or surgical (removal of part or all of the fold).

11. **Medial canthus entropion.** Common in the brachycephalic breeds and often associated with large palpebral fissure and lagophthalmos. Best correction is medial canthoplasty. Many of these breeds have medial canthal entropion and excessive nasal folds. Correction with a medial canthoplasty usually alleviates both problems.

### B. Inflammatory Diseases

1. **Blepharitis.** Inflammation of the eyelids, especially the lid margins, is common but may be overlooked if it is part of a more generalized dermatitis.
   a. Etiologies.
      1) **Bacterial**--most commonly *Staph. aureus*. Juvenile pyoderma/puppy strangles in puppies or staphylococcus hypersensitivity in the adult.
      2) Parasitic--mites, e.g., *Demodex* or *Sarcoptes* in young dogs, *Notoedres* in cats, face flies and *Habronemiasis* in horses.
      3) Metabolic--seborrheic blepharitis associated with generalized seborrhea or allergic dermatitis.
      4) Actinic--(related to sunlight).
      5) Fungal--dermatomycoses.
      6) Traumatic--lye, acids, fire.
      7) Immune-mediated--pemphigus, toxic epidermal necrolysis.
   c. Diagnosis and treatment: similar to any other dermatologic disease including skin scrapings, cultures (bacterial and fungal), and biopsy if necessary. Treat based on
your diagnosis.

1) **Bacterial**—may respond to topical antibiotic-steroid ophthalmic ointment. Often need *systemic antibiotics* and *corticosteroids* and hotpacks as well.

2) In generalized dermatologic disease, establish the underlying cause and treat.

2. **Chalazion.** This is a nodular mass formed by a granulomatous reaction to the oily meibomian secretion which has escaped into surrounding tissue. A blocked duct initiates the process. The mass is usually painless, visible through the conjunctiva, and located near the lid margin. May be associated with chronic allergies/atopy. Treatment is by surgical excision through the conjunctiva. The skin is not excised. Aftercare consists of topical antibiotic-steroid ointment for 5-7 days but may need systemic therapy also. Always submit for histopathology.

   Small chalazion may be lanced and expressed under topical anesthesia. Aftercare is the same as described above.

3. ** Hordeolum** or Stye. This is an inflammation of the glands of Zeis or Moll (external hordeolum) or meibomian gland (internal hordeolum). Treatment includes drainage, topical antibiotic ointment, and hotpacks.

4. **Edema.** This is more of a clinical sign than a disease entity itself. Numerous etiologies.
   a. Allergy.
   b. Insect bites.
   c. Associated with cellulitis.

   Treatment depends on cause but may consist of steroids (topical and systemic), or non-steroidal anti-inflammatories and antihistamines (?) for allergy or insect bites, or antibiotics and non-steroidal anti-inflammatory for cellulitis.
5. **Uveodermatologic Syndrome (VKH-like syndrome)**

Usually seen as depigmentation and/or ulceration of mucous membrane junctions and eyelid margins. Usually see signs of anterior and posterior uveitis also (see Uveal Tract notes). Chronic uveitis may cause secondary glaucoma (see Glaucoma notes). Most often seen in Arctic Circle breeds but can be in any breed. This is an immune-mediated disease of unknown cause. Diagnosis is by clinical signs and/or skin biopsy. A skin biopsy can be diagnostic. Treatment – topical and systemic steroids and oral azathiaprin. Treat glaucoma if present.

C. **Neoplastic Eyelid Diseases**

Full thickness eyelid resection is indicated when lesion involves less than 1/4 to 1/3 of the eyelid margin depending on the length of the eyelid margin. Cryotherapy is often effective with most canine eyelid masses.

1. **Dermoids.** Congenital mass lesion. Not neoplastic. Usually seen in young animals. Most common in cattle. Only rarely will an ocular dermoid extend past the globe onto the lids. In these cases dissect the growth free from the globe first, then use the appropriate blepharoplastic technique to correct the lid deformity.

2. **Meibomian Gland Adenoma. This is the most common eyelid tumor of dogs.** They are most common in older dogs (8 years or older). They are visible through the conjunctival surface and extend into the lid along the meibomian gland. These should be removed if causing irritation. They are nearly always benign. Treat with debulk and cryotherapy or full-thickness lid resection but debulk/cryotherapy is preferred.

3. Adenomas of Zeis and Moll Glands. These are on the skin surface and extend into the lid. They are benign but should be removed if causing irritation.
4. Papillomas. Usually superficial and associated with the skin. Remove if increasing in size. Cryotherapy is effective.

5. Melanomas. Usually superficial and benign. They usually are slow growing and multiple. Cryotherapy is effective.

6. Histiocytomas. These usually appear as raised, hairless, pink nodules which are very rapid growing. They frequently regress spontaneously in 3-5 weeks. This is primarily a tumor of young growing animals.

7. Squamous cell carcinomas. Most frequent in cattle (Herefords and Shorthorns), then horses (light-colored, i.e., Appaloosas and Paints; also Belgians), cats (white), and least frequently, dogs. They may exhibit very rapid growth, are highly invasive, tend to ulcerate early, and will occasionally metastasize (late) to regional lymph nodes or inner organs. Early biopsy and wide surgical removal is indicated. Radiation, cryotherapy, hyperthermia and immune stimulation (BCG) are also advocated. A common history is an ulcerated, nonhealing wound in a cat—think SCC.

8. Basal cell carcinomas. These are much less frequent in animals than in humans. Visually, it is a discrete circular nodule with an ulcerated surface. These are locally invasive but rarely metastasize.

THIRD EYELID

I. Anatomy and Physiology

The third eyelid is well developed in all domestic animals, but in higher primates it is a vestigial structure—the plica semilunaris. The structure varies slightly among species, but in general, it is a T-shaped hyaline (ruminants, dogs) or elastic (horse, pig, cat) cartilage skeleton covered by conjunctiva (palpebral and bulbar) with the gland of the third eyelid enveloping the base of the cartilage. This gland is an accessory lacrimal gland and contributes
to the aqueous portion of the tear film (~35% in dogs). Harder's gland is a gland separate from the third eyelid gland, located deeper in the orbit, and is not present in all animals.

Lymphoid follicles are found over the third eyelid gland on the bulbar surface of the third eyelid in most animals. Follicles are not normally found on the palpebral surface of the third eyelid.

Movement of the third eyelid is passive in all species except the cat and results from increased intraorbital pressure on a fat pad at the base of the third eyelid pushing the third eyelid forward. Thus, contraction of the extrinsic muscles of the eye retracts the globe and causes movement of the third eyelid. Of domestic species, only the cat has a muscle to the third eyelid. This has sympathetic innervation and functions to retract the third eyelid.

II. Function
   A. Protection of cornea.
   B. Production of aqueous portion of precorneal tear film.
   C. Distribution of tear film.
   D. Limited immunological activity.

III. Congenital Disease
   A. Encircling third eyelid--this is a condition occurring primarily in Cocker Spaniels. Treatment is surgical removal of the dorsal band, but this is almost never necessary. Much more often in these breeds (especially Cockers) there may be an encircling dorsal remnant that does not cause clinical problems and needs no treatment.
   B. Pigmentation of the third eyelid is variable depending on hair color of the animal. Lack of pigment may be either unilateral or bilateral. In the canine, the leading edge of the third eyelid is normally pigmented. Nonpigmentation gives a more reddened appearance to the lid. Hypopigmentation predisposes to squamous cell carcinoma in cattle and horses. Cats usually have nonpigmented third eyelids but do not seem to be predisposed to tumors because of this.
   C. Dermoids--these are uncommon and usually involve the globe and cornea as well. Most commonly occur in cattle and dogs. Treatment is surgical excision where necessary.
   D. Eversion of the cartilage (see Acquired Diseases).
IV. Acquired Diseases

A. Prolapse of the gland of the third eyelid ("cherry eye")--this is primarily a disease of young dogs (less than two years), most commonly Beagles, Cocker Spaniels, Pekingese and Bulldogs. The gland protrudes above the free border of the third eyelid between the globe and the third eyelid, and usually becomes irritated and inflamed. The onset is sudden and may be accompanied by excessive tearing, mucoid discharge and a variable amount of conjunctival inflammation.

Regardless of the STT results, we always recommend that the prolapsed gland be surgically replaced. Currently accepted treatments include surgical replacement of the gland by: 1) using the "pocket technique", or 2) suturing it to the deep periorbital tissue. The gland may be surgically excised with ease, but as it contributes to the aqueous portion of the tear film, excision may result in KCS. The gland should not be excised if the tear production is borderline or low or in breeds predisposed to KCS. The third eyelid itself should never be removed. The client should always be advised of the possible occurrence of third eyelid gland prolapse in the other eye.

B. Eversion or inversion of the cartilage--primarily in dogs; occasionally in Burmese cats. It occurs most frequently in young dogs of the large breeds, primarily Great Danes. It is usually idiopathic but can be acquired following injury or improper third eyelid suturing. The cartilage curls either outward (eversion) or inward (inversion) forming a scroll. It is generally a cosmetic issue and does not cause a clinical problem. If it is only cosmetic, no surgical correction is recommended or required. If there is associated ocular discharge, conjunctivitis and discomfort, then surgical correction may be indicated. If necessary, treatment is surgical excision of the deformed piece of cartilage. A saline or saline/epinephrine solution injected in the third eyelid will separate the surfaces and prevent "button-holing" of the conjunctival surface. The conjunctiva on the convex surface is incised and the deformed cartilage isolated by blunt dissection and removed. Avoid leaving any rough edges on the remaining cartilage. The conjunctival incision is closed (if needed)
with 6-0 absorbable suture in a continuous pattern with buried knots to avoid corneal irritation. Aftercare for the above surgical procedures is a broad spectrum antibiotic-steroid ophthalmic ointment for 5 to 7 days. **Another treatment option** is to use a hand-held thermal cautery unit to “melt” the bent cartilage to allow it to move back into a normal position. We are just beginning to try this therapy but it is reported to have good success especially for lesions away from the leading edge of the third eyelid margin.

C. **Protrusion of the third eyelid**--this is a common complaint in small animal practice and has numerous etiologies:

1. **Decreased orbital mass**--dehydration and emaciation leading to loss of orbital fat and volume; the eyes become enophthalmic and the third eyelid protrudes bilaterally. Usually, there will be other associated clinical signs. See often in older dogs.
2. **Decreased ocular mass**--microphthalmia, phthisis bulbi; usually unilateral.
3. Increased orbital mass or pressure--usually neoplasia but can occur with inflammation or abscesses behind the globe. Unilateral usually.
4. **Denervation**--Horner's Syndrome.
5. **Ocular pain**--unilateral corneal ulcer, uveitis, or glaucoma problem leading to globe retraction.
6. **Encephalitis** and meningitis--tetanus, rabies, canine distemper.
7. **Conjunctivitis**--cats primarily.
8. **Idiopathic**--in cats may be associated with gastrointestinal problems. Therapy is dependent on the specific cause. **Do not remove third eyelids.**

D. **Follicular conjunctivitis**--this is a very common disease in dogs in which any prolonged ocular irritation or immunologic stimulus causes follicle development on the bulbar and palpebral surfaces of the third eyelid. Often the follicles will persist even after the initial stimulus is removed. **Presenting signs are a persistent mucoid discharge with hyperplastic follicles leading to a raised, roughened or "cobblestone" appearance.** Mild cases will respond to a topical antibiotic-steroid ointment, but discharge often returns when the medication is withdrawn. **Most cases respond to removal of the follicles**
mechanically with the curved end of a Bard-Parker handle or gauze sponges (being careful not to abrade the cornea). A steroid-antibiotic ointment should be dispensed for 5 to 7 days following debridement.

E. Neoplasia—neoplastic diseases of the third eyelid are not common in dogs, but lymphosarcoma, histiocytoma, adenocarcinoma and hemangioma have been reported. Squamous cell carcinoma occurs in cats but much less frequently than in cattle and horses. If you are unsure of the cause, aspirate or biopsy the lesion to delineate a the cause. The most common therapy for neoplastic processes is to surgically excise the lesion. Care should be taken to preserve as much of the remaining third eyelid as possible. Closure of the conjunctiva over the excision is with 6-0 gut in a simple continuous pattern. The knots should be on the palpebral surface to avoid corneal irritation. Other therapeutic options such as cryotherapy, radiation therapy, or immunotherapy may be used depending on the case.

F. Plasma cell infiltration—this presents as a white-grey bilateral thickening near the margin. Typically, this occurs in German Shepherds. There may be associated chronic superficial keratitis (pannus). Therapy is usually corticosteroids (subconjunctival and topical). Usually prolonged therapy is required.

G. Foreign bodies—often a refractory keratitis and/or conjunctivitis is due to a foreign body lodged behind the third eyelid.

V. Use of the third eyelid as a protective bandage.

A. Third eyelid flap.

Indications—the indications are very few and far between but it can be used to protect cornea during or prior to correction of adnexal disease.

A third eyelid flap does NOT have any healing properties and is no more efficacious than a tarsorrhaphy. This is an overused and misused technique that should probably be avoided, especially in small animals.
The cornea is supposed to be clear but what do I do when it becomes red and cloudy?

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I. Anatomy.

The cornea and sclera make up the tough and protective fibrous tunic of the eye. The cornea is a 42 diopter structure that supplies the majority (about 70%) of the total refractive power of the eye.

The cornea can be best thought of as a collagen stroma covered on the outer surface by 6 to 15 layers of epithelial cells (20-40 µm in domestic carnivores), and on the inner surface by one layer of endothelial cells. It can be described as a “fat-water-fat” sandwich; the epithelium and endothelium/descemet's membrane are hydrophobic while the stroma is very hydrophilic. There is no Bowman's membrane under the epithelium of the cornea of the dog, cat, horse, or cow as there is in man, other primates and birds. The epithelium and endothelium play vital roles in maintaining the transparency of the cornea. Despite conflicting reports of corneal thickness of companion animals, the cornea is approximately 0.55 mm thick in dogs with the central cornea being slightly thinner than the peripheral cornea.

5 layers of the cornea:

1) Pre-corneal tear film
2) Epithelium
3) Stroma
4) Descemet’s membrane
5) Endothelium

A. Pre-corneal Tear Film.

The epithelium of the cornea is protected and nourished by the pre-corneal tear film. This film, which gives the cornea its glistening appearance, is only 6 to 8 microns thick, and it is composed of three layers: (1) mucus layer derived primarily from the goblet cells of the conjunctiva, (2) watery layer produced by the orbital lacrimal gland and gland of the third eyelid, and (3) oily layer produced by the meibomian glands. The tear film has numerous
functions, including lubrication, limited bactericidal properties (lysozymes and some IgA), nutrition for the cornea, removal of debris and general maintenance of optical clarity. **A normal, healthy tear film is critical for the maintenance of corneal health.**

**B. Corneal Epithelium.**

The epithelium of the cornea is an extension of the conjunctival epithelium, with some modification. The normal corneal epithelium is approximately 5-7 cells thick, with a single layer of columnar-shaped basal cells (adjacent to corneal stroma), 2-3 layers of polyhedral (wing) cells and 3-5 layers of stratified, squamous nonkeratinized cells. The epithelium is transparent, free of blood vessels, and very firmly adherent to the underlying corneal stroma.

This firm adhesion is aided by small projections on the underside of the epithelium, called **hemidesmosomes**, that project down into the stroma. The negative pressure or suction created by the stroma's affinity for water, probably also helps keep the epithelium firmly against the stroma. **Normal epithelium is capable of regenerating itself very quickly—in a matter of hours to days.** It turns over approximately every 7 days through mitosis.

The epithelium has an important physical barrier function in preventing the seepage of the pre-corneal tear film into the cornea. It also acts as a barrier to microorganisms, preserving the integrity of all other ocular structures. When the epithelial barrier is breached, microorganisms have access to delicate intracorneal and intraocular structures, creating a potential threat to vision. Edema may also result from breach in the epithelial barrier as the tear film seeps into the water-loving corneal stroma.

**C. Corneal Stroma (substantia propria).**

Stroma represents approximately 90% of the corneal thickness. It is composed of well-organized, parallel layers of mainly collagen fibrils and few keratocytes. Keratocytes are transformed into fibroblasts when deep injury occurs and will form scar tissue. Thin collagen fibrils are uniformly positioned to allow 99% of light to enter the eye without scatter. Collagen fibrils, GAG’s (keratan sulfate, chondroitin sulfate and dermatan sulfate) and glycoproteins make up 15-25% of the stroma. The remaining 75-85% is water. The collagen matrix of the stroma is lipophobic and hydrophilic.
D. Descemet's Membrane.

Descemet's membrane is the basement membrane (10-15 µm thick) of the corneal endothelium. It is lipophilic and hydrophobic.

E. Corneal Endothelium.

The endothelium of the cornea is a single layer of hexagon-shaped cells lining the inner surface of the cornea. The endothelial cell layer is very active metabolically and plays the major role in maintaining corneal transparency. ATP-dependent pumps on the endothelial cells help to actively transport water out of the cornea in order to maintain its relatively dehydrated state. As animals age, endothelial density may decrease as much as 50%.

II. Physiology of Corneal Transparency.

Reasons the normal cornea is clear:
1) No pigment
2) No blood vessels
3) No keratinization
4) Precise arrangement of collagen lamellae
5) Relatively dehydrated

If the sclera and cornea are formed of similar substance, why is the cornea transparent and the sclera white? The best, and currently accepted, theory explaining the difference is the interference theory. The cornea is composed of parallel layers, or lamellae, of collagen lying like pages of a book. These lamellae are composed of collagen fibrils arranged in a regular lattice arrangement, equidistant from one another. The fibrils of adjacent lamellae run at right angles to each other, and each fibril runs from one limbus to the other. Transparency is dependent on this precise arrangement. Conversely, the sclera is composed of interwoven collagen without precise lattice arrangement of the fibrils, rendering it opaque.

Any alteration of the corneal stroma that causes alteration in this regular arrangement results in loss of transparency. Scar formation, following injury of the stroma, results in loss of transparency of
The stroma because the fibers in scar tissue are not in the proper arrangement. Edema separates the collagen fibrils and results in diffusion of light and loss of transparency. The causes of edema are numerous and the etiopathogenesis can be rather complex.

**The stroma is relatively dehydrated.** That is, it would like to take on more water. What maintains this dehydrated state? The epithelium on the outer surface and endothelium on the inner surface act as barriers. When the epithelium is damaged the stroma may double in thickness, and if the endothelium is damaged the stroma may swell to five times normal thickness. Likewise, when edema is seen focally in the cornea, this is usually a sign of epithelial disease (such as a focal corneal ulcer). When edema is seen diffusely in the cornea, this is usually a sign of endothelial disease (such as uveitis or glaucoma). The endothelium is more critical because, besides its role as a barrier to aqueous, the endothelium acts as a physiologic pump and actively removes fluid from the stroma.

### III. Nerve Supply to the Cornea.

The cornea is very sensitive. The nerve supply to the cornea is entirely sensory, via the ciliary nerves which arise from the *ophthalmic branch of the trigeminal nerve* (CN V). Nerves enter the midstroma as myelinated fibers from the limbus and lose their myelin as they terminate as a plexus just beneath the epithelium. These same nerves also provide innervation to the iris and ciliary body. Stimulation of these nerves by any ulcerative or chronic keratitis results in spasms of the iris and the ciliary body. This axonal reflex is a humoral response, which manifests as miosis, hyperemia and uveitis that is termed **reflex uveitis**. This is why **topical atropine** (a cycloplegic and mydriatic), which paralyzes the ciliary body and iris, offers pain relief in corneal injury.

The epithelium is, by far, the most sensitive layer of the cornea. Ninety-five percent of all nerve endings in the cornea are in the epithelium. **The corneal epithelium has more nerve endings per mm than any other tissue in the body.** An abrasion of the epithelium produces severe pain. Pain is related to the area of injury rather than the depth of an injury. There are considerably fewer nerve endings in the deep cornea than the superficial cornea which is why a superficial ulcer is more painful than a descemetocele. **Brachycephalic dogs and cats** have decreased corneal sensation.
compared to other skull shapes which complicates normal blinking and healing in these breeds.

IV. Corneal Wound Healing.

A. Epithelium.

Heals rapidly as follows:

— Epithelial cells migrate to defect after 4 hours (approx. 1-3 mm/day).
— Mitosis is initiated to complete cell layering.
— Normal epithelial cell thickness is reestablished.
— Adhesion between epithelial cells and stroma occurs slowly.

B. Stroma.

Heal slowly and scars readily.

— Initially healed with fibrosis/fibroplasia
— Remodeling leads to gradual restoration of normal thickness, collagen fiber arrangement and transparency
— Vascularization may be an important part of remodeling

C. Descemet's membrane.

— If injured may heal slowly.
— Scars readily.

D. Endothelium.

— Limited mitotic or regenerative capacity in adult dog.
— Cells will change shape and adjacent cells may spread into defect.
V. Corneal ulcers

**Erosion:** loss of a few layers of corneal epithelial without exposure of stroma. Also called “abrasion”. Treat as a simple ulcer.

**Ulceration:** loss of all epithelium with exposure of stroma.

All corneal ulcers can be divided into one of two categories: **simple ulcers** and **complicated ulcers**. Simple ulcers will heal with supportive care. Complicated ulcers require recognition and correction of the complicating factor before they will heal.

**Simple ulcers** are defined by the following criteria:

1) **Superficial** – only epithelium has been lost but no stroma
2) **No evidence of infection** – infection in the cornea usually appears as stromal infiltrate, which is white blood cells migrating within the cornea giving it a yellow/white/tan appearance
3) **Heal in an appropriate amount of time** – epithelium is very mitotically active, and even an ulcer that involves 90% of the corneal surface (if it only involves loss of epithelium and no loss of stroma) can be expected to be healed in 7-10 days. Ulcers usually take 1 day to heal for every 1mm they are wide.
4) **No complicating factors** – no underlying cause for the ulcer can be identified that would need to be corrected.

**Obtaining a diagnosis:**

A simple ulcer can usually be identified on clinical examination by application of fluorescein to the ocular surface. Fluorescein is a water-soluble (hydrophilic) molecule that is normally repelled by the hydrophobic corneal epithelium. When epithelium has been removed, as in the case of an ulcer, the hydrophilic stroma is revealed and fluorescein binds readily to it (called positive fluorescein retention or positive staining). Descemet’s membrane is hydrophobic, so if all the stroma has been lost (as in a descemetocoele) then the bottom of the ulcer will not show any fluorescein retention (but the exposed stroma in the walls of the ulcer will).
Cytology can always be performed to confirm that no infectious organisms are present in the case of a simple ulcer. To harvest cytology, ensure the patient is well-restrained and apply a topical anesthetic (such as proparacaine) to the corneal surface. Cytology can be harvested using a cytobrush, a Kimura spatula, the blade handle end (not the cutting end) of a scalpel blade or a dental applicator brush. The instrument should be brushed gently but firmly against the margins of the corneal ulcer and then wiped gently against a glass microscope slide. Dif-Quick stain is sufficient for most clinical uses. Slides can be submitted to a clinical pathologist for more thorough evaluation.

The cause of most simple ulcers is likely trauma. If you can identify a cause (such as entropion) then the ulcer is no longer simple—it is complicated!

**Treatment of simpler ulcers:**

1) **Topical antibiotics**—the purpose of topical antibiotics in a simple ulcer is to keep the wound from becoming infected. Remember that systemic antibiotics DO NOT achieve sufficient levels in the cornea to be effective—you must use a topical medication. A broad-spectrum antibiotic is most desirable. Triple antibiotic preparations (neomycin-polymyxcin-bacitracin or gramicidin) are ideal.

2) **Atropine**—remember the axonal reflex mediated by CN V that causes reflex uveitis, including spasm of the ciliary body. Atropine causes cycloplegia, or paralysis of the ciliary body, which alleviates the pain that results from the spasm of the ciliary body. Generally once daily administration or one time administration at the time of the first examination is sufficient for most patients. Atropine is contraindicated in patients with glaucoma or those predisposed to glaucoma.

3) **Analgesia**—While atropine does provide some analgesia, we know that superficial ulcers are very painful (remember that the superficial cornea is more densely innervated than the deeper cornea). A systemic non-steroidal anti-inflammatory (NSAID) or an opioid such as tramadol can be used for 3-5 days to provide additional analgesia.

4) **E-collar**—An e-collar may be necessary to prevent self trauma, but is probably not necessary in most cases.
Expected healing course:

The average simple ulcer should be healed in less than a week, and in most cases within 3-4 days. Any prolonged healing should prompt complete and thorough re-examination.

Complicated ulcers are defined by the following criteria:

1) **Deep/stromal loss**— anytime an ulcer involves loss of both epithelium and stroma, it becomes complicated to heal. While epithelium is highly mitotically active, stroma is largely acellular collagen fibers with few keratocytes. When the stroma is wounded, the process of activating keratocytes into fibroblasts that synthesize and replace the collagen is lengthy and prolongs the course of wound healing. Wounds that involve loss of stroma are slower to heal and more likely to develop secondary complications like infection or malacia. An ulcer that has lost all stroma down to the level of descemet’s membrane is termed a descemetocele. Remember that all that stands between the inside the eye and the outside world in a descemetocele is a single layer of endothelium and its basement membrane!

2) **Infection/melting**—Infection is visible in the cornea as yellow/white/tan cellular infiltrate within the stroma. Infected ulcers also tend to be more painful because of the greater involvement of the stroma. The presence of infection can be confirmed with cytology and culture/sensitivity. Keratomalacia, or melting of the cornea is the dissolving of the stromal collagen due to the action of collagenase and protease enzymes. There are two major sources of collagenase and protease: exogenous sources such as infectious organisms (bacteria, fungi) and endogenous sources such as white blood cells (especially neutrophils). Corneal melting can lead to corneal perforation if not treated appropriately.

3) **Do not heal in an appropriate amount of time**—Any corneal ulcer that has not healed within 7 days should be considered a complicated ulcer. In order to determine why the ulcer is not healing, a careful examination must be performed in order to rule out stromal loss, infection or other complicating factors.
4) **Complicating factors are present**—Complicating factors describe a variety of causes of corneal ulceration that must be addressed before corneal wound healing can occur. Examples of complicating factors include KCS, entropion, eyelid tumors, lagophthalmos or inability to blink, ectopic cilia, glaucoma, corneal denervation/CN V deficit and systemic immunocompromise (ie. Diabetes mellitus, Cushings disease). If these underlying factors are not addressed, the ulcer will not heal. Once the factor is resolved, the ulcer should heal without further inhibition.

**Obtaining a diagnosis**

A complete ophthalmic examination is key to making the correct diagnosis. Note that in cases of extreme stromal loss (> 90%), extreme caution should be taken in handling the patient as excessive restraint or struggling on the part of the patient may result in corneal rupture. If corneal cultures are to be obtained, they should be obtained prior to instilling any drops into the eye, including proparacaine or fluorescein as these may inhibit microbial growth. Cytology should also be obtained prior to instilling fluorescein if possible. Cytology and culture/sensitivity should be considered mandatory diagnostic tests in all cases of complicated corneal ulceration, particularly those with stromal loss, infection or melting. The results of cytologic evaluation will guide your initial choice of therapy, and culture/sensitivity will confirm or alter those choices.

If there is extreme stromal loss, avoiding a Schirmer tear test or tonometry is prudent to prevent the initiation of corneal rupture. It is important to perform those tests on the fellow eye, however, since they fellow eye may hold the key to the diagnosis! In a patient with KCS and a melting, infected ulcer, the Schirmer tear test may be within the normal range as the patient hypersecretes tears in the affected eye but the fellow eye may have an abnormally low Schirmer tear test and thus allow the correct diagnosis to be made.

**Treatment of complicated ulcers**

1) **Stromal loss**—If there is > 50% stromal loss, the ideal treatment is surgical stabilization, such as a conjunctival graft. In these cases, the cornea is at risk of rupture with subsequent loss of vision from retinal detachment or chronic uveitis and cataract formation. These patients should be referred to a veterinary ophthalmologist for evaluation. If referral is not an option, manage as an infected/melting ulcer. An e-collar to prevent self trauma is important. In the case of corneal laceration with iris prolapse, referral should be strongly encouraged.
2) **Infection/melting**—Cytology should guide your initial antibiotic choices. If a mixed population of bacteria are observed, a fluoroquinolone such as Ofloxacin 0.3% or Ciprofloxacin 0.3% is a reasonable starting place. An aminoglycoside such as gentamicin may be added if gram negative bacteria are observed, or a cephalosporin or triple antibiotic may be added if gram positive bacteria are observed. Antibiotic therapy should begin q2–4 hours and then decrease as the infection becomes controlled. Fungal keratitis is very rare in small animal patients. Since antifungal sensitivity varies widely with geographic region, consultation with a local veterinary ophthalmologist who has experience with your region is helpful. In central Illinois, voriconazole 1% solution is our most common first-line antifungal. The melting component must be addressed with anti-collagenase and anti-protease therapy. Autologous serum (serum harvested from the patient) is a highly effective anti-collagenase/protease. Serum should be stored aseptically in the refrigerator and replaced every 5 days. EDTA, topical tetracyclines, systemic tetracyclines and N-acetylcysteine are other anti-collagenase/proteases that can be utilized in addition to autologous serum. The frequency of administration depends on the severity of the disease, with q1-2h administration recommended for the most severely affected cases. Referral is appropriate for patients with infected or melting corneal ulcers. An e-collar to prevent self trauma is important.

3) **Not healing in appropriate amount of time**—If a simple corneal ulcer is not healed within 7 days, it must be considered complicated. It is important to then reconsider why the ulcer isn’t healing and look for evidence of stromal loss, infection/melting or other complicating factors. If these have all been ruled out, then consider that the ulcer may be indolent (see section on indolent ulcers).

4) **Complicating factors**—Careful ophthalmic examination will reveal any complicating factors present. It is imperative that these factors be corrected for the ulcer to heal. The treatment will vary with the complicating factor.

Treatment of the complicated ulcer can be...complicated. Recheck examinations may need to be frequent in the case of the infected/melting ulcer. Even if referral is not an option in the case of a complicated ulcer, call your local ophthalmologist to discuss the case if you do not feel comfortable with how to treat.
Corneal perforations

Corneal perforations must be first evaluated for vision. Many patients may lack a menace response due to miosis, hyphema or hypopyon. The clinician should carefully evaluate the patient’s dazzle reflex and consensual PLR to determine the potential for the globe to retain vision. If the globe is visual, surgical repair by an ophthalmologist is recommended for most cases. Medical management as for a complicated ulcer with stromal loss/infection can be used in cases where the perforation is sealed with an iris prolapse. Non-visual and leaking globes should be enucleated. Patients with a corneal perforation should be treated with a systemic antibiotic in order to prevent infection inside the globe (endophthalmitis).

Indolent Corneal Ulcers

Usually seen in older dogs and may be seen more frequently in Boxers. Very superficial nonhealing ulcer with undermining of the epithelium (non-adherent epithelium) at one or more areas along the edge is the classic clinical sign. The disease appears to be a basement membrane defect affecting the adhesion between the epithelium and the underlying stroma. Diagnosing an indolent ulcer is a diagnosis of exclusion. You must rule out all other causes of the ulcer not healing prior to diagnosing ulcer as indolent. We recommend treating indolent ulcers in dogs with grid keratotomy or diamond burr debridement. It is very dangerous to perform a grid keratotomy on an ulcer that has stromal loss, melting or is indolent. A grid keratotomy should never be performed in a cat as the most common etiology of non-healing ulcers in cats is FHV-1, not indolent ulcers as are seen in dogs.
Treatment

Under gentle manual restrain, apply topical anesthesia (proparacaine) to the corneal surface. The corneal surface may additionally be prepared by instilling dilute betadine solution. The non-adherent corneal epithelium is then gently debrided using a dry cotton tipped applicator. All non-adherent epithelium must be removed for the grid keratotomy to be successful. A 25g needle is then used to make fine lines in the anterior stroma, moving from normal cornea, across the ulcer bed and then back into normal cornea on the other side of the ulcer. The entire surface area of the ulcer should be covered. Alternately, a diamond burr debridement can be performed using a diamond burr.

Post-grid keratotomy or diamond burr debridement therapy should be as for a simple ulcer with a recheck exam in 2-3 weeks. Placing a bandage contact lens may provide the patient some additional comfort. If the diamond burr keratotomy has not resolved the ulcer, reconsider that the ulcer may not be indolent (some other factor is keeping it from healing) and consider referral for further evaluation.

VI. Selected Corneal Diseases.

All diseases of the cornea can be categorized as one (or both) of the following: a loss of thickness or a loss of transparency. The key to correctly diagnosing and treating corneal disease lies in the ability of the clinician to recognize which pattern is occurring.

The cornea has a relatively limited repertoire of responses to a wide variety of stimuli. The cornea can ulcerate, melt, vascularize, pigment, scar (fibrosis), or become edematous. Recognizing these patterns of response is the second key to correctly diagnosing and treating corneal disease.

A. Chronic Keratoconjunctivitis Sicca (KCS)

B. Chronic Superficial Keratitis or "Pannus".

This usually bilateral process occurs primarily in German Shepherds and sighthounds but occasionally in other breeds. The lesion is characterized by superficial neovascularization and pigmentation of the cornea. Pannus is a non-ulcerative and non-painful disease. Histopathology
shows a subepithelial infiltration of plasma cells and lymphocytes. The disease is thought to be **immune-mediated** in that no bacteria, fungi, or viruses are implicated. The involvement of B-lymphocytes and the response of the disease to glucocorticoids also support this theory. Exposure to high levels of UV radiation, as found in areas of high altitude such as Colorado, seem to make the disease more refractory to therapy. **Diagnosis is made primarily by the classic appearance of the lesion.** If the disease is left untreated for long periods of time, neovascularization and corneal melanosis may cause blindness.

1. **Treatment.**
   
   a. Prescribe **topical steroid** eye drops (dexamethasone or prednisolone). Topical hydrocortisone is likely NOT strong enough. **Topical cyclosporine or tacrolimus** can also be added.
   
   b. Betamethasone or triamcinolone can be given subconjunctivally if the patient is unresponsive or hard to treat.
   
   c. Adjust the frequency of drops to the minimum needed for control. May see relapses in the summer or fall.
   
   d. Even in cases with severe melanosis of the cornea, treat initially with topical steroids and recheck in a few weeks. In many cases, vision is satisfactory after the inflammation is controlled.

C. **Plasma Cell Infiltration of the Third Eyelid** ("plasmoma", "atypical pannus")—may occur concurrently with pannus.

   Signs: Hyperemia and depigmentation of the third eyelid.
   
   Diagnosis: Plasma cells/lymphocytes found on conjunctival cytology.
   
   Treat the same as pannus, including subconjunctival steroids.
   
   This does not respond as well as corneal disease to topical therapy but this is not vision threatening.
D. **Hepatitis Eye ("Blue Eye").**

"Hepatitis blue eye" refers to the corneal edema caused by inflammation and destruction of the corneal endothelium by the infectious canine hepatitis virus or the canine adenovirus type I (CAV I) vaccine and the Arthus type antigen-antibody reaction that can occur in the anterior segment of the eye. Similar vaccination reactions to the CAV II vaccine have been reported but are much less common. This disease is very uncommon with modern vaccines. Treat as a uveitis: 1. topical anti-inflammatory agent 2. topical atropine if painful.

E. **Endothelial Dystrophy.**

Degeneration of the endothelium results in edema of the cornea. Occurs in middle-aged to older dogs especially Boston Terriers and Chihuahuas, usually bilaterally but not always symmetric. Some feel that topical anti-inflammatory agents may be of benefit. Chronic use of topical steroids may lead to ulceration of the cornea. **Medical treatment:** topical hyperosmotic agents (5% NaCl) may help reduce the development of bullous keratopathy (multiple corneal vesicles). **Surgical treatment:** In moderate to severe cases with bullous keratopathy, thermal keratoplasty can be performed (by an ophthalmologist) to scar the cornea and decrease the risk of recurrent ulceration. **Surgical treatment:** A keratoleptynsis (thin conjunctival flap) may also used to treat and prevent progression.

F. **Herpes Keratitis in Cats.**

Often a history of respiratory infection (Feline Herpes Virus or FHV) is found. In neonatal kittens, FHV is can be a severe, systemic infection. Conjunctivitis and keratitis are some clinical signs that may be seen. In young cats, FHV may present as unilateral or bilateral conjunctivitis with or without clinical signs of respiratory disease. The "dendritic" herpetic corneal ulcer is seen primarily in mature cats. The virus localizes within CN V (trigeminal) ganglion and may remain latent until inciting an inflammatory response. Definitive diagnosis of FHV can be difficult but **polymerase chain reaction (PCR) may be the best test.** In addition, the virus is most easily isolated from acutely ill animals, making identification of long-standing cases and chronic carriers much more difficult but PCR offers a relatively simple and accurate way of screening patients.

Treatment is primarily supportive and symptomatic—topical and systemic (if
respiratory signs present) antibiotics and fluid replacement for animals which are depressed, off feed, and dehydrated. Many of the ocular sequelae are related to secondary bacterial infection, so culture and sensitivity testing may be indicated to aid in choosing an antibiotic.

The current **drug of choice for topical treatment** of feline herpesvirus *in vitro* is **cidofovir 0.5% solution**. It is not commercially available and must be compounded. The advantage of this drug over older antivirals is that it can be administered q12h rather than q3-4h, which improves owner compliance and decreases stress on the patient. Other antiviral drugs include trifluridine, idoxuridine and vidarabine. **Oral lysine** has been shown effective in reducing viral replication and clinical signs in cats (500mg PO q12h for adult cats, q24h for kittens). Oral famciclovir (40mg/kg PO TID) is safe and effective but can be expensive. Famciclovir may be the best drug to use if the cat shows signs of systemic disease, whereas cidofovir may be a better drug if the clinical signs are limited to ocular disease.

Sequelae to FHV include the development of chronic, recurrent conjunctivitis; symblepharon with adhesion of conjunctiva to cornea and variable degrees of distortion of the palpebral fissure; in severe cases there may be perforation of the cornea with eventual phthisis bulbi formation.

Vaccination of breeding stock and young kittens may reduce the incidence and severity of the disease.

**G. Corneal Sequestration in the Cat.**

Also called corneal mummification and "corneal black spot." It is characterized by a keratitis with a central, slightly elevated plaque of black, dried tissue in the center. **The specific cause is unknown but has been associated with brachycephalic breeds, feline herpes virus, nasal entropion, decreased corneal sensation and tear film abnormalities.** The treatment is removal by superficial keratectomy with or without adjunctive tissue replacement (conjunctival flap, corneal tissue or synthetic tissue). The condition may recur.
H. Feline Eosinophilic Keratitis.

Generally of unknown etiology with no age, breed, or gender predilection. Clinically appears as a raised, small, white/pink plaques in cornea, usually originating at the limbus. Diagnosis is confirmed by numerous eosinophils following corneal scraping. Affected cats may also have feline herpesvirus. Oral treatment can be with megestrol acetate (Ovaban®) 5 mg tablet PO daily for 5 - 7 days, then 5 mg every other day for 5 – 7 more doses. The mechanism by which this drug works to treat eosinophilic keratitis is currently unknown. Topical cyclosporine or tacrolimus can be used alone or in combination with oral megestrol acetate. We also use topical or subconjunctival corticosteroids alone or in conjunction with megestrol acetate. If topical steroids are used, antiviral therapy may be necessary (oral lysine and/or topical antiviral therapy) to decrease the chance of increased shedding of virus with steroid therapy. The disease may be seasonally recurrent. Some cats need chronic therapy.

I. Superficial Punctate Keratitis.

Punctate keratitis in the dog is characterized by very small superficial ulcers and epithelial and subepithelial infiltrates that give the cornea a stippled appearance. These dogs typically are quite painful manifested by excessive tearing and blepharospasm. This disease is one exception to the rule of "no steroids with corneal ulceration." Minimal treatment (1-2 times/day) with topical antibiotic-steroid combination drops frequently will cure or control this condition. This treatment should only be attempted if frequent follow-up (at least weekly examination and fluorescein staining) can be done. Topical cyclosporine has also been shown to be effective and is safe to give with corneal ulceration. This disease is uncommon and seen most frequently in dachshunds and Shelties. Consultation with an ophthalmologist is strongly recommended when this diagnosis is suspected.

J. Corneal dystrophy and degeneration.

In the dog corneal dystrophy is characterized by an opaque subepithelial plaque usually located in the axial (center) cornea. The plaque is, most often, sharply delineated and often has a silvery or grey-white appearance. Most are a result of subepithelial infiltration by calcium or cholesterol lipids or salts. The cause is unknown but most are suspected to be inherited. Some dystrophies diffusely involve the entire thickness of the corneal stroma. This
disorder is seen most commonly in purebred dogs. Since condition is non-painful, it does not need treatment in most cases. Corneal dystrophy must be carefully differentiated from corneal degeneration. Corneal degeneration is the accumulation of lipid and mineral in the cornea as the result of keratitis or intraocular disease. It may occur anywhere in the cornea, but is more likely to be perilimbal. Unlike corneal dystrophy, corneal degeneration is often associated with corneal vascularization and epithelial instability which can lead to ulceration and pain. Corneal degeneration can be immune mediated or secondary to corneal or intraocular disease. Treatment may involve topical anti-inflammatories, topical immunomodulators like cyclosporine A or tacrolimus and in extreme cases, keratectomy to remove the affected area +/- grafting.

K. Corneal pigmentation.

Etiologies—distichia, lagophthalmos, KCS, entropion or any chronic keratitis. This is seen more in brachycephalic breeds of dogs, particularly pugs. It is a major cause of impaired vision in the pug breed. Clinical signs—melanosis with or without corneal neovascularization. Treatment—specific for underlying cause. Topical immunomodulators like cyclosporine A or tacrolimus can be used in attempt to thin existing pigment or prevent the progression of pigmentation. A medial canthoplasty may be used to protect the cornea and reduce corneal exposure. A special form of corneal pigmentation is recognized in pugs that is called pigmentary keratopathy. This disease may have a genetic basis in pugs.

L. Dermoid.

An embryological defect in which skin, hair follicles and all, is located on the cornea or cornea and conjunctiva. Treatment—superficial keratectomy. Use antibiotics and atropine postoperatively until surgical site is re-epithelialized.

VII. Diseases of the Sclera

A. Episclerokeratitis—localized inflammatory lesion of the episcleral tissue involving primarily the perilimbal area. Conjunctiva is movable over it but mass is often nodular, immovable, and hard. Usually involves only 1 eye but can be in both eyes. Lesions can be singular
or multiple. Looks like a tumor and often develops suddenly. May also present as mass of the third eyelid. Other names for this disease include episcleritis, nodular granulomatous episcleritis, collie granuloma, fibrous histocytoma, pseudotumor)

Cause: Considered immune mediated.

Treatment: Topical and systemic steroids and/or immunomodulators suchs as cyclosporine A or tacrolimus. In refractory cases, subconjunctival steroid injection and/or azathiaprine may be beneficial.

B. Neoplasia.

1. Squamous cell carcinoma
   — Common in horses and cattle.

2. Epibulbar Melanoma.
   — Need to differentiate from uveal origin.
   — Usually benign.
   — Treatment by local excision (debulk and biopsy) and adjunctive cryoablation or laser ablation
I. Anatomy.

The uveal tract is the vascular coat or layer of the eye which serves an immunologic and nutritive function. The uveal tract consists of the iris, ciliary body and choroid. The anterior uvea includes the iris and ciliary body; the posterior uvea is the choroid. The choroid lays between the sclera and retina in the posterior part of the globe. Finally, vitreous humor fills the space between the retina and posterior aspect of the lens.

The most important function of the uveal tract is to form the blood-aqueous barrier. This barrier is what keeps the intraocular contents protected and separate from systemic blood circulation, which can contain toxins, microorganisms and immune cells that could be harmful to the eye. The blood-aqueous barrier is primarily composed of the tight junctions between the blood vessels in the uvea and the ciliary body epithelial cells. The retina also has similar tight junctions in the retinal blood vessels and between the retinal pigmented epithelium (RPE), which is why the retina is sometimes considered to be part of the uveal tract. When uveitis (inflammation of the uveal tract) is present, the blood-aqueous barrier breaks down. This has the advantage of allowing components of the immune system to enter the eye, but can also be dangerous if the resulting immune response damages delicate intraocular structures, if toxins enter the eye or if microorganisms enter the eye. The immune system behaves differently in the eye than it does in other parts of the body; this is known as immune privilege. Immune privilege helps keep the immune system in check so that normal inflammatory processes do not harm intraocular tissues inadvertently.

A. Iris.

1. Muscles—the only muscles in the body derived entirely from ectoderm.
   a. Sphincter muscle.
      — Constricts the pupil.
      — Smooth muscle in mammals.
      — Parasympathetic control (CN III).
   b. Dilator muscle.
      — Dilates the pupil.
      — Smooth muscle.
      — Sympathetic control (ophthalmic branch of CN V).

2. Vessels.
a. **Major arterial circle.**
   — Incomplete. Located near the iris base.

b. **Minor arterial circle.**
   — Present in primates, pigs and possibly the horse.
   — Located near the iris edge.

3. **Pupil shape.**
   a. **Dog**—circular when dilated and constricted.
   b. **Cat**—circular when dilated but forms a vertically oriented slit when constricted.
   c. **Horse**—horizontally oriented oval.
   d. **Cattle**—horizontally oriented oval.

4. **Pupillary edge.**
   a. **Dog and cat**—pupillary pigment ruff (small projections surrounding the pupillary edge).
   b. **Horse and cattle**—corpora nigra or granula iridica (large, pigmented bodies on the upper, central pupillary edge as well as smaller bodies on the lower, central pupillary edge).

5. **Iris function.**
   a. **Regulate amount of light entering the eye.** The pupil is the hole in the center of the iris that allows light to enter the eye. The iris dilator and constrictor muscles control the pupil size and thus the amount of light entering the eye via the pupillary light reflex (PLR) pathway.
   b. **Maintain the blood-aqueous barrier.** The ciliary body, choroid and retina also participate in this function.
   c. **Plug holes in the cornea.** When corneal perforation occurs, the iris will act as a temporary or permanent plug in the hole. A permanent adhesion between the iris and cornea is called an anterior synechiae.

B. **Ciliary body.**

1. **Muscles.**

   In man, the smooth ciliary muscles are well developed and function to change the shape of the lens so different focal points can be attained (**accommodation**); domestic animals, in contrast, have poorly developed ciliary muscles and therefore a lesser ability to accommodate.
Spasm of the ciliary muscles causes intraocular pain; thus, cycloplegics (e.g., 1% atropine) are used to relax these muscles and decrease pain. In some species (such as birds and reptiles), these are skeletal muscles instead of smooth muscles.

2. Vessels.

The ciliary body is markedly vascularized and has tremendous blood flow.

3. Functions.

   a. Accomodation. The ciliary body processes are attached to the lens zonules which attach to the lens capsule. The contraction and relaxation of the ciliary body muscles changes the shape of the lens, which allows the lens to focus on near or far objects. This process is called accommodation.

   b. Produces the aqueous humor. The ciliary body epithelium produces all the aqueous humor contained in the eye. The enzyme carbonic anhydrase is critical to this process.

C. Choroid.

1. Vessels.

The choroid is markedly vascularized and has tremendous blood flow which supplies nutrition to the outer half of the retina. The oxygen diffusion maximum of the retina is 143 µm. If the retina is thicker than 143 µm, then it will have retinal vessels present.

2. Choroidal function.

The choroid has a critical metabolic role which maintains normal retinal function; the choroid supplies glucose, vitamin A, oxygen, etc., and removes metabolic waste products from the outer half of the retina.

II. Congenital Uveal Abnormalities.

   A. Uveal cysts.
      — Uveal cysts are fluid-filled, generally round to oval, structures surrounded by pigmented epithelium.
      — Form from the pigmented epithelium of the iris or ciliary body.
      — Can remain attached to the anterior uvea or occasionally separate and float freely within the anterior chamber or vitreous cavity.
      — Occur most frequently in the Boston Terrier, Golden Retriever, Labrador Retriever.
      — Major differential diagnosis is uveal melanoma; however, can
distinguish between the two via transillumination (cysts transilluminate whereas melanomas are solid); occasionally ultrasound may be necessary to differentiate a cyst from a melanoma.

— Usually, no treatment is necessary; rarely, cysts located in the anterior chamber cause complications (e.g., corneal edema due to endothelial touch, visual disturbances)—these cysts can be deflated via aspiration using a syringe and needle, but the preferred technique uses laser (a noninvasive method) to deflate the cysts.

B. Persistent pupillary membranes (PPM).
— Developmental abnormality—incomplete rarefaction of the iris tissue that crosses the pupil during embryonic stages.
— Arise from collarette of iris—on the anterior surface of the iris
— may adhere to another section of iris (iris-iris PPM); adhere to the anterior lens capsule (iris-lens PPM); or adhere to the corneal endothelium (iris-cornea PPM).
— Iris-lens PPM and Iris-cornea may be associated with cataract or corneal scarring, causing visual impairment
— Treatment: no treatment is necessary for most PPMs.
— Diagnosis: typically remains static.

C. Iris coloboma.
— Typically uncommon.
— Caused by incomplete closure of embryonic fissure.

III. Acquired Uveal Abnormalities.

A. Iris atrophy.
— Senile—aging change is most common.
— Characterized by an irregular pupillary ruff, holes (transillumination defects) in the iris stroma (pseudopolycoria) or a sluggish, incomplete pupillary light reflex.
— No treatment available nor necessary.
— Important rule out for dilated, nonresponsive direct pupil light reflex

B. Uveitis.

1. Definitions:
— Uveitis—inflammation of part or entire uveal tract
— Iritis—inflammation of the iris.
— Cyclitis—inflammation of the ciliary body.
— Anterior uveitis (rarely called iridocyclitis)—inflammation of the iris and ciliary body.
— Posterior uveitis (choroiditis)—inflammation of the choroid.
— Chorioretinitis—inflammation of the choroid and adjacent retina—"chicken or egg"—hard to always know which came first
— **Endophthalmitis**—inflammation of the anterior and posterior uveal tract
— **Panophthalmitis**—inflammation of the entire uveal tract and sclera

2. **Clinical signs.**
   a. **Anterior uveitis.**
      — Ocular pain: can manifest as epiphora, blepharospasm, photophobia, and enophthalmos with secondary elevation of the nictitans.
      — Conjunctival hyperemia (caused by local vasodilation due to inflammatory mediators).
      — Decreased intraocular pressure (caused by decreased production of aqueous humor by the inflamed ciliary body).
      — Miosis (caused by action of inflammatory mediators in the aqueous humor causing the iris sphincter muscle to contract).
      — Corneal edema (caused by dysfunction of the endothelium as the aqueous humor composition changes and is not nourishing the endothelium properly).
      — Corneal neovascularization.
      — Aqueous flare (increased protein, fibrin, and cells in the aqueous humor due to inflammatory breakdown of the blood-aqueous barrier).
      — Hypopyon (most extreme manifestation of aqueous flare, conglomeration of WBC/fibrin/protein in the ventral anterior chamber).
      — Hyphema.
      — Keratic precipitates (cellular [macrophage] and fibrinous deposits on the posterior surface of the cornea; i.e., the corneal endothelium) (±).
      — Swollen (edematous) iris.
      — Congestion of iridal blood vessels or neovascularization (rubeosis iridis).
      — Anterior or posterior synechia (adhesion of the iris to the corneal endothelium or anterior capsule of the lens, respectively).
      — Cataract (caused by the changes in the aqueous humor composition and accumulation of metabolic wastes in the lens or due to posterior synechiae).
      — Glaucoma secondary to pupillary block (total, 360 degree, posterior synechiae, iris bombe), peripheral anterior synechiae, development of a preiridal fibrovascular membrane (PIFVM) and/or compromise of the iridocorneal angle by accumulation of inflammatory debris.
   
   b. **Posterior uveitis.**
      — Decreased vision.
      — Retinal edema, hemorrhage.
      — Subretinal exudate (serous or granulomatous) with secondary retinal separation.
      — Vitreal inflammatory debris.
Retinitis.

a. Signs rarely isolated, choroid usually involved—hence chorioretinitis
   Active vs. inactive.

   **Active**—hyporeflective area with indistinct borders; vascular engorgement;
   perivascular sheathing of vessels; retinal hemorrhages; retinal detachment; progressive
   enlargement of lesion.

   **Inactive**—hyperreflectivity—over the tapetum; depigmentation or pigment
   hypertrophy in nontapetal fundus; decreased vessel size, sharply defined borders.

b. Etiologies—fungal (blastomycosis, histoplasmosis, cryptococciosis, coccidiomycosis);
   rickettsial (Ehrlichia, Rocky Mountain Spotted Fever, Lymes); bacterial-septicemia;
   viral-distemper; toxoplasmosis; hypertension; acquired neoplasia – lymphoma and
   melanoma as well as others; congenital neoplasia - medulloepithelioma;
   uveodermatologic syndrome, parasitic migration; protothecosis; uveodermatologic
   syndrome;
   Toxoplasmosis, FeLV, FIV, and FIP in cats.

Retinal hemorrhage—There are numerous causes of retinal hemorrhage that cannot be differentiated
without additional history, clinical findings, and/or further diagnostic testing. **In our common**
domestic species, trauma is an unlikely cause of retinal hemorrhage.

a. Hypertension—Either primary or secondary. Generally >200 mmHg for patients to have
   retinal hemorrhage and detachment. Precapillary vasoconstriction of retinal arterioles
   leads to smooth muscle necrosis which leads to vascular dilation and leakage.

b. Thrombocytopenia—Usually will see other signs of bleeding in the body. Decreased
   platelet numbers. Examples: Immune-mediated thrombocytopenia or Ehrlichia.


d. Disseminated intravascular coagulation.

e. Hyperviscosity syndrome—Multiple myeloma monoclonal gammopathy, increased
   IgG, IgM or IgA reported.

f. Radiation-induced—Secondary to radiation therapy.

h. Senile.

i. Anemic retinopathy—Anemia induced hypoxia of retinal vessels leads to venule dilation
and increased capillary fragility. There is some debate if this phenomenon exists on its own (RBC loss) or is part of diffuse bone marrow suppression affecting RBCs, WBCs and platelets.

**Retinal Detachment.**

Misnomer in that it is actually an intraretinal separation. The separation occurs at the embryologic separation of the RPE and the photoreceptors. The outer layer of the retina, when detached, is removed from the choroid which supplies its nutrition. Irreversible changes may occur because of the high metabolic needs of the retina.

Many potential causes:

a. Inflammatory/infectious: secondary to some chorioretinitis with subretinal exudate.

b. Hypertension: secondary to serous subretinal effusion. The **most common cause of a serous retinal detachment with intraretinal and/or vitreal hemorrhage is systemic hypertension.**

c. Idiopathic/immune-mediated/steroid responsive: rule out other causes first.

d. Traction: secondary to vitreal hemorrhage or inflammation.

e. Trauma: **rare** cause of retinal detachment in most domestic species unless the trauma is penetrating.
Below is a relatively complete list of diseases associated with uveitis in dogs.

Algae
— Protothecosis.

Bacterial
— Brucellosis.
— Borrelia (Lyme Disease).
— Leptospirosis.
— Bartonellosis.
— Septicemia (pyometra).

Fungal
— Blastomycosis.
— Coccidioidomycosis.
— Cryptococcosis.
— Histoplasmosis.

Immune Mediated
— Phacolytic (lens induced)—due to cataracts.
— Immune-mediated thrombocytopenia.
— Phacoclastic (lens rupture).
— Uveodermatologic syndrome (VKH-like).

Metabolic
— Hypertension leading to retinal detachment/intraocular hemorrhage.

Parasitic
— Dirofilaria.
— *Toxocara canis* (ocular larval migrans).

Protozoan
— Leishmaniasis.
— Toxoplasmosis.

Rickettsial
— Ehrlichia (canis/platys/risticii).
— Rocky Mountain Spotted Fever
— Lyme disease

Viral
— Adenovirus (postvaccinal blue eye).
— Distemper.

Misc.
— Coagulopathies.
— Hyperviscosity syndrome.
— Idiopathic — most common cause in any species.
— Retinal detachment.
— Neoplasia.
— Granulomatous meningoencephalitis
— Trauma.
— Ulcerative keratitis—antidromic axonal reflex.
3. **Diagnosis.**

   a. **History.**
      — Vaccination status.
      — Travel history, i.e., region → blastomycosis vs. coccidiomycosis.
      — Indoor vs outdoor lifestyle.
      — Acute vs chronic nature.
      — Previous medication (what, how much, how long).

   b. **Complete physical examination** – to search for any other signs of systemic disease.

   c. **Complete ophthalmic examination.**
      — Especially important to evaluate IOP by tonometer
      — Evaluate response to mydriatics. Pupils should dilate completely within 20 minutes of administering topical tropicamide. If the pupils do not completely dilate, this can be sign of uveitis.

4. **Causes of uveitis in dogs.**

   a. When evaluating a patient for uveitis, **the clinician must determine if the uveitis is caused by intraocular disease or is an ocular manifestation of systemic disease (OMSD).** The most common **ocular** cause of uveitis is cataract leading to lens-induced (also called phacolytic) uveitis and reflex uveitis associated with corneal ulcers. In dogs, approximately 60% of uveitis cases that are NOT associated with other ocular disease are idiopathic, and 20% are associated with infectious diseases. It is important to know which infectious diseases are common in the area you practice in.

   b. When a systemic cause of uveitis is suspected, a **systemic workup** should be performed. This should include: complete blood count, serum chemistry profile, urinalysis, thoracic radiographs and abdominal ultrasound. Specific tests for infectious diseases can be run based on the geographic area the patient lives in. Here in central Illinois, we run titers for common tick-borne diseases (Ehrlichia canis and platys, Rocky Mountain Spotted Fever, Lyme disease) and urine antigen assessment for Blastomycosis dermatidis on all our canine patients with uveitis.

   **Other tests may be indicated** by the type of clinical signs the patient exhibits. A patient with hyphema should also have their blood pressure assessed and tests of platelet number, platelet function and clotting function assessed. If the posterior segment (including the vitreous and retina) cannot be visualized because of the severity of disease in the anterior segment, an **ocular ultrasound** is indicated to assess the inside of the globe.
b. **Lipemic aqueous** is a clinical sign that is observed in patients with concurrent hyperlipidemia and anterior uveitis. When lipemic aqueous is observed, the patient should be evaluated for both hyperlipidemia and causes of uveitis. Hyperlipidemia may result from systemic lipid abnormalities or dietary indiscretion.

c. **Uveodermatologic syndrome** (VKH-like syndrome or Vogt-Koyanagi-Harada syndrome). This ocular manifestation of systemic disease most commonly affects artic circle breeds of dogs (ie. Huskies). It results in depigmented and ulcerative skin lesions of the mucocutaneous junctions and concurrent uveitis. Biopsy of affected skin is diagnostic in most cases. Treatment is lifelong administration of immunosuppressive systemic medications.
5. **DISEASES THAT CAN CAUSE UVEITIS IN CATS:**

Many of the same diseases listed under dogs also apply to cats.

**More commonly diagnosed diseases in cats include:**

**Bacterial**
- Bartonellosis.

**Fungal**
- Cryptococcus.
- Histoplasmosis.

**Protozoan**
- Toxoplasmosis.

**Viral**
- FeLV.
- FIV.
- FIP.

**Misc.**
- Hypertension.
- **Idiopathic – most common cause in any species.**
- Lens induced.
- Neoplasia.
- Septicemia.
- Trauma.
- Ulcerative keratitis.

a. When a systemic cause of uveitis is suspected, a **systemic workup** should be performed. This should include: complete blood count, serum chemistry profile, urinalysis, thoracic radiographs and abdominal ultrasound. Specific tests for infectious diseases can be run based on the geographic area the patient lives in. Here in central Illinois, we run tests for FeLV, FIV, FIP, Toxoplasmosis and Bartonella on all our feline patients with uveitis.

b. **Systemic disease is a more common cause of uveitis in cats** than in dogs; fewer cases of uveitis are idiopathic in the cat compared to the dog.
6. **Therapy for uveitis.**

Topical therapy should be instituted immediately, whereas appropriate systemic therapy should follow diagnosis of the underlying disease.

a. **Topical corticosteroids**—(Posterior uveitis necessitates systemic anti-inflammatory agents.)
   - Prednisolone acetate 1% - best.
   - Dexamethasone sodium phosphate 0.1% - very good.
   - Betamethasone and hydrocortisone are poor alternatives because they do not penetrate the cornea well. DO NOT USE.

b. **Subconjunctival corticosteroids.**
   - These formulations are rarely used by practitioners because they come in repositol formulations that cannot be removed. If the patient develops a corneal ulcer after receiving a repositol steroid injection, vision-threatening infection and melting may occur.

**Topical and subconjunctival injection of corticosteroids are contraindicated with concurrent corneal ulceration.**

c. **Mydriatic/cycloplegic.**
   - Atropine. This will dilate the pupil (decrease chance of posterior synechia) and stabilize the blood-ocular barrier. In cases where secondary glaucoma is possible or probable, monitor the IOP carefully as topical atropine closes the drainage angle and may increase the IOP.

d. **Systemic corticosteroids.**
   - Identify etiology.
   - Use with great caution with diabetes mellitus. Use judiciously and in conjunction with appropriate antimicrobials in patients with infectious disease.

e. **Topical nonsteroidal agents.**
   - May be used alone or in conjunction with corticosteroids.
   - Are safe in the presence of most corneal ulceration.
   - Flurbiprofen 0.03% solution
   - Diclofenac sodium 0.1% solution
   - May be used in conjunction with systemic steroids

f. **Systemic nonsteroidal agents.**
   - Are especially beneficial to begin systemic therapy while you are waiting on test/titer results.
   - Contraindicated where generalized bleeding tendencies exist.
   - Carprofen, Deramaxx or Meloxicam in appropriate species.
Systemic antimicrobial therapy.
— Will penetrate the blood aqueous barrier during inflammation.
— Only necessary if you can document intraocular infection (quite rare)
  OR if corneal penetration or perforation has occurred.

7. Consequences of uveitis.

Uveitis has blinding consequences for the patient when left untreated. The following are major complications of untreated uveitis.

a. **Glaucoma.** Chronic uveitis leads to the formation of a fibrovascular membrane on the surface of the iris termed a **pre-iridal fibrovascular membrane (PIFVM).** This membrane grows across the surface of the iris and across the opening of the iridocorneal angle, preventing aqueous humor from draining normally from the eye and leading to secondary glaucoma. Once a PIFVM forms, it cannot be removed, surgically excised or dissolved; preventing its formation is essential for preventing secondary glaucoma. Treatment with topical anti-inflammatories to control the uveitis as quickly as possible is the most effective way to prevent or delay PIFVM formation and secondary glaucoma. Iris bombe can also lead to secondary glaucoma (see below).

c. **Cataract.** The lens is dependent on normal aqueous humor for nutrition and removal of waste products. Under chronic uveitis conditions, the composition of the aqueous humor changes and toxic metabolites accumulate in the lens, leading to lens fiber cell death and cataract.

d. **Retinal detachment.** Inflammation of the underlying choroid and cellular exudates from the choroid can lead to detachment of the overlying retina.

e. **Posterior synechiae.** Synechiae are adhesions between the iris and another ocular structure. Anterior synechiae are adhesions between the iris and cornea; posterior synechiae are adhesions between the iris and anterior lens capsule. Posterior synechiae decrease the mobility of the pupil and the ability to appropriately regulate the amount of light entering the eye, which impairs vision.

f. **Iris bombe.** Iris bombe is a 360 degree posterior synechiae of the iris. When this occurs, aqueous humor can no longer flow through the posterior chamber, through the pupil, into the anterior chamber and out the iridocorneal angle. Instead, the aqueous humor is trapped behind the iris. This leads to anterior displacement of the peripheral iris against the iridocorneal angle and secondary glaucoma.
Seeing the lens more clearly.

Ralph E. Hamor, DVM, MS, Diplomate ACVO

The lens is subject to two major disease states: loss of transparency and loss of normal position or shape. Understanding then normal anatomy and physiology of the lens is critical to understand lens diseases. Synonyms that can be used to describe the lens include the latin roots “phac-“ and “phak-“. The word “lenticular” means “of the lens” and can be used interchangeably with the word lens.

Embryology and Physiology

1. **Lens is formed from surface ectoderm that is placed in position by infolding.**
   
   Note that the surface of the epithelium is inside and what will become the lens capsule is now on the outer surface. Posterior epithelial cells become the primary lens fibers. Anterior epithelial cells become the lens epithelium. The basement membrane of the epithelial cells (which is now on the exterior surface) becomes the lens capsule. **The lens capsule is much thicker (10 to 12 times) anteriorly than posteriorly.**

2. The lens epithelial cells under the anterior lens capsule vary in activity. There is a central region which is an area of little cellular reproduction, a germative region just anterior to the equator and an equatorial region. Lens fibers are formed by the germative region. Mitosis occurs and lens epithelial cells are pushed inward where they elongate and become lens fibers. Each fiber as it elongates curves around the deeper and older formations toward the anterior and posterior poles of the lens. The tips of these fibers meet in a radiating pattern of short lines knows as suture lines. The suture lines usually form a "Y" on the anterior surface of the lens and an "inverted Y" on the posterior surface.

   The nuclei of the lens fibers are located in the equatorial region in an area called the lens bow. As the fibers are continually pressed inward by newly forming fibers, they lose their nuclei. The lens continues to grow throughout life, albeit at a decreasing rate, and the older fibers are continually compressed toward the center forming the nucleus. **Nuclear sclerosis is a term applied to highly compacted nuclear lens**
fibers. It gives a blue-grey, opalescent appearance to the center of the lens, and can be differentiated from senile or other cataracts by viewing the retina through the nucleus with the ophthalmoscope. **Nuclear sclerosis is transparent—you can see through it with an ophthalmoscope.** Nuclear sclerosis is usually bilaterally symmetric, which can help differentiate it from cataract. It is generally seen in older animals (> 7 years of age for dogs).

**Chemical Content of the Lens**
1. The lens is about **65% water** (which is relatively dehydrated).
2. **Protein** is the main other component. The protein consists of crystallines: alpha, beta, gamma, and albuminoid. The precise ratio of crystalline proteins helps maintain lens transparency.

**Metabolism**

The clarity of the lens is influenced by the state of hydration. The state of hydration is related to metabolic activity and electrolyte balance. Glucose is the major source of energy. The metabolism is limited by the avascular state of the lens and low oxygen supply. **The lens is completely dependent on the aqueous for nutrients.** Glycolysis is the major pathway of energy metabolism. It is eliminated via the aqueous. There are several other enzyme systems and pathways for glucose utilization.

**Transparency**

The lens maintains a transparent state via several mechanisms. Like the cornea, it is avascular, non-pigmented and has no keratinized epithelium. The lens fibers, similar to the collagen fibrils of the cornea, are arranged in a precise interlocking pattern that allows light to pass through undisturbed. The lens fiber cells have few organelles within them, which causes minimal disruption of light as it traverses the lens.
Function

The normal function of the lens is to focus light rays on the retina to allow optimal image processing and vision. To perform this function, the lens must maintain its normal position and transparency. Focusing of light is achieved via accommodation. The lens is normal stabilized and held in place in the center of the eye via linear zonules, which attach to the lens at the equator and then attach to the ciliary processes of the ciliary body. Contraction or relaxation of the ciliary body musculature causes changes in the tension of the zonules and thus changes in the shape and precise position of the lens. This process, called accommodation, is responsible for the eye’s ability to focus on either near or far objects. When the lens becomes opaque, it no longer can transmit light in an organized fashion from the outside world to the retina, creating distortion in the light rays and thus visual deficits. When the lens is shifted from its normal position, the ability of the eye to focus on near or far objects is impaired and thus vision becomes distorted. An eye that lacks a lens (known as an aphakic eye, or an eye with aphakia) lacks the ability to focus on near objects. Likewise, a lens with an abnormal shape will not have a normal ability to focus light on the retina and will create a visual deficit (such an a microphakic (too small) or spherophakic (too round) lens).

Pathology

In the cataractous lens, various biochemical mechanisms become damaged—thus resulting in hydration from osmotic effects. These changes may result in such clinical forms as spokes, fissures, lamellar separation, dot-like opacities, rosettes, etc. Insoluble proteins increase; whereas the soluble proteins decrease. As these biochemical mechanisms begin to fail, other electrolytes and lipid and glucose metabolic pathways are affected. Na\(^+\) and Ca\(^{++}\) ion retention and loss in lens ATP progresses and eventually results in an opaque cataract.

Examination of the lens

Examination of the lens should be performed after mydriasis has been achieved by instilling a mydriatic such as tropicamide 1% solution. The entire lens cannot be examined unless the pupil is fully dilated. Differentiating nuclear sclerosis and cataract is MUCH easier after the pupil is dilated! Remember to assess the pupillary light reflexes (PLRs) prior
to dilating the pupils, carefully noting any abnormalities. It is important to remember that **having a cataract should not affect the PLR**. While cataract causes light to be disorganized as it passes through the cataractous lens, it does not prevent illumination of the retina. The PLR should be normal, even with a mature cataract. If PLR abnormalities are noted, other ocular or brain disease may be present. The lens equator cannot be visualized in a normal lens. If the lens equator is visible, an abnormality of lens shape or position must be present.

**Diseases of lens shape**

The most common disease of lens shape is **microphakia**, a lens that developed abnormally and is smaller than normal. Often this abnormality is seen in conjunction with other developmental intraocular abnormalities. Most cases do not require treatment beyond monitoring unless concurrent cataract is present. A dilated examination is the only way to diagnose microphakia. Microphakia must be differentiated from a subluxated lens.

**Spherophakia** is a term used to describe a rounder than normal lens. This is a relatively uncommon abnormality that usually requires a slit lamp biomicroscope (and hence an ophthalmologist) to diagnose. Most cases do not require treatment beyond monitoring unless other ocular abnormalities are present.

A **coloboma** is a congenital absence of normal tissue. A **coloboma of the lens** usually appears as a flattened region of the equator of the lens. This abnormality may be seen in conjunction with other developmental intraocular abnormalities. Most cases do not require treatment beyond monitoring unless concurrent cataract is present.

**Diseases of lens transparency: cataract**

**Stages of Cataract Development**

These refer to the appearance of the lens regardless of the etiology of the cataract or the age of the animal.

1. **Incipient**—the very earliest and smallest cataract you can see. Very little percentage of the lens is opaque.

2. **Immature**—more of the lens is involved than with incipient. You can still see a tapetal reflection and may be able to observe some retinal detail.
3. **Mature** — a solid, opaque, white marble. No tapetal reflection or retinal detail can be seen. **Important to remember** — *even with a mature cataract, the PLR’s are normal (as long as the retina is normal).*

4. **Hypermature** — lens is starting to shrink and reabsorb. Capsule is frequently wrinkled and equatorial area has ragged, scalloped edges. Can be difficult to differentiate from immature.

5. **Morgagnian** — nucleus liquefies last and may sink to bottom of lens when the cortex liquifies.

**Classification of Cataracts in Dogs by Age of Animal**

1. **Congenital** — present at birth; often nuclear, sometimes nuclear plus cortical. Consider removal if cortex is involved. Makes no statement about etiology.

2. **Juvenile** — occurs in young dogs (up to about 6 years of age; usually at 2 to 3 years). Makes no statement about etiology; however, in many breeds, juvenile cataracts are hereditary.

3. **Senile** — seen in older dogs (exact age varies with breed). Usually not hereditary and is related to decreased anti-oxidant function and degeneration in older animals.

**Classification of Cataracts in Dogs by Cause of Cataract**

1. **Genetic** — The most common cause of cataracts in dogs is hereditary. Many purebred breeds of dogs are affected. Cataracts are usually but not always bilateral and may have variable age of onset. The appearance, age of onset and expected progression vary by breed. Not all genetic cataracts progress to cause complete vision loss, but many do. Genetic cataracts are much less common in non-canine species.

2. **Diabetic cataracts** — related to abnormal glucose metabolism in lens of diabetic dogs (quite rare in cats); The normal anaerobic glycolysis of the lens is overwhelmed and metabolism is shunted to the sorbitol pathway (**aldose reductase** is the rate limiting enzyme), excess sorbitol accumulates in the lens, “fluid” is osmotically drawn into the lens and breaks the lens fibers to form cataract; bilateral, rapid forming. Clinically patients often exhibit polyuria/polydipsia (PU/PD) and have elevated blood glucose levels.
3. **Secondary to PRA**—common in Poodles, Labradors, Irish Setters, etc. Check history for evidence of blindness or poor dim light vision before cataracts developed. ERG needed in many cases to be sure. Exact mechanism of unknown

4. **Secondary to uveitis**—since the lens is dependent on the aqueous humor for its nutrition and for the removal of waste products, the lens becomes malnourished and may accumulate toxins when the composition of the aqueous humor changes negatively during uveitis (increased protein, increased fibrin, increased inflammatory by-products)

5. **Traumatic**—common example is after penetrating trauma such as a cat scratch that can perforate the cornea and the lens capsule. Blunt trauma is less commonly associated with cataract.

6. **Nutritional**—Esbilac milk replacer in wolves and large breed dogs (not considered a significant modern problem, seen historically when nutritional composition of milk replacers were inadequate for lens development)

7. **Electric shock**—usually anterior subcapsular in location

8. **Radiation**—causes ↓ epithelial cell mitosis—young animals more susceptible.

9. **Secondary to iris-to-lens persistent pupillary membranes**—Remnants of embryologic iris tissue adhered to the anterior lens capsule may be associated with underlying cataract.

10. **Secondary to hyaloid artery/tunica vasculosa lentis**—During embryonic development, the lens is surrounded by a vascular system that arises from the hyaloid artery known as the tunica vasculosa lentis. This vascular system is critical for normal lens development but rarifies prior to birth. Abnormally developing eyes may have some remnants of this vascular system, known collectively as **Persistent Hyperplastic Primary Vitreous/Persistent Tunica Vasculosa Lentis (PHPV/PTVL)**. This congenital abnormality may have a genetic component in some breeds, but is relatively uncommon. When it occurs, it is often associated with cataract and is an important differential for cataract in young dogs and whenever blood is observed within the lens in association with cataract.
Classification of Cataracts by Location of Opacity in Lens

1. **Capsular**—opacity confined to lens capsule.
2. **Subcapsular**—most of opacity involves cortex directly beneath lens capsule.
3. **Cortical**—between the capsule and the nucleus
4. **Nuclear**—opacity primarily in center of lens (nucleus). Frequently congenital and nonprogressive.
5. **Equatorial**—most involvement in area of lens equator (near where zonules attach).
6. **Polar/Axial**—Usually a focal, central opacity in the center of the visual axis.

These terms are frequently modified with words like anterior and posterior and/or combined to give a complete description, i.e., posterior capsular and subcapsular juvenile cataract.

Cataracts may also be described by the shape of the cataract within the lens (punctate, cuneiform, vermiform, etc). **When vacuoles are visible within the lens, this is a sign that cataract is actively being produced.**

Detrimental effects of cataract on the eye

**Lens-induced Uveitis** (phacolytic uveitis)—any cataract, especially immature, mature and hypermature, will cause inflammation. This is due to leakage of lens proteins through the intact lens capsule and is known as phacolytic uveitis. Treatment is with topical anti-inflammatory agents (steroid or nonsteroidal) and systemic therapy in severe cases. Chronic lens-induced uveitis can lead to secondary glaucoma, retinal detachment, posterior synechiae and keratitis. **All cataracts larger than incipient in size should be treated with a topical anti-inflammatory for the remainder of the patient’s life to prevent lens-induced uveitis and it’s painful sequelae.** Treatment options include topical NSAIDS (diclofenac 0.1% or flurbiprofen 0.03%) or topical steroids (prednisolone acetate 1% solution). **Topical NSAIDS are generally safer for long term use,** especially in diabetics.

**Secondary glaucoma**—When lens-induced uveitis has not been treated, the chronic inflammation can lead to the formation of a fibrovascular membrane on the surface of the iris termed a **Pre-Iridial FibroVascular Membrane (PIFVM).** This fibrovascular membrane
arises from the blood vessels on the surface of the iris and can extend to cover the opening of the iridocorneal angle, effectively blocking aqueous humor from draining out of the eye. This leads to secondary glaucoma. Treating lens-induced uveitis can prevent or significantly delay the formation of a PIFVM.

**Phacoclastic uveitis**—Penetrating trauma to the lens capsule disrupts lens fibers, leading to a cataract. When there has been a traumatic breach of the lens capsule, lens epithelial cells and lens fiber cells are liberated within the eye. Since these cells develop within the confines of the lens capsule, there is no self-tolerance for the cells of the lens. An overwhelming and significant inflammatory response ensues, which is exceedingly difficult to treat and frequently leads to blindness via endophthalmitis (inflammation of all chambers within the eye), secondary glaucoma and/or retinal detachment. Penetrating corneal trauma (most often a cat scratch in small animals or vegetation in large animals) is the most common cause of traumatic lens capsule rupture. **Treatment is controversial.** In a paper by Paulsen et al 2012, 50% of dogs or cats lost vision with a traumatic lens laceration. In the past, emergency lens removal was always recommended. In this paper, medial therapy was significantly likely to result in maintenance of vision, especially if the patient had good corneal wound apposition without continued aqueous leakage or uveal prolapse. **Prompt referral is indicated** and was associated with a positive outcome.

**Treatment for cataracts**

The only treatment available to restore vision once cataract has formed is surgical removal of the cataract. There are no eyedrops, pills or solutions that dissolve cataract, despite an abundance of false information on the internet! A scientific report regarding a topical aldose reductase inhibitor showed that TID administration of a drop that acted to inhibit aldose reductase in diabetic dogs may have some promise in inhibiting the formation of cataract in diabetic dogs. This drug needs a significant amount of further investigation and is not commercially available as of 2011.
Cataract surgery

Pre-Cataract Surgery Work-up: Prior to surgery, the patient’s general health status needs to be evaluated with a complete physical examination as well as bloodwork and urinalysis. If the patient is a diabetic, the diabetes needs to be reasonably well regulated. We routinely assess fructosamine levels as well as urine culture prior to surgery since many diabetic dogs have occult urinary tract infections that can complicate their recovery from surgery. An electroretinogram and an ocular ultrasound are performed prior to cataract surgery to confirm retinal function and retinal attachment, respectively. In patients with hypermature cataracts or in predisposed breeds, a prophylactic laser retinopexy is recommended to decrease the risk of retinal detachment after cataract surgery.

Modern cataract surgery is now performed most often via phacoemulsification, which uses Ultrasonic fragmentation/emulsification of the lens through a 3mm incision. Phacoemulsification surgery is the surgical treatment of choice for lens extraction in most veterinary species, especially with intraocular lens implantation. Success rates far exceed previous extracapsular and intracapsular lens extraction procedures. This technique also allows the implantation of a replacement intraocular lens. Without the replacement lens, the patient will have good vision at a distance but blurry vision close up. The most common reason NOT to implant a lens at the time of surgery would be surgical complications that prevent lens implantation (such as a tear or hole in the posterior lens capsule, preventing the lens capsule from being stable enough to hold the lens implant).

Advantages
a. Maintains a formed anterior chamber thereby reducing the chance of inadvertent contact between surgical instruments and delicate intraocular structures.
b. Procedure is rapid in comparison to standard extracapsular and intracapsular extraction procedures.
c. High rate of success (90-95%).
d. Can operate on both eyes at time of surgery.
e. Optimum method for implanting artificial intraocular lenses in the remaining lens capsule (“in the bag”) or the artificial lens can be sutured in place behind the iris (“sulcus”).

**Disadvantages**

a. Cost for purchasing the phacoemulsification unit and adequate operating microscope.

b. In rare cases, the canine lens is too hard to fragment adequately.

**Laser cataract surgery.**

Currently is a common misconception that cataracts can be "removed" with lasers. There is no currently available technique for removing cataracts with laser. Possibly in the future, cataract surgery will involve use of both a laser and aspiration system.

**Diseases of lens position: subluxation and luxation**

Lens subluxation and luxation refer to the lens becoming dislocated from its normal zonular attachments. **Subluxation** implies that some zonules are still attached and the lens is only partially dislocated. **Luxation** implies that all zonular attachments have been lost and that the lens is completely dislocated from its normal position. Subluxation proceeds complete luxation in almost all cases. Lens luxation can be described as either **primary** or **secondary**.

**Primary lens luxation**

Primary lens luxation is seen most commonly in jack russell terriers and related breeds (rat terriers, Parson’s russell terriers, tibetan terriers) as a genetic defect. A genetic test is now available. Affected dogs have **zonular dysgenesis**, which leads to their zonules weakening and ultimately dissolving in early middle age. This leads to instability in the lens position, starting initially with subluxation and ultimately leading to complete luxation of the lens. The condition is usually bilateral and is associated with glaucoma in many dogs.

**Primary posterior luxation** refers to the lens falling into the vitreous after all zonular attachments have been lost. Clinical signs include deep anterior chamber, iridodenesis and
lens visible posteriorly displaced in the vitreous. Complications of posterior lens luxation include retinal detachment and glaucoma. Many dogs can maintain vision for months to years with a posterior lens luxation, particularly if they are treated with a miotic agent to make the pupil small and prevent the lens from coming forward and being entrapped in the anterior chamber. **Posterior luxations are preferable to anterior luxations as they are not painful for the patient.** Remember that a dog with a complete posterior lens luxation will have very poor near vision without a lens in a normal position to allow it to focus on near objects.

**Primary anterior luxation** refers to the lens coming forward and being trapped in the anterior chamber. This condition develops acutely (despite the fact the zonular degeneration has been progressing for some time) and is associated with pain/blepharospasm, tearing, focal corneal edema and glaucoma. The best treatment for the preservation of vision is removal of the lens before glaucoma leads to vision loss. Anterior lens luxations can be removed via phacoemulsification or intracapsular lens extraction. Concurrent surgical treatment for glaucoma may also be indicated. Prompt referral is indicated in these cases. If surgical removal of the lens is not an option, medical management for the patient’s comfort (including pain medication and anti-glaucoma medication) can be attempted but often ends in enucleation. It is important to warn the client that the condition is usually bilateral and to start the dog on a topical miotic in the fellow eye to prevent anterior luxation of the other lens.

**Secondary lens luxation**

**Secondary lens luxation** results from loss of zonules caused by other intraocular disease. **Chronic uveitis** with its associated inflammatory debris and by-products can lead to degeneration of the zonules. **Uveitis is the most common cause of lens luxation in cats and horses.** Chronic lens induced uveitis, when left untreated, may be associated with an increased rate of lens luxation (note that the lens will be cataractous in these cases). **Chronic glaucoma** leads to buphthalmos (enlargement of the size of the globe), which causes zonules to stretch and break. **Intraocular neoplasms** may displace the lens and cause breakage of zonules. **Trauma** is rarely a cause of lens luxation, and when observed is often associated with major skull fractures and other intraocular disease.
Treatment of secondary lens luxation is often unrewarding, as the globe is usually severely affected by the primary disease process. Anteriorly luxated lenses may be surgically removed in rare cases. Posterior luxations likely do not need treatment beyond treatment for the underlying disease process.

Lens subluxation

Lens subluxation can be most easily observed when the pupil is dilated and an aphakic crescent (space between lens equator and pupillary margin) is visible. Other clinical signs include vitreous in the anterior chamber, iridodensis, phacodensesis or unequal anterior chamber depth. **Lifelong topical miotic therapy to prevent anterior lens luxation or early surgical removal of the lens are possible treatments for primary lens subluxation.** Treatment of secondary lens subluxation requires treatment of the underlying ocular disease process.
Ocular neoplasia: Save both the patient and vision.

Dr. Ralph E. Hamor DVM, MS, DACVO

Although ocular and orbital tumors of dogs and cats are not frequently encountered, they are potentially blinding and may carry significant risk to the animal's life. The biologic behavior of ocular and orbital tumors depends on the tumor type, tumor location, and the species that presents with the tumor. Accurate histologic identification of the tumor type is crucial to case management and prognosis. When confronted with an ocular or orbital neoplasm, one must first determine whether the tumor is primary (with or without metastasis) or secondary to a systemic neoplasia. This determination is based on clinical signs, systemic signs (if any), and tumor type. Ocular neoplasia can masquerade initially as chronic uveitis or glaucoma so neoplasia must be considered with these clinical signs, especially in older patients. For example, one of the most common causes of spontaneous intraocular hemorrhage in an older patient, especially dogs, is an intraocular neoplasm. Orbital neoplasia most commonly presents as nonpainful exophthalmos. Exophthalmos secondary to orbital neoplasia must be differentiated from exophthalmos secondary to orbital cellulitis.

PRIMARY NEOPLASMS OF THE CANINE GLOBE:

Anterior uveal melanoma (AUM) is the most common primary neoplasm of the dog. Iridal melanomas usually present as focal, dark, raised lesions on the anterior surface of the iris in young dogs. These neoplasms are slow growing, cause little intraocular disease, are benign histologically, and are very rare to metastasize (6/179 in the literature at that time). Canine AUM's most commonly occur in dogs greater than seven years of age and are usually benign, both histologically and behaviorally.

The clinical presentation is based on the primary site of origin of the neoplasm. Frequently, the patient will exhibit changes in the color, shape, and texture of the iris or ciliary body. In dogs, the neoplasm is more discrete in contrast to feline AUM which is most often diffuse. Typically, a smooth, raised, pigmented lesion is seen growing from the iris or ciliary body. Pigmentation of the mass does not confirm the presence of melanoma, as some melanomas are nonpigmented. It is also possible for a nonpigmented ciliary body neoplasm to push the anterior surface of the iris forward and mimic an AUM. Other clinical signs typical of any intraocular neoplasm may be identified. As with any primary ocular tumor, this neoplasm will progressively enlarge and cause secondary uveitis and glaucoma if not treated. Uveal cysts may mimic the appearance of an AUM. Transillumination generally allows one to differentiate between the two masses. Uveal cysts usually transilluminate whereas AUM's do not.

Diagnosis can be attempted by fine needle aspiration or incisional biopsy. Fine needle aspiration of an anterior uveal neoplasm usually has limited side effects especially if the mass is located within the anterior chamber. An incisional biopsy does require intraocular surgery and may be best referred to a veterinary ophthalmologist. Ocular ultrasonography, especially high-frequency ocular ultrasonography, can provide more accurate information as to the extent or site of origin of the
neoplasm especially if the ocular media is not clear. An enucleation can also provide a diagnosis but is usually reserved for painful or nonvisual globes.

Forms of treatment include resection, cryosurgery, enucleation, or laser photocoagulation. Of all of these, laser photocoagulation has demonstrated the most promise to cause remission, shrink, or slow the growth rate of primary intraocular neoplasms in dogs. The benefit of laser photocoagulation is that it is possible to save vision and treat the neoplasm with a minimum of ocular side effects. Because pigmented tissues preferentially absorb laser energy, one would expect that pigmented neoplasms would be treated more successfully than nonpigmented ones. In fact, laser photocoagulation has shown efficacy in nonpigmented ocular neoplasms in dogs as well. Potential side effects from laser photocoagulation include hyphema, vitreal hemorrhage, corneal edema, mild anterior uveitis, corneal scarring and cataract formation (if the mass is adjacent to the lens). Aside from scarring and potential cataract formation, side effects are transient and usually resolve with treatment within two weeks. Neoplasms confined to the ciliary body have responded the most favorably to this method of treatment. Because most primary ocular neoplasms in dogs have an extremely low metastatic potential, we feel that the use of laser photocoagulation provides a safe and effective alternative to enucleation. If there are signs of severe secondary uveitis or glaucoma, we recommend an enucleation and histopathology. Prior to any treatment, the patient should have a thorough evaluation for any evidence of systemic metastasis including a complete physical examination, complete bloodwork, thoracic radiographs, and abdominal ultrasonography. When canine AUM's do metastasize the lungs, liver, kidney, spleen, adrenal gland, and heart can be affected. It is also possible for a systemic melanoma to spread to the eye from a distant site.

Canine epibulbar melanomas arise in the sclera adjacent to the cornea and typically present as smooth, raised, pigmented masses at the scleral limbus that may encroach onto the cornea. Systemic metastasis of this neoplasm has not been reported but they can be locally invasive. If allowed to grow, they can invade the globe, cause uveitis and secondary glaucoma, and necessitate enucleation. Proposed methods of treatment include full-thickness resection with homologous or synthetic grafting, partial resection, cryosurgery, or laser photocoagulation. Because of the complications association with full-thickness resection and the difficulty in finding replacement tissue, we feel that laser photocoagulation or cryosurgery are the optimum treatments. The earlier these are performed, the more efficacious and safe the treatment will be.

Choroidal melanomas also tend to occur in older dogs. In contrast to human beings, these neoplasms exhibit benign characteristics histologically and behaviorally. They occur very rarely and usually demonstrate slow, expansive growth that eventually necessitates enucleation. As they enlarge, they can cause retinal atrophy and detachment. Clinically, ophthalmic evaluation reveals a well-delineated, raised, subretinal, pigmented mass. Again, ocular ultrasonography may aid the diagnosis when the ocular media is not clear.

Anterior uveal epithelial neoplasms consist most commonly of adenomas and adenocarcinomas of the ciliary body and are the second most common primary intraocular neoplasm in dogs. They are usually nonpigmented, white to pink, slow growing, and occupy the posterior chamber. They typically do not cause profound secondary ocular disease until they are rather large. The difference between adenomas and adenocarcinomas is a histopathologic differentiation and does not generally
affect the prognosis. Both types can invade local tissues but metastasis is rare. As with canine AUM’s, laser photocoagulation may provide the best option for maintaining vision and providing effective treatment if severe secondary uveitis or secondary glaucoma is not present.

**Medulloepithelioma** has been reported rarely in the dog and arises from embryonal neuroepithelium. These neoplasms tend to occur in young dogs but can be slow growing and may not be evident for a few years. The clinical appearance of this neoplasm is very similar to a ciliary body adenoma or adenocarcinoma. Regional extraocular extension or metastasis has not been reported in dogs.

**PRIMARY NEOPLASMS OF THE FELINE GLOBE:**

Melanoma is the most common primary ocular neoplasm in cats. **Feline anterior uveal melanoma** (AUM) often presents as a diffuse pigmentation and thickening of the anterior iris surface. As the disease progresses, the neoplastic cells cause thickening and distortion of the iris as well as obstruction of the filtration angle that leads to secondary glaucoma. This must be differentiated from diffuse iris melanosis which causes diffuse iridal pigmentation without thickening and distortion of the anterior iris surface. This clinical differentiation can be very difficult. Whenever the anterior surface of the iris is raised or if the normal iridal architecture is obscured, melanoma must be suspected.

Cytology or histology may give some diagnostic information. Histologic samples can be gained by performing an iridectomy and will provide you with more accurate information about cell structure and invasion. Because 50-60% of feline AUMs are reported to metastasize, it is crucial to evaluate the cat for metastasis at the time of diagnosis. Metastatic disease can occur several months to 2-3 years after diagnosis and may not be affected by enucleation. The liver and lung tend to be the primary site of initial metastasis. The presence of secondary uveitis and especially secondary glaucoma is associated more frequently with metastasis. Histologically, a large number of mitotic figures is also associated with metastasis. It is still quite difficult to give owners good prognostic information even with a biopsy. It can be difficult if not impossible to differentiate melanoma from melanosis clinically. We find that cytology and, more often, histopathology provide us with much better information to accurately inform and make recommendations to the owner. Depending on the location of the lesion, a small iridectomy is relatively easy to obtain and is well tolerated by the globe. This procedure, however, may be best performed by an ophthalmologist.

Again, prior to iridectomy or enucleation, we evaluate the thorax (radiographically) and the abdomen (ultrasonographically) for metastasis. If metastasis is present or strongly suspected, we recommend consultation with an oncologist. If ocular malignant melanoma is found or is strongly suspected, we recommend early enucleation and histopathology. The presence of melanoma cells within the scleral vessels is closely associated with distant metastasis. We also recommend re-evaluation for metastasis every two to three months for a year if histopathology of the globe demonstrates malignant AUM. If the mass is small, localized to a small portion of the iris, and not invading the drainage angle, we have performed an iridectomy to remove the entire iridal mass. With this situation, it is crucial to have histopathology performed to determine if the entire mass has been removed and we are more comfortable if the histopathology demonstrates a benign lesion. If
Iridectomy demonstrates diffuse iris melanosis or a benign melanoma, we will observe the patient closely for any signs of malignancy but do not routinely enucleate. If, at any time, the globe develops secondary uveitis or glaucoma, we recommend enucleation and histopathology. Because malignant AUM is frequently associated with metastasis that is life threatening, we would rather remove a visual globe than risk a patient's life. This has to be balanced against not removing a visual globe unnecessarily. If the diagnosis is not clear, we recommend referral to an ophthalmologist.

**Feline Post-traumatic Sarcoma:** Numerous cases of intraocular sarcoma have been reported in cats with a history of ocular trauma. The time period between the initial trauma and the development of an intraocular sarcoma can be several months to many years. If examined histologically, almost all of the cases have severe lenticular disease and it has been suggested that the sarcomas may have originated from lens epithelial cells. These sarcomas often demonstrate malignant behavior with extension to the optic nerve, orbit, and brain and metastasis to distant sites has been reported. Because of this behavior, early enucleation is recommended. If there are any signs of orbital extension such as exophthalmos and/or third eyelid elevation, the extent of tumor invasion should be evaluated prior to enucleation by orbital ultrasonography, computerized tomography (CT) scan, or magnetic resonance imaging (MRI). In our experience, CT scan or MRI provides better information about the extent of orbital and brain invasion than orbital ultrasonography.

**Feline Limbal Melanoma:** This neoplasm is clinically very similar to canine epibulbar melanoma and is also typically benign. It is, however, more important in cats to be sure that the mass is scleral in origin and has not grown through the sclera from the anterior uveal tract. Thorough intraocular examination and gonioscopy can aide in this determination. Treatment is as with canine epibulbar melanoma.

**SECONDARY NEOPLASMS OF THE CANINE AND FELINE GLOBE:**

Secondary neoplasms of the eye of dogs and cats are not common but are seen with some regularity in a referral ophthalmology practice. Hematogenous spread of systemic neoplasia can occur as the ciliary body and choroid have a significant blood supply and are, in fact, one of the most vascular organs in the body. The clinical signs associated with secondary neoplasia are dependent on the amount of and the location of the affected ocular tissues. Secondary neoplasms can occur as solitary masses but more commonly manifest as diffuse lesions because the spread occurs through vascular tissues. In the posterior segment (retina and choroid), secondary neoplasms may appear as diffuse or multifocal hyporeflective lesions in the retina and choroid. They may even appear as intraretinal or subretinal hemorrhages. In the anterior segment (iris and ciliary body), secondary neoplasms tend to mimic diffuse anterior uveitis with iridal hyperemia, iridal thickening, aqueous flare, and hyphema. As signs of anterior uveitis worsen, the incidence of secondary glaucoma increases. Secondary glaucoma occurs due to blockage of aqueous outflow by posterior and/or peripheral anterior synechia or by physical clogging of the drainage angle with inflammatory or neoplastic cells. One would expect secondary neoplasms to affect both eyes if the eyes are involved, however, any or all of these ocular signs can occur unilaterally or bilaterally. If ocular spread of a systemic neoplasia is suspected, a thorough systemic evaluation of the patient should be
instituted. This includes a physical examination and bloodwork including a complete blood count, biochemical profile, and urinalysis. We also recommend thoracic radiography and abdominal ultrasonography to evaluate for the location of the primary neoplasm and the presence of other metastasis. As with primary neoplasia, ocular ultrasonography may be of benefit especially if the ocular media is not clear.

**Lymphosarcomas (LSA) are the most common secondary neoplasm to affect the eye of both dogs and cats.** The ocular clinical signs are usually diffuse and mimic anterior uveitis. Choroidal lesions and optic neuritis can also be present. If optic neuritis is present, one has to consider that the central nervous system is affected and institute additional appropriate therapy. In dogs and cats with ocular lesions from LSA, one can usually identify systemic involvement without too much difficulty. In both dogs and cats, ocular LSA carries a worse prognosis than cases without ocular lesions. In *dogs with LSA*, about one-third of patients exhibit ocular signs with diffuse anterior uveitis being the most common ocular clinical sign. The presence of ocular lesions and lymphadenopathy is associated with Stage V disease using the World Health Organization protocol and suggests that the patient has hematologic cell involvement. This stage usually represents a poorer prognosis for life expectancy. In *cats with LSA*, anterior or panuveitis is the most common clinical sign of ocular disease. Cats are more likely than dogs to present with unilateral signs and may appear systemically healthy at the time of initial examination. The association of LSA and feline leukemia virus (FeLV) remains so routine testing for FeLV should be performed on all suspected cases. Because of the strong association of FeLV and LSA, we recommend that an indirect fluorescent antibody test of a blood smear or bone marrow be performed on all negative enzyme-linked immunosorbent assay FeLV screening tests.

**Adenocarcinomas are the second most commonly reported secondary neoplasms in dogs and cats.** They are more commonly seen in dogs than cats. Many types of adenocarcinomas have been reported to spread to the eye in both dogs and cats. These secondary neoplasms tend to be more solitary or discrete and are more often unilateral than bilateral. Other secondary neoplasms can be found in both dogs and cats but are less commonly seen, especially in cats. A thorough ocular examination should be a part of any evaluation of a patient with systemic neoplasia. It is often impossible to differentiate secondary neoplasms simply by a clinical ophthalmic evaluation. Many of the ocular signs are similar and the exact identification can only be determined by histopathology.
NEOPLASMS OF THE CANINE AND FELINE ORBIT:

The dog and cat have an incomplete bony orbit as opposed to horses and ruminants. The orbit consists of the frontal, lacrimal, zygomatic, presphenoid, basisphenoid and palatine bones. The lateral orbital wall in the dog and cat is completed by a collagenous orbital ligament that attaches the frontal process of the zygomatic bone to the zygomatic process of the frontal bone. The masseter muscle completes the orbit posterolaterally and the zygomatic salivary gland and medial pterygoid muscle fills the floor of the orbit. The lacrimal gland is located dorsolaterally beneath the frontal bone in the lacrimal fossa. Vascular elements, nerves and adipose tissue are also present. Any of these tissues can be the primary source of orbital neoplasia. Secondary neoplasms can invade the orbit from adjacent sites (sinus, oral cavity) or metastasize to the orbit from distant sites.

Orbital pathologic processes involve one or more of 3 anatomical compartments: 1) within the extraocular muscle cone; 2) outside the cone but inside the periorbita; 3) inside the orbit but outside the periorbita. The orbit cannot be examined directly; therefore orbital disorders are evident only indirectly. Orbital disorders are characterized by clinical signs that alter the function, appearance, or position of the globe, eyelids or ocular adnexal structures. The orbit is a confined space with no area for its contents to expand. Primary and secondary clinical signs of orbital disease are the hallmark of orbital disorders. Primary clinical signs include: 1) exophthalmos, 2) enophthalmos and 3) deviation of the globe (strabismus). Secondary clinical signs can include chemosis, swelling of lids and periorbita, elevation of the third eyelid, pain upon opening the mouth (if present), lagophthalmos, exposure keratitis, visual impairment, abnormal PLR's, scleral indentation resulting in overlying retinal detachment, mild to moderate increase in intraocular pressure, and facial asymmetry.

A thorough history and physical examination are prerequisites to the diagnostic workup of all ophthalmologic and orbital problems. When orbital disease is suspected, initial examination should include palpation of the eye and periocular structures, digital retropulsion of the globe and careful examination of the oral cavity. Compare the size of palpebral fissures, palpate the orbit, observe eyelid carriage, position of eyelids and third eyelid, location and mobility of the globe within the orbit and the presence of ocular discharge. The globe can be retropulsed if there are no space occupying lesions in the orbit.

The prognosis for orbital neoplasia has historically been poor. This may be most related to the number of tumors that are malignant. Ninety-one percent of orbital tumors in dogs and 90% in cats are histologically classified as malignant. With early intervention and aggressive therapy, the prognosis improves dramatically. The most common clinical sign of orbital neoplasia is slowly progressive, unilateral exophthalmos. In contrast to orbital cellulitis, pain is not a prevalent sign upon opening the mouth, and fever or leukocytosis is absent. The average age at diagnosis for both dogs and cats is approximately 9 years while the average age for a patient with orbital cellulitis is 4 years. The intraocular pressure of the globe is usually within the normal range unless the exophthalmos is so severe that the eyelids are pressing on the globe which can lead to increased IOP. In dogs, most orbital neoplasias are primary (74%) and the most common types of orbital neoplasia are osteosarcoma, meningioma and fibroma/fibrosarcoma. In contrast, most cats have
secondary neoplasia (71%) and the most common types are squamous cell carcinoma, lymphosarcoma, carcinoma and melanoma.

The clinical diagnosis of orbital neoplasia is based upon the previously noted signalment and associated clinical signs. The exact location, tissue involvement and histologic diagnosis are crucial to effective therapy, but is complicated by the orbital anatomy. It is difficult, if not impossible, to appropriately diagnose orbital neoplasia without more elaborate diagnostic imaging modalities (orbital ultrasound, CT, MRI) and invasive tissue sampling (fine needle aspirate, Tru-cut biopsy, orbital exploration). Skull radiographs are only beneficial if there is extensive bony involvement. Therapy is based on tumor type, location, involvement of associated tissues and the presence or absence of metastasis. If orbital neoplasia is suspected, a complete tumor staging is required. At a minimum this should include a CBC, chemistry profile, UA, thoracic radiographs and abdominal ultrasound. Once the tumor type has been identified, a specific therapy can be formulated for each patient. Our service works closely with the oncology service to determine the most effective therapy for these patients. Therapy for primary neoplasms is usually based on surgical removal of the tumor. This can be an orbitotomy with tumor removal, an orbital exenteration (removal of all orbital contents including the globe), or orbitectomy (removal of all orbital contents and part or all of the bony orbit). Depending on tumor type, adjunctive chemotherapy and/or radiation therapy can be included. Therapy for secondary neoplasms often involves adjunctive chemotherapy and/or radiation therapy. Surgical debulking of a secondary orbital tumor may be indicated to improve the efficacy of adjunctive therapy. As previously indicated, early diagnosis and aggressive imaging modalities dramatically improve the short and long-term prognosis for orbital neoplasias. Each year, we can offer newer and more effective therapies for orbital neoplasias. For this reason, early referral of the patient to an ophthalmologist may offer the patient a better prognosis.