

THE LENS

Paul E. Miller, DVM, Diplomate ACVO

Objectives

1. Review lens embryology, anatomy, and physiology and be able to correlate these with clinical lens diseases.
2. Know the congenital anomalies of the lens.
3. Understand the terminology, etiology, and therapy of cataracts.
4. Understand the pathophysiologic causes and treatment of lens luxations.
5. Understand the pathophysiology and treatment of lens-induced uveitis.

I. EMBRYOLOGY - Explains many lens diseases. The lens is an inverted epithelium with the basement membrane (lens capsule) on the outside, thereby isolating lens proteins from the developing immune system. The lens consists of concentric layers of fibers with the older, inactive fibers in the center, and the younger, growing fibers peripherally. The region of the lens affected by an opacity can permit determination of the time an insult occurred in development. Also, cataracts which form peripherally are likely to progress (since the insult is currently occurring) whereas many nuclear cataracts which are surrounded by clear cortex tend to remain static. The tunica vasculosa lentis develops from the hyaloid artery and surrounds the posterior lens. The anterior lens receives blood from the anterior tunica vasculosa lentis which extends from the iris. Avascular remnants of these structures may be seen in adults as hyaloid remnants or as persistent pupillary membranes.

II. ANATOMY AND PHYSIOLOGY - The lens and cornea are unique in that they are living tissues which are optically transparent. The lens maintains transparency by having a highly ordered, critically spaced arrangement of fibers which scatter only 5% of the incident light.

A. Lens Anatomy - Pupil dilation allows more of the lens to be seen.

1. **Zonules** (suspensory ligaments) - Suspend the lens in the pupil and attach the ciliary body to the elastic lens capsule to facilitate accommodation.
2. **Patellar fossa** - A depression in the anterior vitreous in which the lens rests. The anterior vitreous face is strongly attached to the posterior lens capsule.
3. **Lens capsule** - Lets the become more spherical when zonular tension is relaxed.

4. **Lens fibers** - These lamellarly arranged lens epithelial cells have lost their nuclei, are less metabolically active, and form "Y" sutures as they join. The cortical cells are younger whereas the nuclear cells are older, more irregular, and less transparent.

B. Physiology of the Lens

1. Lens capsule is semipermeable and lens nutrition is supplied by the aqueous humor since the lens is avascular.
2. Lens metabolism is low and primarily involves glucose via anaerobic glycolysis (the rate of which is controlled by the enzyme hexokinase and the amount of glucose).
3. Lens proteins - The lens is very high (35%) in protein and is therefore sensitive to protein deficiency.
 - a. In young animals, most lens proteins are soluble (alpha, beta and gamma crystallines).
 - b. Lenses with cataracts contain more insoluble proteins.
 - c. With age, some crystallines become insoluble which is important in senile cataractogenesis.
 - d. The lens capsule immunologically tends to isolate lens proteins from the immune system.
 - e. **Nuclear Sclerosis** - The lens continues to grow slowly throughout life with compression of the nucleus making the lens less elastic and less able to accommodate for near vision. The aging, compressed nucleus normally becomes "cloudy" or "milky" and is differentiated from a cataract by the fact that the fundus is still visible through the sclerotic region.

C. Function of the Lens - Adjustable refraction (bending) of light rays to focus them on the retina.

1. Second most powerful refractive surface (air-cornea interface most refractive).
2. As classically described, near vision requires lens thickening.
 - a. Ciliary muscles constrict, zonule tension decreases, and the elastic lens capsule causes axial thickening (a more spherical) lens. For distance vision the ciliary muscles relax, zonule tension increases, and the lens thins axially.

3. Most domestic animals have poor accommodation (2-3 Diopters) compared to man (up to 14 D) due to weaker ciliary muscles. Some domestic mammals may accommodate by moving the lens anteriorly or posteriorly rather than causing lens shape changes.
4. Birds - Have very good accommodation as well as superior retinal development (many avian species have two foveae).
 - a. Have a lens pad where zonules attach to lens equator.
 - b. Have ability to change length of eyeball (telescope effect using scleral ossicles).

III. DISEASES OF THE LENS - Lens diseases can be categorized as: 1) congenital defects; 2) loss of accommodation; 3) decreased transparency (cataracts); 4) abnormal position (subluxation and luxation); and 5) creation of inflammation (lens-induced uveitis).

A. Congenital Lens Defects - Since the lens develops so early in gestation, defective lens development tends to be associated with other severe defects which may be fatal or at the very least significantly impair ocular development.

1. **Vascular related anomalies of the lens** - Probably the most common clinical congenital defects of the lens.
 - a. **Persistent pupillary membranes** - The most common congenital defect. The anterior remnants of the tunica vasculosa covers the pupil up to 2 weeks post birth and usually undergoes post-natal lysis by 3-5 weeks of age (some animals may take several months for lysis to be completed). If they persist in adults PPMs can be identified by their origin from the iris collarette region and extension from iris to iris, iris to lens, or iris to cornea. Treatment is rarely required. Persistence into adulthood may have a heritable component.
 - b. **Persistent hyperplastic primary vitreous/persistent hyperplastic tunica vasculosa lentis** - Fibro-vascular remnants of fetal structures may cause opacification of the lens capsule, cataract, or posterior lenticonus (out-pouching of the posterior capsule of the lens). Suspect this problem in young dogs with cataracts and intra-lenticular hemorrhage.
2. **Uncommon congenital lens anomalies:**
 - a. **Microphakia** - An abnormally small lens. May lead to lens luxation.
 - b. **Lens coloboma** - a notch-like defect in the lens.

- c. **Peter's anomaly** - the developing lens placode fails to separate from the cornea resulting in an opaque cornea and lens.

B. Loss of accommodation

1. **With aging (presbyopia)** - The anterior lens capsule thickens and the lens nucleus hardens (nuclear sclerosis). Not a major problem for most domestic animals because of a limited accommodative range, although is the reason why many people over 40 years of age need reading glasses.
2. **Following cataract surgery** - Most post-op cataract patients do well despite large refractive errors. (A dogs normal visual acuity is 20:80 meaning it can see from 20 feet away what a normal person could see from 80 feet away. After lens extraction the aphakic dogs visual acuity is about 20:800). Artificial intraocular lenses (IOLs) to replace the focusing ability of the lens have been developed for humans and dogs, and are in the process of being developed for cats, horses and other species.

C. Cataracts - Any opacity of the lens or its capsule. Cataracts are probably the most common cause of treatable vision loss in the dog.

1. **Pathogenesis** - Related to alterations in lens metabolism. Any irregularity in the 3-dimensional spacing of the lens fibers resulting from changes in lens hydration, protein conformation, cell metabolism, electrolyte imbalances, or cell membrane stability can disrupt lens transparency and result in light scattering (cataract).
2. **Classifications and definitions** - Numerous classification schemes are used simultaneously to describe cataracts.

a. When they occur

- 1). **Congenital** - Present at birth. Tend to be nuclear and may have clear cortex around them. They may or may not progress or be inherited.
- 2). **Juvenile** - Developing before adulthood (1-2 yrs of age in dogs).
- 3). **Adult** - Occur in adult animals.
- 4). **Senile** - Aged animals. (Beyond nuclear sclerosis).

b. Where they occur - Important in that many inherited cataracts occur in the posterior cortex area.

- 1). **Structure affected** - capsule, cortex or nucleus.

- 2). **Location in the lens** - anterior or posterior, equatorial or polar (axial), zone (capsular, subcapsular, cortical, nuclear).

c. Stage of development

- 1). **Incipient** - Small opacity and vision is maintained.
 - 2). **Incomplete (immature)** - Vision is impaired and the fundus is seen indistinctly. A tapetal reflex, however, is still seen.
 - 3). **Intumescent** - A swollen, opaque lens which may cause secondary glaucoma due to mechanical compression of the drainage angle.
 - 4). **Complete (mature)** - Entire lens is opaque with no tapetal reflex or fundus visible.
 - 5). **Resorbing (hypermature)** - The cortex may liquefy and permit visualization of the fundus around the opacity. These can be identified by noting wrinkles in the anterior lens capsule or "sparkles" in the lens which consist of very fine particles that reflect light much as snow reflects sunlight. Often these type of cataracts are associated with lens-induced uveitis. May also see when the cortex "dries out" resulting in a smaller lens that may pull away from the zonules and luxate. Occasionally limited vision is restored in some patients but this is very unpredictable.
 - 6). **Morgagnian cataract** - A hypermature lens with liquefied cortex and the solid nucleus sinks to the bottom.
- d. Rate of development** - Stationary or progressive. Helps determine if surgery is needed.
- e. Lens consistency** - Important primarily for surgery. Cataracts in young animals tend to be soft whereas those in older animals tend to be hard.
- f. Etiology** - The most useful method but the most difficult to determine.
- 1). **Inherited**- May/may not be congenital and are probably the most common cause of cataracts in dogs. Can appear at any age and may involve just the lens or be part of multiple ocular abnormalities. In dogs the location, age of onset, progression pattern, and inheritance differ by breed. Diagnosis and prognosis is based on breed, clinical appearance, age of onset, evaluation of related animals, and test breedings.

2). **Nutritional** - Especially protein deficiencies.

- a). Amino acid deficiencies in puppies fed Esbilac^R or kittens fed KMR^R milk replacers.
- b). Protein deficient diets and starvation states.
- c). Various amino acid and vitamin deficiencies (A, E and riboflavin) as well as electrolyte imbalances.

3). **Toxic** - Either congenital or acquired. Clinically significant toxins include:

- a). Disophenol (dewormer) - transient or permanent cataracts, especially in pups.
- b). Hygromycin B (anthelmintic) - Pigs.
- c). In humans and in experimental animals, corticosteroids, epinephrine, chlorpromazine, and parasympathomimetic miotics (especially phospholine iodine).

4). **Inflammatory/infectious** - Usually due to altered aqueous humor or lens metabolism.

- a). Uveitis-induced cataracts - Probably the most common cause of cataracts in cats and adult horses.
- b). BVD in cattle - acquired in utero.

5). **Senile degeneration** - May be seen in elderly animals secondary to the cumulative effects of chronic exposure to ultraviolet light and perhaps oxidizing stress.

6). **Radiation and electric shock** - Usually seen in patients undergoing radiation therapy for neoplasia in which the eye was in the field - or in animals that have experienced an electric shock from chewing on electric cords.

7). **Metabolic**

- a). **Diabetes mellitus** - Common. Diabetic cataracts are often intumescent with a rapid onset. A blood glucose should be performed on all dogs with rapid onset bilateral cataracts, especially if they have "water" or "Y" suture clefts. Elevated glucose in the aqueous overloads the enzyme hexokinase in glycolysis and forces glucose into the aldose reductase pathway thereby producing impermeable sorbitol and drawing water into the lens making "water cleft" cataracts. Eventually coagulation of lens protein occurs. Good control of blood glucose can prevent diabetic cataracts, but once clefting and protein coagulation occurs the changes are irreversible.

b). Cataracts have also been reported in cats and dogs with hypocalcemia (hypoparathyroidism, and nutritional secondary hyperparathyroidism).

8). **Traumatic** - Lens capsule rupture and lens fiber disruption draws aqueous into the lens, resulting in opacification. Lens protein release also may lead to lens-induced uveitis.

3. Therapy of Cataracts

a. **Medical** - Of extremely limited value and consists of only palliative therapy in patients where surgery is not an option.

1). **Dissolution** - Despite claims in the popular press, vitamins, nutritional supplements etc. have not been shown to be any better than placebo because of the natural dissolution (hypermaturity) the lens may undergo. Experimentally a topical aldose reductase inhibitor has shown some promise in preventing “sugar cataracts” in dogs. This may have some utility in the prevention of diabetic cataracts in dogs, although longer term clinical trials are required.

2). **Prevention** - Tighter regulation of diabetes may prevent or slow the onset of diabetic cataracts.

3). **Palliative**

a. **Atropine** - Pupil dilation may permit vision around an axial cataract (careful using in breeds prone to angle closure glaucoma). Use once every 2-3 days.

4). **Anti-inflammatories** - Topical/oral corticosteroids, and aspirin/carprofen may decrease lens-induced uveitis associated with lens resorption. Occasionally, in very young dogs (<1 yr of age) limited vision may be restored as the cataract resorbs. Lens-induced uveitis, however, must be controlled to avoid secondary glaucoma, retinal detachments etc. which may again cause blindness.

b. **Surgery** - Treatment of choice in most animals with vision impairing cataracts. This procedure is often very successful and is usually best performed by a specialist who regularly performs cataract surgery. Early diagnosis and patient selection, however, are critical to success.

1). **Primary care veterinarian-factors related to a successful outcome.**

- a). It is essential that the primary care clinician be able to recognize the presence of cataracts prior to complete lens opacification and to help screen patients that would benefit from lens extraction. The primary care clinician should give the client the opportunity to have lens extraction surgery performed when the statistical chances for success are the greatest - which is before complete lens opacification.
- b). Any patient with progressive cataracts which impair vision in one or both eyes should be referred prior to the onset of complete opacification. This results in a greater likelihood of a successful surgical outcome and reduces the cost to the client because it may allow examination of the fundus for PRA, retinal detachments etc. and avoid the cost of an ERG or ocular ultrasound.
- c). Animals should be referred prior to the onset of lens resorption (hypermaturation) because the onset of lens-induced uveitis reduces the surgical success rate at 6 months post-op from 90% to 50%. Again, early referral will permit the optimum timing for surgery and highest chance of success.

2). Animal-related factors to a successful outcome.

- a). The animal should be in good general health as determined by physical examination, and preoperative screening consisting of a CBC, chemistry profile, urinalysis, and fecal examination. Diabetics should be well regulated as determined by a glucose curve.
- b). The affected eye ideally should be free of other ophthalmic abnormalities such as KCS, pannus, glaucoma, uveitis, retinal disease, etc. Pre-op ERGs, and ocular ultrasound should be performed pre-op if the fundus cannot be seen.
- c). The animal should tolerate being treated by both the hospital staff and the owner. Surgery is seldom successful in aggressive dogs, foals that are not halter broken, or if the owner cannot treat the pet.
- d). Surgery should be performed before 6 mos of age in foals. Cataracts in adult horses are usually secondary to chronic uveitis and are poor surgical candidates.

3). Client-related factors to a successful outcome.

- a). The client must be familiar with the pros and cons of lens extraction and accept the risk:benefit ratio.

- b). The client must be willing to bear the expense and time commitments associated with surgery and post-op visits.

4). Surgeon-related factors to a successful outcome.

- a). The surgeon should be familiar with the methods of, and regularly performing, lens extraction surgery.
- b). The least amount of ocular trauma should occur.
 - i). Phacoemulsification - Breaks up and aspirates a cataract through a small (3.0 or 3.2 mm) incision. The procedure of choice in most eyes with vision impairing cataracts and this technique has greatly improved cataract success rates in animals.
 - ii). Extracapsular cataract extraction - An older method of lens extraction which requires a large (20 mm) incision. Now usually performed in cases in which the lens is very hard and not easily phacoemulsified.
- c). Any post-operative refractive errors should be corrected to the greatest degree possible. This means that artificial lenses should be implanted in good candidates and avoided in animals likely to have significant complications associated with the IOL.

D. LENS LUXATION - Lens displacement. Occur due to zonular disruption, lens shrinkage (hyper mature cataract), or buphthalmia.

1. Etiology

- a. Traumatic** - Infrequent and usually carries a poor prognosis due to other intraocular damage.
- b. Spontaneous** - Zonular abnormality especially in terriers.
- c. Secondary**
 - 1). To chronic uveitis and zonule dissolution.
 - 2). To a hyper mature cataract and lens shrinkage.
 - 3). To glaucoma and globe stretching with zonule disruption.

2. Signs of lens luxation - The eye may appear quiet or very inflamed (especially if

glaucoma is present).

- a. The anterior chamber is shallow in anterior luxation or subluxation, and deep in posterior luxation/subluxation. There may or may not be iridonesis (iris trembling).
- b. The lens may be partially or totally in anterior chamber.
- c. An aphakic crescent is seen in lens subluxation.
- d. Corneal edema - seen in anterior luxation with the lens in contact with the corneal endothelial surface.
- f. +/- Glaucoma due to pupillary block by the lens or vitreous, vitreous infiltration of the drainage angle, or secondary to chronic uveitis.

3. **Treatment of lens luxation** - A referral surgery

- a. **Acute anterior luxation** with glaucoma in a potentially sighted eye is an emergency and best treated by immediate lensectomy. Topical atropine or tropicamide may be beneficial on an emergency basis as pupil dilation may allow the lens to fall back into the posterior chamber. Removal of a luxated lens is more difficult than standard cataract extraction because of the risk of vitreal loss and secondary retinal detachments
- b. **Subluxations** - Occasionally an attempt is made to "trap" the lens in the posterior chamber with miotics (demecarium bromide, sometimes latanoprost). This can precipitate glaucoma, however, if the pupil should dilate (perhaps from owner noncompliance), and the lens falls forward into the pupil. Redosing the miotic then constricts the pupil around the lens, impairing outflow and raising IOP.
- c. **Posterior lens luxation** - Lens extraction can be difficult. In some cases it may be better to try to trap the lens behind the pupil with miotics and use topical corticosteroids to control uveitis.
- d. **Chronic luxation** with blindness and pain is best treated by enucleation or evisceration and prosthesis.

E. LENS-INDUCED UVEITIS - Occurs in two basic forms clinically; 1) a severe form associated with traumatic tears of the lens capsule, and 2) a usually milder form associated with leakage of lens protein from a cataract.

1. **Lens Rupture** - Results in severe uveitis usually due to a penetrating wound or occasionally secondary to severe blunt trauma to the globe. Often these injuries cause other damage, i.e., corneal laceration, hyphema, iris prolapse, retinal detachment, etc.

- a. **Signs** - The capsular tear may be hard to see. History suggests penetration i.e. cat scratch, gunshot etc.
 - 1). Other signs of trauma such as a corneal laceration, hyphema, anterior uveitis, perhaps a tear in the lens capsule or cataract formation.
 - 2). In chronic cases there may just be a miotic pupil, deep anterior chamber, and smoldering anterior uveitis with or without posterior synechia in addition to the corneal scar from the injury.
 - b. **Treatment**
 - 1). **Aggressive surgical therapy in acute injuries** - The eye and vision may be saved in some patients by removing the lens and suturing the corneal wound. This is a referral procedure. Enuclerate very severe cases.
 - 2). **Conservative therapy** - If necessary, the corneal laceration is sutured and treat with topical and systemic antibiotics/corticosteroids and topical atropine. Often these patients are blind and the eye is chronically inflamed if lens extraction is not performed at a latter date.
 - c. **Prognosis** to retain vision is guarded due to the severity of the inflammation and concurrent injuries.
2. **Cataract Associated Lens-induced Uveitis** - Very common clinically and can range from a mild to severe uveitis (perhaps as a result of how much lens protein is leaking through the capsule). It differs from an uveitis-induced cataract in that in LIU the cataract came first followed by uveitis. Suspect in any red eye with a cataract.
- a. Hypermature or rapidly swelling intumescent cataracts.
 - b. Results from exposure of immunologically isolated lens protein to the immune system.
 - c. Although lens-induced uveitis in young dogs is generally more severe in the short-term, it has a better prognosis than does the chronic cell mediated granulomatous uveitis seen in older dogs.
 - d. Young dogs (< 1 yr of age) may experience sufficient lens resorption to allow some limited vision. Usually, however, glaucoma and retinal detachment are a sequela of chronic LIU, and it is relatively uncommon for dogs ≥ 3 yrs of age to have sufficient resorption for vision to return.

e. Signs of lens-induced uveitis

- 1). Acute - Episcleral injection, perilimbal "flush," corneal edema, anterior chamber cells and flare, iritis, miosis, cataract or ruptured lens, low IOP.
- 2). Chronic - Posterior synechia, iris bombe, occlusion of the filtration angle with inflammatory debris and possibly secondary glaucoma.

f. Treatment of lens-induced uveitis

- 1). Topical and systemic anti-inflammatory agents.
- 2). Treat glaucoma if present (remember that miotics intensify uveitis). Epinephrine may be helpful.
- 3). Lens extraction has high long-term failure rate in cases of chronic LIU.
- 4). Enucleation or evisceration and prosthesis if the eye is blind and chronically painful.