

EVALUATION AND COLORS (opacities) OF THE CORNEA

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Corneal functional anatomy

No discussion of the cornea is complete without at least a brief and basic anatomy review. This is a shamelessly simple but not dumbed down lesson; it's truly a way to think about the cornea clinically during evaluation and disease interpretation. Understanding the function of the cornea allows understanding of the anatomy to follow naturally. The function of the cornea is two-fold. It is a defensive barrier between the outside world and the inside of the eye (which allows vision and thus is fairly important for most creatures to do their jobs). Additionally, as a glorified window, the cornea transmits and bends light. In order to perform these functions, the cornea is intact and pretty strong AND, it's clear (so the animal and you can see through it).

The anatomical components and features that give rise to these corneal defense and clarity functions include the corneal layers (from outside in): the tear film, the epithelium, the stroma (making up the majority of the corneal thickness), Descemet's membrane (the basement membrane of the endothelium) and the endothelium (a non-regenerative single layer of cuboidal epithelial cells lining the inside of the cornea / front side of the anterior chamber). And, they include the cornea's make up: with it being avascular, lacking pigment, being relatively dehydrated and with intensely organized collagen fibrils.

Corneal relative dehydration is governed by the epithelium, which is a "water-hating" mechanical barrier to fluid uptake by the "water loving" stroma – this is why with corneal ulcers, where the epithelium is missing, there is associated edema; and it is governed by the endothelium, which is similarly a mechanical barrier but also and most importantly, contains a Na-K ATPase pump that constantly pumps water out of the cornea.

The cornea's PERFECTLY regularly arranged collagen fibrils also contribute to clarity and a nice analogy to make sense of that is to recall that transparent glass and glass block are both made of the same material but it is the organization (specifically the variation in band gaps in different glasses, which are considered amorphous solids) that dictates whether a photon of light passes through or is absorbed or reflected. The cornea and the sclera are both made up of mostly similar collagen and yet the cornea is clear and the sclera opaque white, and this is due to the regular collagen arrangement in the cornea.

Corneal evaluation

Examination

With an understanding of what the cornea is supposed to do, what about it gives rise to that and thus what it is supposed to look like, you can start to examine it. First off, just look at it!! Do not be intimidated by the different anatomy and physical exam skill set requiring different equipment, or the different differential list and treatments including drugs and surgeries (requiring different and expensive instruments and with fragile, un-forgiving tissue), or the often highly owner-visible outcome and level of importance/value on eyes.

Examination equipment

What do you need to look? Really, if you could only have one thing for this, I'd recommend it be a Finnoff transilluminator. Other options include direct or panoptic ophthalmoscopes (as light sources and usually NOT via the ocular for corneal examination) or a good penlight and some loupes for magnification. A hand-held slit lamp or slit lamp biomicroscope

Examination technique

Start with a lights on, hands off exam – this is where you make your across the room observations, looking for overt rubbing at the eye(s), squinting, ocular discharge, periocular redness or swelling, and corneal cloudiness, redness or surface changes. You also can make an initial visual function assessment as the animal moves about in the lobby or exam room and you talk to clients about the history and presenting complaint.

Next up is a lights on, hands on exam – an exam table is often helpful here to get the patient's head and face at your eye level. Check the head, face, eyelids and each eye in turn for overt issues, then assess each eye in turn with direct, diffuse AND focal illumination for a quick overview.

For lights off hands on exam, an exam table and proper, steady head restraint, are even more important. Using a transilluminator or an ophthalmoscope with the light aperture set to a large spot and light intensity high enough to permit/facilitate the exam but also still reasonable comfort and tolerance by the patient, start arm's length away and use retroillumination (back-lighting with the tapetal reflex) to assess pupil size, shape and symmetry and notably, to highlight even subtle changes / opacities / interruptions in the clear optical media (including the cornea) that you might otherwise miss. Seeing them at this stage will allow you to be aware of them and look for and localize (cornea, anterior chamber, lens, vitreous) and define them on further specific exam whereas I guarantee, many would be missed altogether on up close and personal exam if not "spotted" here first. It's akin to jumping to 40 or 100x on a microscopic evaluation of a cytology specimen. Again, just look for anything "off" even if you know nothing about eyes. The beauty of this is that the cornea is normally intact, smooth and clear, so anything altering its surface or opaque, is abnormal.

Next up is close corneal inspection using diffuse and focal (i.e., with the light source closer to the eye, +/- smaller light aperture/spot) direct illumination at a variety of angles and

across the entire corneal surface. Look for appropriate sheen (versus lackluster/dull/dry or gritty surface), any opacities, and any other surface irregularities

You might stop there, but if you want to get into this cornea business a little, the meat of the matter is with a focused slit beam (and ideally magnified view) exam. You can either “be a slit lamp” – use a focused slit aperture light (from a slit lamp or direct or panoptic ophthalmoscope using the slit or smallest spot) and ideally magnified view (through magnifying head loupes of some sort) at a convergent angle OR use an actual slit lamp (hand held Heine, Eidolon, etc. or slit lamp biomicroscope) to provide you both.

Project the small and sharply focused light source obliquely across/through the eye to create an optical cross section/Purkinje images. This allows the observer to localize and determine depth of lesions within the corneal stroma, as well as to assess for corneal thickening/expansion/raised lesions and/or corneal stromal loss/thinning/devoting. These principles also apply to the anterior chamber, lens and anterior vitreous.

The concept (physics of light / optics, not really ophthalmology at all) behind slit beam use relies on passing light being bent differently by different substances and thus highlighted at interfaces of different / transitions from different media (with Purkinje images) such as from air to tear film/corneal epithelium – Purkinje image #1; and from aqueous humor to the anterior lens capsule. If we go more in depth, though, really there are more of these transitions: 1 - from air to tear film/corneal epithelium, 2 - from corneal endothelium to aqueous humor in the anterior chamber, 3 - from aqueous humor to the anterior lens capsule, and 4 - from the posterior lens capsule to the vitreous (Figure 1). Understanding the ocular cross sectional anatomy and these transitions and how associated visualized light from an obliquely projected slit beam appears across them normally, and also how it may be altered by lesions/disease states allows excellent exam capability, demonstrating localization and depth of lesions within the ocular structures. Figure 2 provides a diagrammatic example showing the distortion of the first and second Purkinje images with a thickened cornea, a mid-depth stromal corneal opacity (between the first and second highlighted Purkinje images), corneal endothelial debris (right up against the second Purkinje image), aqueous humor flare, cell and fibrin clot (all between the second and third Purkinje images), an anterior cortical lens opacity or cataract (just behind the third Purkinje image), and anterior vitreal cell (behind the fourth Purkinje image) (Figure 2A); and the distortion of the first and second Purkinje images with a thinned cornea (specifically a Descemetocoele, where they essentially touch because there is no remaining stroma between them) (Figure 2B). This highlighting / identification of corneal thinning is a very important function of a slit beam as not all stromal / deep corneal ulcers look “divoted” to the naked eye even with close inspection, and yet recognizing such stromal loss or thinning of a cornea is a critical part of corneal disease assessment.

Other diagnostics

Schirmer tear test (STT)

A healthy tear film is essential to maintain a healthy cornea and thus the STT is a component of a thorough corneal evaluation. It is performed with the goal of ruling in or out an aqueous tear deficiency having a role in corneal disease. In veterinary medicine, the routinely

clinically utilized Schirmer tear test I uses a standardized STT strip to provide a quantitative measure of the basal plus reflex aqueous component of tear production in response to a noxious stimulus over one minute. (The rarely used Schirmer tear test II provides a quantitative approximation of the basal aqueous component of tear production with the ocular surface topically anesthetized and dried.) Normal canine reflex tear production (STT I) is equal to or greater than 15mm of wetting in one minute. Wetting values between 10 and 15mm are borderline and should be serially monitored with significance interpreted in conjunction with history and clinical signs and findings. Notably, the STT does not fully assess tear quality, and thus it may be normal despite a tear film lipid or mucin deficiency or abnormality and associated ocular surface disease.

STT technique and interpretation “pearls”

The STT (I) should be performed FIRST in the ophthalmic examination, before anything aside from your initial peek and without topical anesthetic, lubricants, etc. applied, to reduce the effect of reflex tearing from ocular manipulation and stimulus.

You should always* check both eyes as it may provide a built in control/normal or at least frame reference or important information to take into account. For example, the STT I of an eye affected with a painful (and reflex tear promoting) corneal ulcer may be stimulated into the normal range by the problem, prompting a missed diagnosis of a contributory tear film issue if the other eye (perhaps measuring low due to underlying keratoconjunctivitis sicca (KCS) in both eyes) is not assessed.

*The STT should not be performed in the face of deep corneal ulceration or other cases of significant corneal thinning and thus fragility/risk of perforation/rupture. Even minor trauma of the STT may also be contraindicated in a recently healed non-healing corneal ulcer with still fragile / weakly adherent corneal epithelium. Finally, though most species of animals can develop dry eye (and associated ocular surface/corneal disease) warranting it as a differential diagnosis consideration to always have at least in the back of your mind, the STT is usually only routinely performed/assessed in dogs, and infrequently performed in cats, exotic species, etc., as it may be difficult to interpret (e.g., normal cats may have a STT I of 0mm of wetting in one minute) or there may not be available normal reference value ranges. The phenol red thread tear test provides an alternative option for measurement of basal plus reflex aqueous tear production in cats' and smaller animal species' eyes.

Tear film break up time (TFBUT)

Again, because a healthy tear film is essential to maintain a healthy cornea, the TFBUT is a component of a thorough corneal evaluation. It is performed with the goal of ruling in or out a qualitative (lipid and/or mucin) tear deficiency having a role in ocular surface or corneal disease. This test measures the time it takes for a uniformly distributed (through the observer manually blinking the eyelids after fluorescein dye application, then holding them open) layer of fluorescein dye (highlighting the tear film) to break up or dissociate from the corneal surface and form dark spots. Normal TFBUT is ~20 seconds and this is reduced (accelerated) in many ocular surface disease states.

Other methods of tear quality assessment

Tear film quality may also be evaluated through meniscometry (measuring the tear meniscus radius), interferometry (measuring tear film thickness and the lipid layer), meibometry (measuring the meibomian lipid along the eyelid margin) and or conjunctival biopsy with analysis of goblet cell density/index, as these cells are responsible for producing the mucin component of the tear film.

Fluorescein and Rose Bengal staining

These stains evaluate the surface (tear film and epithelium) health of the cornea and are thus also integral to thorough corneal evaluation.

Fluorescein dye

Though fluorescein dye has many uses in ophthalmology, including assessment of tear film quality through TFBUT above, assessment of nasolacrimal duct patency (Jones test) and assessment for active aqueous humor leakage via a corneal wound (Seidel test), the most common is to detect corneal ulceration through fluorescein staining. Fluorescein dye (which is hydrophilic) is normally not retained by the “water hating” epithelium, but when that is not intact or missing, it is taken up by the “water loving” stroma and highlights the epithelial defect / stromal exposure. This is best viewed after application of fluorescein dye +/- saline eye wash rinsing, with a cobalt blue filtered light source in a dimly lit or dark environment.

Fluorescein technique and interpretation “pearls”

Fluorescein dye solutions are excellent growth media for bacteria and should not be saved/stored once made up.

Fluorescein “pseudostaining” uptake is not uncommon where a STT strip contacted the cornea, especially if the animal’s tear film is unhealthy; with tear film disorders; and/or corneal surface irregularities (gritty or raised lesions; or facets (epithelialized stromal loss or healed corneal ulcers with residual thinning) where dye may pool).

Two types of corneal ulcers may have characteristic fluorescein staining patterns. In primary or secondary superficial non-healing (“Boxer” or “indolent”) ulcers, fluorescein may slowly leak under the defining loose epithelial edge, resulting in an area of bright green uptake surrounded by hazier uptake with time. With Descemetocoeles, which it may be safest to not stain with fluorescein to reduce patient and ocular manipulation and increased risk of perforation, the exposed hydrophilic stromal walls take up fluorescein but the hydrophobic Descemet’s (“water hating” epithelial basement membrane) does not. It is exposed because by definition with this type of ulceration, there is extreme (total) stromal loss down to that layer.

Rose Bengal dye

Rose Bengal staining is used in the same manner as fluorescein (though viewed with non-filtered white light), but detects / is taken up by devitalized (not necessarily missing) epithelium and or regions deficient in tear film mucin.

Corneal cytology

Cytologic evaluation of corneal lesions is indicated in cases with corneal infiltrate. After application of proparacaine or other topical anesthetic, a cytobrush or back end of a scalpel blade is used to collect a sample from the infiltrated cornea by gentle scraping (this may be dangerous and even contraindicated in cases of deep corneal ulceration at risk of perforation). If the lesion is epithelialized (fluorescein negative), it will be less likely to yield a diagnostic sample unless iatrogenic corneal ulceration is created; the pros and cons of doing so for this test must be weighed. Regardless, the sample is spread onto a clean glass microscope slide and allowed to dry. Clean (no “ears or rears”) diff-quick staining of the slide allows in-house cytologic evaluation, or unstained slides may be submitted to a clinical pathologist for assessment.

Corneal cytology technique and interpretation “pearls”

Again, sample the area of / the infiltrate (where the “action” is), not the surrounding cornea or conjunctiva.

On analysis, look for epithelial cells, which indicate a good sample, and assess their health and for intracellular organisms, inclusions, etc.. Also look for inflammatory cells and assess who’s there? how many? status? Similarly, look for organisms including bacterial (cocci, rods), fungi/yeast, as well as dysplastic or neoplastic cells.

Corneal culture and sensitivity

Culture of corneal lesions is indicated in cases with corneal infiltrate, especially if infection suspected. Ideally, sample(s) are collected early in the corneal evaluation, without topical anesthetic if safely/comfortably possible, using a microtip culturette swab gently rubbed over the area of infiltrate. Be careful to avoid contamination with the conjunctiva, eyelids, etc.. These may be used to inoculate growth medium plates or sent to a microbiology lab (prompt plating maximizes yield) for aerobic bacterial culture and sensitivity. Fungal culture in small animals is uncommonly indicated in cases of specific predisposition/concern (patient status (systemically and/or topically immunocompromised), infiltrate plaque, cytology results); but almost always indicated in addition to bacterial culture in horses and other large animals due to their increased environmental risk of fungal keratitis. Sensitivity results should be interpreted “with a grain of salt” as well as taking in to account the clinical picture, as with topical therapy safely achievable drug concentrations may exceed those tested and yield different results.

Serial evaluation and response to therapy

Serial monitoring evaluation to gauge disease progression, especially with assessment of response to empiric or specific directed treatment, can be very useful in the evaluation of corneal lesions. Never underestimate the value of rechecks to help you determine what is coming and what is going / what is active or inactive!

Corneal biopsy

Biopsy of the cornea may be indicated for refractory, especially progressive mass or other undiagnosed corneal lesions and this may be diagnostic (via cytology and or histopathology) and or therapeutic. Corneal biopsy is generally a referral procedure and is frequently combined with adjunct therapy (cryotherapy or other).

Corneal lesion interpretation

Corneal opacities – the color wheel

So now we know how to look at and evaluate the cornea; what do we do with what we see? Interpretation begins with having a list of differentials for the corneal opacities or corneal colors.

Red

Red corneal opacities include: vascularization/vessels, granulation tissue and stromal hemorrhage/blood – all indicating chronic corneal irritation (keratitis). Less common red corneal opacity differentials include hemangioma/hemangiosarcoma and conjunctiva (pink-red) such as after grafting/flap surgery or via aberrant migration onto the cornea.

Brown / black

Brown corneal opacities include: pigment, neoplasia (limbal/conjunctival or iris/ciliary body melanocytoma/melanoma), dematiaceous fungal infection, foreign body (usually plant material) and sequestrum (cats only).

Corneal pigment may arise/migrate from the conjunctiva (superficial) and indicate chronic corneal irritation and/or previous vascularization (keratitis); arise/migrate from the endothelial limbus (endothelial pigment migration) as a usually incidental finding in middle-aged and older dogs; or it may have come from the iris through persistent pupillary membrane attachment, anterior synechia, corneal perforation with iris prolapse, iridociliary cyst exfoliation or rupture, or iridociliary mass exfoliation or contact.

Feline corneal sequestra may be from faint/weak tea staining to golden brown to burnt cookie to brown (to black) in color. They indicate chronic corneal irritation associated with breed/facial/ocular conformation and or feline herpes virus 1 infection.

Silver

Metallic foreign bodies may present silver corneal opacities.

Blue

Blue corneal opacification may be subtle/hazy grey-white “blue” to overt blue; and focal to diffuse. It indicates corneal edema, which can arise from epithelial (ulceration) and/or endothelial dysfunction (dystrophy, degeneration, endothelitis/uveitis, glaucoma, direct damage from lens luxation or other contact (ppm, cyst, synechia, neoplasia)), or leakage from corneal vascularization of any cause. In addition to blue opacification with corneal edema, the cornea thickens and bullae (blisters) may be present.

White

White corneal opacities are trickiest because they have the most differential diagnoses that are also often harder to differentiate. The differentials include: scar/fibrosis, Haab’s stria, infiltrate (cells present that should not be) and deposit; and as above, when more subtle (and not blue), edema.

Corneal scar/fibrosis may be subtle/hazy grey-white to dense white; and focal or diffuse. By definition it is “inactive”, and usually appears that way. Considering the clinical picture (history – e.g., previous issue now static and comfortable; ophthalmic exam findings – e.g., “quiet eye”, relatively well-defined opacity (at least with close and critical inspection), fluorescein negative, etc.) may help allow determination of a white corneal opacity as scar.

Haab’s stria(e) are grey-white, softly linear Descemet’s membrane (deep corneal) defects occurring with or after elevated intraocular pressure (glaucoma).

Corneal infiltrate may present as diversely as its causes (from infectious, sterile/immune-mediated inflammatory, to neoplasia or cystic) and thus appear creamy yellow/green-white, “soft or melting” to “white-white”, as well as sometimes thickened/raised, cystic or plaque-like, all mostly/usually with ill-defined borders. The presence of corneal infiltrate, both because it is by definition an active and potentially eye threatening condition, and because it has varied underlying causes with different therapies, warrants at least consideration of signalment, history, overall ophthalmic examination findings and further corneal diagnostic evaluation (cytology, culture, serial evaluation and response to therapy +/- biopsy) to aid differentiation and diagnosis as discussed above.

Examples of corneal infection associated infiltrate (from subtle to plaque (raised) include infected corneal ulcers and stromal abscesses (bacterial or fungal).

Examples of sterile/immune-mediated inflammation include German Shepherd-like pannus and feline eosinophilic keratitis.

Keratic precipitates (KPs) are technically corneal opacities (usually in the white category though they may also be red or brown depending on their cell type) but indicate intraocular, not corneal disease (specifically uveitis). KPs are white blood (white, creamy yellow to tan in visible color), red blood, pigmented or neoplastic cells in the anterior chamber smattered against the corneal endothelium (generally more inferiorly due to gravity and aqueous humor convection current).

Neoplastic corneal infiltrate may have variable appearance from thickened/raised, grey to white-white, or pinkish/vascularized lesions. The most common (whitish) corneal tumor types are squamous cell carcinoma and papilloma. (The other most common corneal neoplasias are hemangioma/hemangiosarcoma (red as above), and melanoma (arising from, and brown as above)).

Corneal epithelial inclusion cysts may occur after trauma (commonly surgical or not always witnessed (spontaneous?)) “implants/entraps” surface epithelium within the corneal stroma. They are usually clear-ish to “fatty”-creamy-yellow-white fluid-filled/cystic (round, raised/nodular/thickening the cornea) structures. They may enlarge with time and potentially cause usually minor complications (though they can be full thickness and even rupture in to the eye), and thus may warrant intervention from “de-roofing” and debridement, to excision via keratectomy.

Corneal deposits generally have sharp borders, though they may be irregular. Lipid/cholesterol deposit opacities are usually sparkly or opalescent and occur with inherited corneal dystrophy (typically seen in young dogs of certain breeds (Cavalier King Charles Spaniel, Boxer, etc.) as bilateral and symmetric, non-painful lesions); post-inflammation (degenerative); topical steroid use (steroid keratopathy); systemic metabolic disease (hypothyroidism or other issue with fat metabolism); or infrequently solely high dietary fat intake. Mineral deposit opacities are usually more chunky, like a “dried soap bar”, sometimes plaque-like, and may slough like scabs. These occur with calcific corneal degeneration, which is an age related / degenerative process in older and often metabolically compromised dogs, with secondary ulcerative keratitis as a common complication; post-inflammation (degenerative); or systemic metabolic disease (uncommon mineral imbalance, hyperadrenocorticism). Corneal drug precipitates are infrequently seen with topical ciprofloxacin, and rare other medications, administration.

Green

Aside from the occasional green plant foreign body, green corneal opacities are seen with positive fluorescein staining / fluorescein dye uptake, defining corneal epithelial loss or defect (erosion/abrasion/ulceration) +/- or stromal exposure. Corneal ulceration indicates trauma, an unhealthy / predisposed cornea (e.g., from KCS), or viral infection (herpes – a rare true primary epithelial pathogen); and when present risks secondary infection thus warranting topical antibiotic therapy until resolved.

Pink

Pink corneal opacities include Rose Bengal dye uptake (indicating corneal epithelial devitalization and or mucin deficiency), conjunctivalization (from previous surgery or aberrant migration), neoplasia, or vascularization/granulation tissue especially when combined with corneal edema and or fibrosis, which make them appear less red.

Haired skin &/or conjunctiva

Dermoids (choristomas) or aberrant islands of haired skin and or conjunctiva with or without pigment may occur on the cornea, resulting in opacification.

“Zebras”/other weirdos

It is not possible to predict all corneal opacity “colors” or other appearances and thus every differential, but the information above provides pretty close to an exhaustive list. And if you can detect and identify the opacity, you’re well on your way to making the diagnosis....appropriate management (intervention, monitoring, implications) follows from there. Voila, corneal disease made simple/simpler.

Corneal ulcers and alterations of thickness

Seeing and identifying an opacity and differential diagnosis list is most of the story but for corneal examination and interpretation, there is a little more besides opacities.

Corneal erosions/abrasions/superficial ulceration (by definition not affecting the thickness of the cornea) may be diagnosed with positive fluorescein staining/uptake and

frequently associated discomfort, ocular discharge and redness, and or focal, usually relatively mild, corneal edema.

Corneal ulceration with stromal loss (thinning the cornea) is where the use/importance of a slit beam to determine depth and thus urgency and option considerations come in to play. These stromal ulcers may be superficial, mid or deep (including down to Descemet's membrane (Descemetocoele)); sometimes obviously "divoted" or thinned as indicated by clearing in an otherwise cloudy and thickened corneal region (where little to no stroma remains to be opaque with edema and vessels in the surrounding area), but sometimes very hard to judge depth. In addition to determining their depth, appropriate corneal ulceration management is aided by assessing for and addressing any associated corneal infiltrate, "softness/melting/malacia and or (reflex) uveitis, as well as taking in to account lesion vascularization and location.

Corneal facets are areas of epithelialized (fluorescein negative) stromal loss (thinning) post previous ulceration.

Increased corneal thickness may occur with vascularization, edema*, infiltrate, or neoplasia/cysts as above.

Summary and Purkinje image figures

Armed with these differential considerations for almost every corneal lesion/disease, assessment/interpretation includes looking for/processing opacities, loss of thickness, or thickening, and then appropriate diagnostic testing. The other eye and the clinical picture (signalment dictating breed predispositions and or environmental risk; history – general, ophthalmic including topical and other medications/exposure and response; ophthalmic signs and exam findings; and systemic status) may also provide very useful information to guide and refine differential diagnosis and ultimate case management.

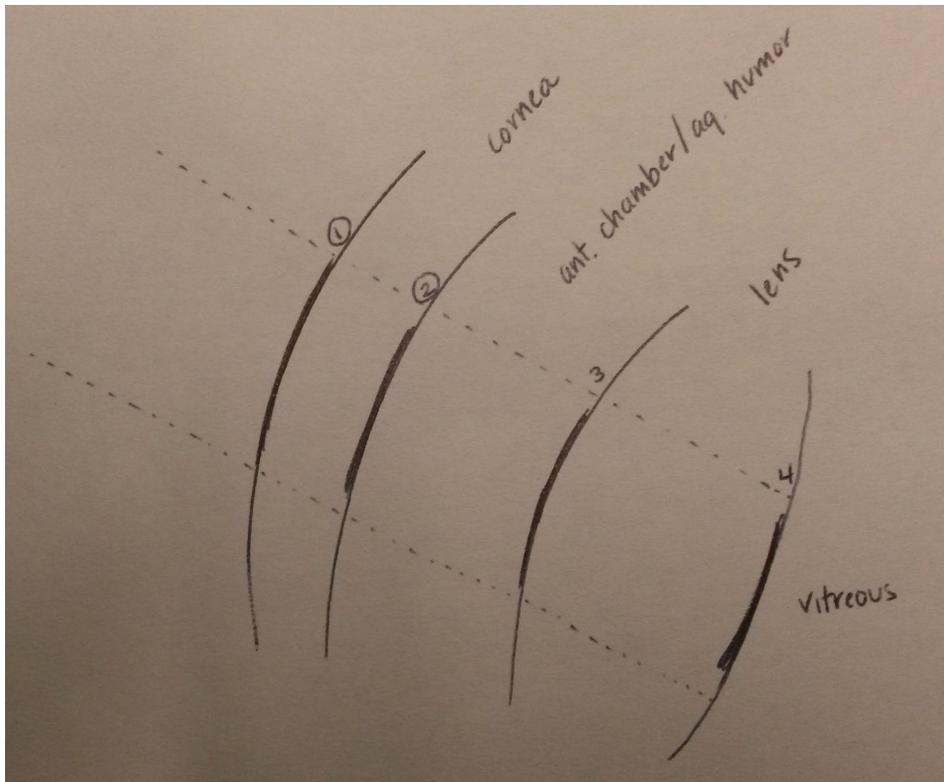


Figure 1 The Purkinje images. Light from a slit aperture is projected from left to right and across the eye. 1- from air to tear film/corneal epithelium, 2- from corneal endothelium to aqueous humor in the anterior chamber, 3- from aqueous humor to the anterior lens capsule, and 4- (often difficult to visualize without mydriasis) from the posterior lens capsule to the vitreous. This view and these images highlight the outside and inside of the cornea and its uniform thickness, the uniformly deep anterior chamber, and the anterior and posterior lens surfaces with the vitreous behind it.

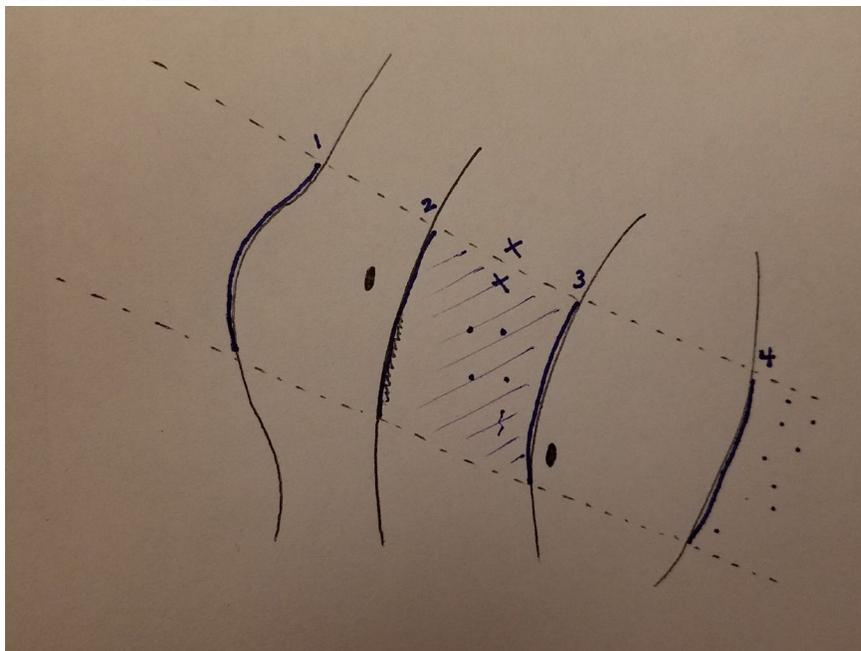


Figure 2A The Purkinje images highlighting and allowing localization of pathology. Light from a slit aperture is projected from left to right and across the eye. This view and these images highlight the thickened cornea, mid-depth stromal corneal opacity, corneal endothelial debris, aqueous humor flare, cell and fibrin clot, an anterior cortical lens opacity or cataract, and anterior vitreal cell.

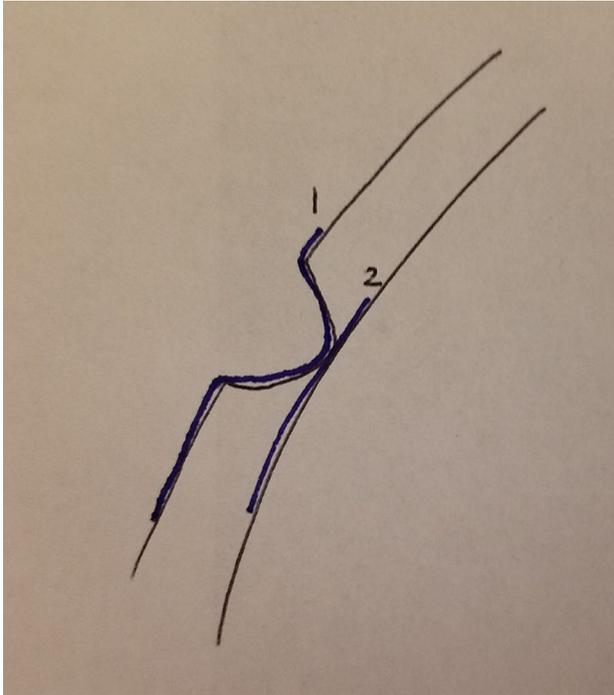


Figure 2B The Purkinje images highlighting and determining depth of pathology. In this diagrammatic cross sectional representation of a Descemetocoele, light from a slit aperture is projected from left to right and across the eye. This view and these images highlight the thinned cornea with Purkinje image 1 approaches 2 because there is no corneal stroma remaining between them.

THE LENS AND CATARACTS

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This lecture will briefly review clinically relevant lens anatomy and examination techniques to help identify and localize cataracts. It will then cover in depth different classification schemes of cataracts including causes. Finally, treatment of cataracts will be explained with concentration on a soon to be available promising medical treatment for diabetics, as well as surgery and indications for such.

With respect to clinically applicable lens anatomy, it is often useful to think of and explain the lens like a peanut m & m shaped like a regular m & m. It is comprised of the (continuous anterior, equatorial and posterior) lens capsule and anteriorly, the associated epithelium as the “candy shell”, the cortex as the chocolate, and the dense central nucleus as the peanut. The actual lens cells or fibers are elongate, arising from the metabolically active equatorial region or lens bow and spanning from the front to the back of the lens, meeting at / forming the lens sutures. After being produced at the equator lens cells are sequentially compressed in to the lens center by new growth/cells.

A cataract, by definition, is any opacity within the lens. Such opacities occur due to disruption of the normally perfect/orderly lamellar arrangement of the lens fibers and thus light's passage through/interaction with (refraction (bending of light) and reflection) the structure. This disruption in varying degrees, may then affect the ability of the lens to “do its job” of focusing light (through refraction) and images onto the retina, with light scatter and ultimately blurred vision. Despite this potential visual impairment (with loss of menace response and/or object tracking), even with a complete cataract, the afferent (retina, optic nerve) and efferent (parasympathetic fibers of cranial nerve III, iris sphincter / pupil constrictor muscle) arms of the pupillary light reflex should be intact/functioning, and the pupil should react normally to light.

To evaluate for cataracts, especially to pick up more subtle and/or posterior lesions, first perform an ophthalmic examination from arm's distance away using a light source (pen light, transilluminator or otoscope head, direct ophthalmoscope (set at 0 diopters if looking through the ocular) in a darkened area. Collect a tapetal reflex to “back-light” the lens. Lens opacities will block the tapetal reflex and be highlighted as a darker or shadowed area within the pupil. Then perform a closer evaluation, ideally with a slit beam or other focused and bright light source (creating an optic cross section view or image) +/- magnification to localize a cataract within the lens and pharmacologic mydriasis (pupil dilation) with short-acting/diagnostic tropicamide (a topical anti-cholinergic / parasympatholytic agent). An optic cross section view provides Purkinje images where the first beam highlights the cornea, the black space the anterior chamber, the second beam the anterior lens capsule, the Tyndall effect of light scatter through the lens (protein) thickness including the anterior cortex, the nucleus and the posterior cortex, and finally the third beam the posterior lens capsule.

Cataract cause classification scheme / reasons for cataract development

Cataracts may be classified and named/diagnosed within several different categories, including their reason for development, size, location within the lens and age of onset.

Inherited/genetic

This is the most common cause of cataracts in dogs. In this species cataracts should thus be presumed inherited until proven otherwise (known diabetes, trauma, etc.). Canine inherited cataracts occur in many breeds and in some there is a classic appearance. One common example is dominantly inherited triangular incipient posterior polar cataracts of Golden and Labrador Retrievers as well as some other large breed dogs. Fortunately these only rarely progress to cause clinical significance for the individual patient, but obviously affected animals should not be bred to avoid worse issues in the offspring.

Metabolic

Diabetes mellitus – This is a common cause of canine cataracts; the incidence of cataract formation in diabetic dogs is 80% within 16 months of diagnosis (Beam, S; Correa, MT; Davidson, MG. *Vet. Ophthalmol.* 1999; 2(3) 169-172), while it is rare in diabetic cats. Diabetic cataracts are usually bilateral, complete, develop rapidly and cause vision loss. Due to their tendency to occur and progress rapidly, they also commonly have Y suture clefting.

Cataracts occur with diabetes due to altered lens metabolism of glucose. In a normoglycemic state, lens metabolism of glucose occurs first via breakdown of glucose by the enzyme hexokinase to glucose-6-phosphate. In a hyperglycemic state, hexokinase is overwhelmed and glucose metabolism is shifted to the enzyme aldose reductase and a pathway that produces sorbitol, which accumulates in the lens cells. Sorbitol is a large, osmotically-active molecule, and its accumulation ultimately leads to lens cell swelling and rupture. The disruption of lens fibers then leads to cataract formation.

Hypocalcemia – This is an uncommon cause of cataracts with a typically bilateral, multifocal punctate appearance similar to a “snow-globe” opacity appearance within the lens. This should not be confused with that appearance within the vitreous, which indicates asteroid hyalosis, a degenerative or post-inflammatory change not uncommonly seen. The ophthalmic examination with an “optic cross section” is used to differentiate these locations/depth within the eye.

(Post-)inflammatory (in a way, toxic)

Inflammation (uveitis/vitritis of any of many causes (systemic or local/ocular)) is the most common cause of cataract formation in cats and horses. Particularly in those species then, but in dogs as well, it is important to look for hallmarks of (current/active with anterior chamber flare +/- relative miosis, red eye and low intraocular pressure and) prior inflammation (uveitis), including posterior synechiae (adhesions of the iris to the lens) and iris hyperpigmentation. Patients/eyes with cataracts in this category are generally poor candidates for cataract surgery due to significantly increased risk of post-operative complications of retinal detachment and secondary glaucoma.

Traumatic

Cataracts may be caused by **blunt or sharp/penetrating trauma to the eye**. Blunt cataracts are usually actually caused by inflammation/uveitis (“toxin”) caused by the trauma. Sharp cataracts may occur due to direct lens fiber disruption as well as from uveitis. Blunt traumatic cataracts are managed as any other along with any other traumatic injury and likely uveitis present. Sharp traumatic cataracts are similarly managed but lens capsule integrity must also be considered as lens capsule tears pose an additional problem. Capsular tears greater than 1.5mm in length generally will not self-seal and this can lead to severe lens-induced uveitis that is refractory to treatment (phacoclastic uveitis) – an exception to this rule is found in puppies, which can often (though not always) overcome severe phacoclastic uveitis. Generally though in cases of phacoclastic uveitis, treatment is thus more urgent cataract surgery not only to address the lens opacity as with typical cataract surgery, but also and almost more importantly to remove the inflammatory-inciting leaking lens material from the eye before secondary complications (retinal detachment, glaucoma) occur. In cats lens capsule damage is associated with the risk of post-traumatic sarcoma development, thus especially with sharp traumatic cataracts, long term close monitoring and ultimately possibly enucleation over cataract surgery is warranted.

Electrocution may cause cataracts and is most often encountered in young animals chewing on electric cords or with lightning strikes. Obviously there may be other issues/injuries to attend to that “trump” the lens opacities.

Dietary

Nutritional cataracts may occur in orphaned or nutritionally supplemented/supported puppies (and some other species) fed milk replacer due to arginine and other amino acid deficiency. Some ophthalmologists advocate adding beef or liver baby food to the milk replacer to reduce this risk. Milk replacer-related cataracts typically occur bilaterally at the nuclear – cortical junction and fortunately, usually don’t progress and in fact become relatively smaller with age as the lens grows around them and compresses them centrally.

Age-related or senile / degenerative with oxidative stress

These cataracts are incredibly common in older dogs with cumulative damage to the lens cells (by UV light radiation, free radicals, etc.) but fortunately rarely affect vision and thus are often rightfully benignly neglected. They are often located at the equatorial cortex and wedge-shaped, as well as punctate cortical lesions.

Radiation induced

In addition to UV light radiation contributing to inducing senile cataracts as above, radiation induced cataracts have been reported to occur in 10-28% of dogs with the eye in the field of ionizing radiation, even when appropriately/adequately protected or shielded. They generally occur 6-12 months following radiation therapy. They often start in the lens equator, as well as anterior and posterior subcapsular regions. They may or may not progress but are rarely treated surgically because of ocular surface / corneal disease (dry eye, keratitis) that is even more common in eyes in fields of RT +/- radiation retinopathy change preempting good candidacy and prognosis. Additionally there is often the “big-picture” disease and systemic status to consider in these cases (i.e., why the patient was receiving RT in the first place).

Toxic

Toxic cataracts may occur after exposure to certain drugs, most notably though still infrequent and not well described, ketoconazole. Toxic cataracts may also occur secondary to exposure to “natural” toxins such as those released into the vitreous and ultimately permeating the posterior lens capsule and lens tissue, from dying retinal cells (dialdehydes). This is common in dogs with progressive retinal atrophy (PRA) and is important to recognize as these patients are not good surgical candidates. This cause of / association with cataracts is one major reason for performing electroretinograms to assess retinal function before cataract surgery is performed, as if it is abnormally low, surgery may not be indicated to remove the opaque lens because the visual impairment is also and regardless (without treatment options available), retinally based. Prior to going down the road of pursuing pre-operative testing for cataract surgery though, signalment (PRA and secondary cataracts common in Labs and Poodles) and history can help suggest this underlying disease in patients being evaluated for cataracts as owners (especially when probed) often report dim light visual deficits and even blindness before, THEN the ocular cloudiness/opacity (of the cataracts).

Anomalous/congenital

Congenital cataracts by definition are present at birth. They may be due to developmental “hiccup” or less often, inherited.

Vascular

Aberrant retention of (sometimes hyperplastic) ocular fetal vasculature (which may be inherited or a random developmental “hiccup”) that normally regresses before or soon after birth, may result in cataracts (usually congenital) if it contacts the lens. Examples include iris to lens persistent pupillary membranes (ppms) anteriorly and persistent hyaloid artery (potentially with blood or bleeding into the lens if there is an associated defect of the back of the lens (posterior lenticonus and or absent capsule/capsular coloboma))/persistent (hyperplastic) primary vitreous/persistent (hyperplastic) tunica vasculosa lentis (PHPV/PHTVL) posteriorly.

Infectious

Infection within the lens may occur via septic implantation during penetrating trauma. This may result in cataract formation and progression even years after the inciting incident. The most common example of this scenario is after penetrating cat scratch/claw trauma/injury.

In rabbits, *Encephalitozoon cuniculi* (usually through intrauterine transplacental vertical transmission though spore ingestion or even inhalation is possible) or *Pasteurella* may infect the lens and or iris forming an abscess/granuloma and associated cataract, as well as uveitis. *E. cuniculi* lens abscessation and cataract has also been described in cats (rare).

Iatrogenic/post-operative

After cataract surgery, some degree of post operative faint hazy to even dense white opacification of the retained lens capsular bag, left in place to hold an intraocular lens implant if placed and or serve as a barrier to vitreal prolapse, is expected. This is called (posterior) capsular opacification (PCO) or capsular after “cataract” or capsular fibrosis and occurs due to migration and abnormal proliferation of residual viable lens epithelial cells that are not completely removed or killed at surgery.

Cataract size classification scheme

Punctate

With the advantage of slit lamp biomicroscope evaluations, this is first category, which is as it sounds, a pinhead sized opacity.

Incipient

These cataracts involve less than 10% of the lens volume and typically don't affect vision. They can easily be missed on exam, especially when posterior, if diffuse retroillumination to back-light them with the tapetal reflex is not employed. Additionally, due to their small size and varying with location, they may be best visualized after pharmacologic mydriasis or dilation of the pupil (with tropicamide).

Incomplete (immature)

These opacities involve greater than 10% of the lens volume but not the entire lens. As this is obviously a broad category, it is sometimes further subdivided into early and late incomplete cataracts. These lesions variably affect vision, depending on their size and location within the lens.

Complete (mature)

These cataracts, as their name implies, involve the entire lens and are almost always associated with visual impairment (though slightly variable due to variable density of the opacity and "coping" function/ability of the patient).

Resorbing (hypermature)

These cataracts are starting to liquefy; sort of the body's way of doing its own cataract surgery. Cataract resorption often occurs with chronicity but also in very rapid-onset and progressive cataracts, for example in inherited, juvenile cataracts of Cocker Spaniels and several other breeds. Hallmarks of resorbing cataracts include a sparkly appearance, wrinkling of the anterior lens capsule, a deep anterior chamber and sometimes discernable (on exam itself and definitely with ocular ultrasound) decreased lens thickness. As lens resorption and leakage of lens proteins out of / through the lens capsule and into the eye often causes phacolytic lens-induced uveitis, other signs to look for are those associated with intraocular inflammation, including anterior chamber flare +/- relative miosis, red eye, low intraocular pressure, posterior synechiae and a velvety smooth and/or hyperpigmented iris. An uncommon specific type of resorbing cataract is a Morgagnian cataract, which occurs when the lens cortex is so markedly resorbed away that the residual nucleus sinks inferiorly within the lens capsule.

Intumescent

In these cataracts, the lens fibers and thus the lens itself becomes markedly swollen and stretching the lens capsule. This results in shallowing of the anterior chamber and sometimes secondary pressure elevation or even overt glaucoma. It can also result in rupture (bursting) of the lens capsule (usually posteriorly where it is thinnest or near the equator) and then phacoclastic uveitis. This type of cataract is most commonly associated with diabetes (rapid onset osmotic cataract) or other rapidly progressive cataracts.

Cataract location classification scheme

Recall the lens anatomy. An incomplete or smaller cataract can occupy a specific/focal region(s) within the lens and can thus be classified based on this location as below. During clinical examination, the location of lens opacities is most readily and best determined using a slit beam to create an optic cross section or slice through the eye and lens, highlighting the anterior and posterior lens capsule with bright, convex and concave respectively, lines of light, and then assessing relative depth and position of lesions.

Capsular

Capsular cataracts may affect the anterior or posterior lens capsule or shell. They rarely progress. Typical causes include uveitis, congenital / developmental abnormalities (especially incomplete regression of the embryologic vascular supply to the lens) and genetic.

Subcapsular

Cataracts just under the capsule may be anterior or posterior.

Cortical

Cortical cataracts may affect the anterior or posterior cortex. Anterior cortical cataracts are more likely to progress than posterior cortical ones.

Equatorial cortical cataracts involve the equator or periphery of the lens and are often missed or difficult to see without retroillumination and ideally, for more thorough evaluation / assessment, pharmacologic mydriasis or pupil dilation. Cataracts in this location often progress (unless senile) because this is the most metabolically active region of the lens.

Nuclear

Nuclear cataracts form in utero and are thus usually congenital. They may be inherited or associated with developmental accidents or “hiccup”. Fortunately they rarely progress and in fact, relatively-speaking, often become smaller with age as the nucleus is compressed centrally within the lens.

Cataract age of onset classification

Congenital

By definition, congenital cataracts are present at birth. They may or may not be inherited.

Juvenile

Juvenile cataract develops after birth and varying with breed, up to about six years of age. They are very commonly inherited in cause.

Senile

As the name implies, senile cataracts occur after about 6-10 years of age. Age-related cataracts are very common and one study documented some degree of cataract formation in all dogs greater than 13.5 years of age (Williams, DL; Heath, MF; Wallis, C. Vet. Ophthalmol. 2004; 7(1): 29-35). Fortunately these usually do not significantly affect vision nor progress.

***Nuclear sclerosis** is a normal age-related opacification of the lens nucleus associated with increased density due to lens fiber growth around it throughout life (without increase in lens size/volume) and resultant compression centrally. In dogs and cats it begins around age 6 years – though not really generally visibly so until 8-10 years. In humans it begins about age 40 years and results in decreased accommodative ability and presbyopia. Nuclear sclerosis should be differentiated from a true cataract opacity and can be as the former generally does not affect vision (whereas a complete or near complete cataract in the same central location likely would); and with nuclear sclerosis the tapetal reflex is still present and the fundus/retina can be visualized (not be the case with a complete or near complete cataract). Finally, differentiating nuclear sclerosis from cataract is often easier with pupil dilation allowing visualization of the clear(-er) cortical halo around the dense central nucleus.

Cataract therapeutic interventions

Once cataracts are identified and ideally classified, treatment options come into play. In terms of medical management, there have been some highly publicized/advertised/marketed topical therapies that are touted to “melt away” cataracts. The old adage that says if it sounds too good to be true it probably is applies here. These eye drops are generally anti-oxidants, specifically N-acetyl carnosine and other ocular health vitamin supplement agents marketed under several names. They may in fact reduce oxidative damage to the lens and in a controversial study (as lens changes were very subtle and difficult to measure objectively with photographs as lighting and angle of exposure alter the results significantly and are nearly impossible to keep totally consistent, and the principle investigator refutes the findings stating his words have been manipulated by the pharmaceutical companies) did decrease lens opacity in cases of nuclear sclerosis and incomplete cataracts (Williams, DL; Munday, P. *Vet. Ophthalmol.* 2006; 9(5) 311-316. However, they do not eliminate or slow further progression of significant cataracts that we see in dogs that actually warrant treatment due to their visual impact (late incomplete and complete), probably due to the relatively large size of the canine lens and the high density of cataract opacities in this species. The bottom line is that these may be “useful” for cases where treatment is not really indicated as there is no visual impairment or other complication, but not for those already visually impaired. Furthermore, these medications are generally expensive, and can provide a false sense of security to clients as they think they’re managing things with the drops and thus seek veterinary evaluation and attention later in the disease course when secondary changes like lens induced uveitis, resorption, lens luxation, retinal detachment and/or secondary glaucoma, etc. may have already occurred with chronicity, and now preempt successful intervention.

Ocu-GLO Rx™ is a maybe more worthwhile oral nutraceutical containing a combination of 12 safe (and effective in generally supporting and protecting ocular health and normal function, boosting overall immune health, and scavenging destructive free radicals) antioxidant ingredients and formulated specifically for dogs. Considered a vision supplement, it is probably most useful in potentially delaying progression of retinal disease (progressive retinal atrophy (PRA) and other degenerative diseases, maybe sudden acquired retinal degeneration syndrome (SARDS) and immune-mediated retinopathies, etc) and cataracts that are secondary to such retinal disease (toxic cataracts) or prior to formation/early diabetic cataracts. It will not reduce existing opacities but depending on cause, might delay progression of such, and has possible

utility in decreasing post-cataract surgery capsular scarring/fibrosis opacification. Finally, Ocu-GLO Rx™ may also benefit (and it is certainly unlikely to harm though it is expensive) other ocular disease conditions such as uveitis, glaucoma, and Golden Retriever uveitis.

A more promising potential medical therapy for diabetic cataracts is the use of aldose reductase inhibitors. This has been shown to be effective in delaying the onset and severity of cataracts in galactosemic (essentially an experimentally induced diabetic state) (Sato, S; Mori, K; Wyman, M; et. al.. Exp Eye Research 1998; 66(2) 217-222) and more recently diabetic dogs, and may ultimately also even be effective in treating these cataracts once they occur. Unfortunately these drugs (topical and systemic) are not commercially available for use at this time.

Cataract surgery

Considering these issues with medical treatment options, at this time, surgery is the only proven and reliable, effective way to restore vision lost due to cataracts. Surgery employs phacoemulsification or ultrasound energy to break up the opaque lens and it is irrigated and aspirated out of the capsule. The success rate in good/ideal candidate canine patients is 90-95%.

The ideal candidate for cataract surgery is:

- systemically healthy or at least managed/regulated/stable,
- a manageable patient - intensive post-operative medical therapy and follow-up are vital to success and the patient, client/owner and veterinary ophthalmologist must be able to tolerate and handle this!
- has vision affected by cataract/is impaired or functionally blind at least in the affected eye(s), making the potential benefit/gain of surgery worth the cost/risks,
- has no or at least controlled lens induced uveitis - previous or refractory intraocular inflammation poses an increased risk of post-operative complication(s), especially retinal detachment and glaucoma)
- does not have lens resorption – if present, this significantly increases the risk of pre-existing or post-operative retinal detachment
- has normal pre-operative electroretinogram (ERG) and ocular ultrasound (normal lens shape and no capsule disruption, non-degenerate vitreous (as when present slightly increases the risk of retinal detachment), no pre-existing retinal detachment, no residual embryologic vascular supply)

Risk factors for cataract surgery sort of naturally follow from the above list of qualities/factors of an ideal candidate. Specifically though, risk factors include lens induced uveitis (LIU) and lens resorption as above; breed predisposition to retinal detachment (in Bichon Frises and some other breeds as well as patients with significant vitreal degeneration); breed predisposition to glaucoma (Cocker Spaniels and many other breeds predisposed to primary glaucoma (and thus also secondary) with/by goniodysgenesis (an abnormal (narrowed) drainage angle)); and being a Boston Terrier – multiple studies have shown that the single biggest risk factor for serious (potentially devastating with ultimate blindness and loss of the eye/need for removal due to pain) post-operative complications (corneal ulceration, inflammation, retinal detachment, GLAUCOMA) is being a Boston Terrier!

Several of the potential complications of surgery are eluded to above but most importantly, as they are vision threatening and in the latter case, painful, include retinal

detachment and glaucoma. At surgery, inability to place an intraocular lens implant may occur, though even in this case, vision should still be improved, though far-sighted or hyperopic, like our vision underwater. Other possible issues include infection (potentially devastating endophthalmitis as the eye does not tolerate/handle infection and the associated secondary inflammation well); corneal ulceration, chronic and refractory inflammation/uveitis, posterior synechiae which may be cosmetic, increase the risk of secondary glaucoma or rarely be visually significant; and especially in young dogs, lens fiber regrowth often inciting lens induced uveitis and possibly though rarely affecting vision again – sometimes warranting surgery to alleviate the stimulus of inflammation and any visually significant opacity (remove regrowth).

Also as mentioned above when discussing the ideal candidate for cataract surgery, indicated/appropriate pre-operative testing includes electroretinogram (measuring/assessing hopefully normal/adequate retinal function) and ocular ultrasound (hopefully ruling out pre-existing retinal detachment, etc. as above). These tests are warranted as for good surgical candidates likely complete or nearly so cataracts preclude retinal examination and these tests allow the best possible evaluation and assessment to determine that the retina “checks out” okay. If it does not, it probably doesn’t make sense to remove the cataract through somewhat invasive, expensive surgery – this is sort of like the situation if there is no film/data card in the camera, there’s no point in removing the lens cover.

Other cataract pre-operative testing indicated includes screening lab work to assess for underlying systemic disease that may have caused the cataracts in the first place but more importantly for safe candidacy for general anesthesia and aggressive peri- and post-operative anti-inflammatory medical therapy needed with this procedure. In diabetic patients for the same reasons, glucose regulation should be good and stable (clinical signs controlled, blood glucose curves with nadirs not lower than 80mg/dl and peaks less than 350mg/dl; fructosamine < 450-500). It is expected that they will suffer some dysregulation with the stress of anesthesia and surgery, and frequently with necessary aggressive peri-operative anti-inflammatory therapy, etc., so it is ideal if everyone is comfortable and on-board with where they were and stay the course without reactionary insulin dose changes in the “rough” period shortly afterwards. Additionally in diabetic patients a urine culture, even if not indicated by the sediment findings of the urinalysis, should be performed pre-operatively as these dogs are prone to silent urinary tract infections and any bacteria in the body can seed the eye particularly when peri-operative uveitis breaks down the blood aqueous barrier. Bacterial infection within the eye can result in devastating endophthalmitis, frequently with vision and ultimately eye loss (enucleation). For this same reason, the skin (and ears) should be assessed, especially in allergic or otherwise predisposed patients, for signs of pyoderma (and otitis). In the case of UTI or pyoderma, appropriate antibiotic therapy should be initiated and continued through a negative culture and possibly the post-operative period to reduce risk of infection especially with intraocular lens implant (nidus potential). Finally, another pre-operative requirement or at least strong recommendation is good/reasonable periodontal health, again due to the risk of bacteremia with periodontal disease readily seeding the eye at surgery. Thus if/as indicated by oral/dental disease, a dental cleaning should be performed at least two weeks prior to cataract surgery, with peri-procedural antibiotics as indicated and also just time for expected bacteremia to clear. Though this all may seem excessive, remember that cataract surgery is an elective procedure

with significant risk. Having all of the “ducks in a row” in an ideal candidate can maximize success.

Surgery is performed with phacoemulsification under an operating microscope. An incision is made superiorly in the cornea paralleling the limbus. A capsulorrhexis (hole in the anterior lens capsule) is then made to access the lens contents. The phaco. needle delivers ultrasound energy to fragment the hard nucleus of the lens while continuous irrigation and aspiration flushes and vacuums it out. The remaining lens cortex is then aspirated out of the hopefully still intact (it is very thin and easy to rupture or tear during the procedure) lens capsular bag. An intraocular lens is then inserted into the capsular bag. These are generally foldable acrylic lenses of varying diameter sizes as indicated for the patient, and in dogs usually with dioptric power of 41 to restore normal/emmetropic vision (through bending of light rays through/by the lens into focus on the retina) in the majority of patients. They are injected with special cartridges and instruments. Previously and sometimes still currently on occasion, a rigid polymethylmethacrylate lens is used – this requires a larger corneal incision and generally longer surgical time. Regardless, the corneal incision is then closed and the road to recovery begins. The postoperative therapy is as important as what happens in the operating room / at surgery – it is absolutely vital to the success of the procedure and entails initially somewhat intense topical and systemic anti-inflammatory medications (ultimately slowly tapered as indicated) and close/frequent monitoring with serial rechecks at increasing intervals. Because the inflammatory response incited by dogs to exposure to their own lens proteins (with any pre-operative lens induced uveitis and then at and after surgery itself) and the ultrasound energy requirement (high and long) to break up the relatively large and dense canine lens (about 8 times the size of a human lens and usually operated relatively later in the game when the lens is harder...) result in significant inflammation, afterwards weeks to months and even years are spent combating / hopefully controlling it and many canine post-cataract surgery patients remain on some level of topical therapy and monitoring long term to forever.

What if cataract surgery is not an option? It may not be elected or the patient may not be a candidate, etc.. In these cases, it is still indicated to monitor and treat any lens induced uveitis (with topical anti-inflammatory medication) to avoid or at least decrease the risk of discomfort and secondary glaucoma or other complications. Occasionally, if lens resorption occurs and is advanced, without in the process inciting significant inflammation and causing retinal detachment or secondary glaucoma, it may result in enough clearing of the lens and visual axis that some vision (albeit far sighted/de-focused) may be restored/gained.

In terms of visual impairment, if only one eye is affected, most veterinary patients function essentially normally, though longer-nosed and highly visually reliant working dogs may demonstrate some/more deficits on the affected side and astute owners may notice this. If patients are bilaterally affected and visually impaired to even completely functionally blind, fortunately the vast majority of dogs adapt amazingly well and have good quality of life, especially when their vision loss is gradual (with slow onset or progressing cataracts) or given time to adjust even when it is rapid. They will frequently memorize their environments and some owners don't even recognize how impaired they are. However, with things out of place or novel environments, not surprisingly they may have more trouble, so ideally their environments should be kept as stable as possible to help them adjust and cope. This and other useful tips are

available through many great resources for owners of visually impaired pets, in book and online forms.

GET TO KNOW THE NICTITATING MEMBRANE

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Conjunctiva review

Reminder that the conjunctiva (conj) is the light pink (vascularized with thin vessels) tissue/mucosa that lines the eyelids and eyeball and allows smooth movement of the eyelids and globe. It has lymphoid tissue/immune function, frequently pigment (melanocytes/melanin), and connective tissue. It is not sterile (surface microbial flora – mostly gram + bacteria).

Palpebral conjunctiva lines the inside of the eyelids, reflects back at the fornix and then somewhat loosely lines the front of the globe (up to the limbus) as the bulbar conjunctiva. Palpebral conjunctiva of the third eyelid lines its outer/anterior side and bulbar conjunctiva of the third eyelid lines its inner side.

Nictitating membrane

Nictare = to blink in Latin.

The nictitating membrane/membrana nictitans, nictitans, TEL, haw, palpebra tertia, or plica semilunaris, as its name implies, is an eyelid structure. It lies between the inferior eyelid and the cornea in the nasal/medial inferior conjunctival fornix. It is variably pigmented with the margin (or leading or free edge) and a portion of the palpebral or anterior face (aspect/side) commonly pigmented. This variation, particularly when asymmetric can give rise to concerns of pathology (may create optical illusion of abnormal position, etc. or make an eye seem “red”).

Poorly defined attachments secure the base of the NM to the periorbita surrounding the inferior rectus and inferior oblique extraocular muscles. Musculature of the NM is largely vestigial in domestic species and movement is generally passive (except in cats where there is some muscular contribution to active protrusion) across the eye with retraction / retropulsion of the globe (in the former case by the retractor bulbi m innervated by the abducens n (CN VI)) – some animals with eyelid or exposure related conditions may “learn” to blink with the NM in this manner.

Movement (except in birds) is from inferior nasal/medial where the NM originates, to superior temporal/lateral.

Normal NM position is determined by a combination of orbital, eyelid and globe conformation and sympathetic tone of orbital and periocular smooth muscles, which govern globe position within the orbit and thus the NM’s passive movement associated with that position.

Again, lined on both sides by conjunctiva that allows its smooth movement.

Like “regular eyelids” it serves to provide physical protection to the globe/ocular surface/cornea. It also has important functions in contribution to tear production as well as distribution and drainage of the tears / tear film across the ocular surface through blinking. Finally it serves an

immune function through the presence of lymphoid tissue (CALT), specifically numerous superficial lymphoid follicles on its bulbar surface.

The conjunctival bi-lined (tightly adherent at the free margin, loose deeper and over the gland) nictitating membrane gains structure / support / rigidity from its internal T cartilage with a vertical portion extending perpendicularly from near its margin/free edge towards the inferior medial canthus/orbit where its base is encircled by the gland, and its horizontal portion extending near (about 1.5mm away) and along its margin or the leading edge.

The gland of the NM is located at the (orbital) base of the third eyelid on its bulbar or back side, again, at the base of the vertical T cartilage – hence, like the cartilage, it is not visible in the normal state. The gland is seromucoid and in the dog, has adrenergic and (denser) cholinergic innervation. In the pig and many rodents, a portion of the gland or a separate Harderian gland is found deeper within the orbit.

Tear film

Recall tear film is trilaminar with outer fatty / oily layer, middle aqueous portion (with up to 50% produced by the GNM), then mucin layer. There is a basal tear production and then an additional reflex component in response to stimuli. Tear film disease may have roots in NM disease.

Nictitating membrane examination

Look at it! Appearance, position, movement. Palpebral and bulbar aspects.

Diagnostics: cytology, culture and sensitivity, biopsy, response to therapy, work up of underlying issue

Nictitating membrane disease conditions

Abnormal position/movement – Horner syndrome, orbital disease, enophthalmos of other cause, tetanus, dysautonomia, Haws syndrome, physical restriction,

Inflammation, follicles – episcleritis (nodular granulomatous episcleritis), follicular conjunctivitis, pannus (“atypical”)

Follicular conjunctivitis: young, usually large breed dogs; response to environmental exposure; possible precursor to overt allergic conjunctivitis; bulbar conjunctival follicles with variable irritation; treatment = topical steroid +/- anti-histamine; rinsing

Glandular disorders including prolapsed gland of the NM and post-operative complications; keratoconjunctivitis sicca

Prolapsed gland of the nictitating membrane (PGNM): Inherited (or post-inflammatory) weakness of connective tissue attachment anchoring GNM; treatment = surgical repositioning / replacement; risks = keratoconjunctivitis sicca, cyst formation, failure/recurrence

Cartilage anomaly/eversion

Young large breed dogs; chronic exposure conjunctivitis and associated redness & discharge, but mainly cosmetic; may predispose to, cause or be associated with PGNM;

treatment = benign neglect, medical management (lubricant, steroid), manual correction, third eyelid flap, excision of bent cartilage portion, thermal cautery to straighten

Tumor/mass – inflammatory (immune-mediated), infectious (esp. parasitic), neoplastic

Neoplasia – adenoma / adenocarcinoma of GNM most common primary tumor but many possible – lymphoma, mast cell tumor, melanoma (AGGRESSIVE here), squamous cell carcinoma, hemangioma/hemangiosarcoma (USUALLY more benignly behaving)

Trauma – laceration, other damage; foreign body – look!!

Excision – with risk of iatrogenic keratoconjunctivitis (sicca)

EXCERPTED FROM

Drs. Katie Diehl and Kate Myrna present:

OPHTHALMOLOGY SURGERY WET LAB

UGA College of Veterinary Medicine Continuing Education

Athens, GA

August 7, 2016

INTRODUCTION

Ophthalmic surgery instruments/supplies

Small, sharp and precise! Designed to be handled with the fingertips under adequate lighting and often with magnification.

Essential instruments include:

Barraquer wire eyelid speculum (small or pediatric)

Tissue forceps

-Delicate Adson or other rat tooth 1 x 2 forceps

-Bishop-Harmon forceps (1 x 2 0.5mm teeth for eyelids; 1 x 2 0.3mm teeth
(delicate) for eyelids and conjunctiva)

-(0.3mm Colibri-style forceps for conjunctiva)

Scalpels and blades

-#3 Bard-Parker scalpel handle with #15 blade for eyelids

-(Beaver handle/chuck with #6400 or #6500 blade for conjunctiva)

Scissors

-Stevens tenotomy scissors (curved or straight)

-Westcott tenotomy scissors (spring action handles) for conjunctiva and fine

suture

Needle holders

- Derf needle holders / drivers for 5-0 to 4-0 suture material/needles
- Microsurgical needle holders (fingertip-controlled, spring action handles; curved or straight, locking or non-locking) for 6-0 and smaller suture material/needles

Additional useful instruments and supplies include:

Clear plastic, adhesive drapes (Steri-Drape™), Schaedel cross action towel clamps, tongue depressors or Jaeger lid plate, Jameson caliper or STT strips, cotton tipped applicators, cellulose sponge spears (Weck-Cel® sponges), 2x2 or 3x3 gauze sponges, irrigation cannulas, Jameson muscle hook, Gelfoam®, small Metzenbaum scissors, small Mayo scissors, Mosquito and Kelly hemostats, sterile tubing for stents, IV catheters

Surgeon's stool, adequate lighting – options via Universal Surgical Instruments

Ocular surface lubricants: Celluvisc/hyaluronic acid, Genteal gel, Puralube

Small clippers

Magnification – OptiVisor, surgical loupes

Instrument Care

Ophthalmic instruments are easily damaged and quickly worthless unless properly handled.

Storage: Store in a separate pack (various specialized trays are available) where instruments cannot rub against each other or individually wrap and sterilize them.

Cleaning: After use, rinse with distilled water and gently brush to remove blood and tissue. Subsequent ultrasonic cleaning with mild detergent, distilled water rinsing and air drying is best. Inadequate cleaning results in rust, which can be removed by soaking affected instruments for 12hrs in equal parts ethyl alcohol and aqueous ammonia.

Sterilization: Gas sterilization is best. Small sections of silicone tubing may be placed over instrument tips to reduce risk of damage during packing and sterilization. Steam autoclaving may be used but may dull instruments and cause corrosion. Cold sterilization is not recommended.

MOST DULLING AND CORROSION of instruments IS DUE TO IMPROPER CLEANING AND HANDLING.

Ophthalmic Suture

Suture **needles**: Ophthalmic microsurgical needles have "spatula" tips to allow suture to pass in the same layer (lamellae) of the tissue without cutting deeper or shallower. The higher the number assigned to a needle the smaller its radius of curvature. Handle (some 5-0 and all) 6-0 and smaller suture material/needles with microsurgical needle holders as Derf needle holders will bend the needles.

Suture **material**:

Absorbable for subcutaneous, conjunctival and episcleral tissues

Polyglactin 910 (vicryl) – generally braided except very small sizes; good tensile strength for ~20 days; fairly reactive

Poliglecaprone 25 (Monocryl) - monofilament

Polydioxanone (PDS II) - monofilament

Nonabsorbable for skin

Monofilament nylon – chronically strong and inert

Braided nylon – strong and inert with softer tags; requires additional throws to hold knot; wicking potential in between monofilament nylon and silk

Silk – braided with potential wicking (uncommon issue if sutures removed in timely manner (~10 days))

Ophthalmic surgery patient considerations

Anesthesia

-For extraocular procedures, sedation/anesthesia is much the same as for other surgeries.

-In sedated/anesthetized animals, **exposure-related corneal damage** risk is increased due to altered palpebral reflexes with frequent lagophthalmia and decreased tear production. Un-operated eyes should be generously lubricated with an artificial tear

ointment. Operated eyes (unless being enucleated) should also be lubricated with artificial tear solutions/gels or irrigating saline.

-**Monitoring** anesthetic depth is often more difficult in ophthalmic surgery because of the presence of draping over the animal's head. Pulse, pulse quality, respiratory rate, blood pressure and ECG should be observed.

-Traction on extraocular muscles and the optic nerve or pressure on the globe may incite the **oculocardiac reflex**, with resultant bradycardia or even cardiac arrest. Both the anesthetist and surgeon should be aware of this potential, avoid it if possible and quickly correct it if encountered, by promptly releasing the globe and when resuming intervention, proceeding more gently.

Patient and surgical field preparation: Differ slightly with procedure, but in general:

-Elevate the down eye off the table (with a rolled towel under the neck or otherwise) to prevent it from trauma and/or contacting a pool of betadine that has run off from preparation of the eye to be operated.

-**Trim the eyelashes** near flush with the eyelid margin with small scissors lightly coated with K-Y jelly or artificial tear ointment along the blade away from the cornea to catch cut lashes and reduce risk of them contacting the ocular surface/being retained there.

-When applicable (eyelid procedures, enucleation, etc.), carefully **clip** an appropriately sized border around the margins of the eyelids using a #40 blade on an electric clipper or other small electric clipper. Gently blot the area with tape to pick up remaining loose hairs.

-Either **lubricate** the ocular surface before clipping to protect it from stray hairs OR do so AFTER cleaning/rinsing the conjunctiva (including fornices) post clipping to reduce risk of loose hairs actually getting caught up in the lubricated ocular surface.

-To avoid excessive lid and conjunctival edema, BE GENTLE. All antiseptic preparations are toxic to intraocular structures, and should not be used to flush the conjunctival sac if the corneal/scleral shell has been breached or intraocular surgery is anticipated.

-Conjunctival sac prep: Rinse and wipe with dilute (half-strength aqueous / "weak tea") povidone-iodine solution (NEVER SCRUB) with flushes of sterile saline. Sterile cotton tipped applicators should be used to apply and wipe the povidone-iodine, taking care not to touch the cornea. The fornix should be swabbed first working out toward the eyelid margins. Rinse immediately with saline and repeat the cycle for a total of three times.

-Periocular skin prep: Prepare with gentle alternate applications of dilute (half-strength aqueous / "weak tea") povidone iodine solution (NEVER SCRUB and NEVER chlorhexidine which may cause a severe toxic keratitis) and sterile saline. Work from the eyelid margins outward. Repeat the cycle for a total of three times.

Patient and Surgeon Positioning:

-Patient: Depending on the surgery to be performed, the animal is placed in dorsal or lateral (or ventral for some eyelid and third eyelid procedures) recumbency with the **head close to the head of the table** and rotated such that the **palpebral fissure of the operated eye is parallel to the table/floor**. This position allows improved ease of focus especially if magnification is used for surgery. Vacuum (Vac-packs), sandbags, or other moldable beanbags or other padding or supports, as well as adhesive tape, to maintain this head position are particularly helpful for ophthalmic procedures, again especially those requiring magnification. **Be careful to avoid excessive kinking of the neck with impact on patient ventilation / CO2 level.**

-Surgeon: The surgeon usually **sits** at the head of the table, **resting his or her forearms for stabilization**. Care must be taken to not put pressure on the patient or anesthetic equipment.

Postoperative Care:

-Trauma to the surgical site should be avoided and this is accomplished by ensuring a smooth anesthetic recovery and placement of an Elizabethan collar as needed.

-Discomfort should be managed with appropriate anti-inflammatory and/or opioid medications.

-Indicated medical therapy, monitoring and follow-up should be pursued as indicated.

THIRD EYELID FLAP

Indications: Uncommonly performed to encourage/expedite healing of non-healing corneal ulcers when bandage contact lenses are not retained, tolerated or effective. **Or to “un-train” everted third eyelid cartilage anomalies.**

Presurgical considerations:

-A third eyelid flap is **contraindicated for corneal ulceration complicated by infection, malacia, and/or stromal loss (including perforation)**

-A third eyelid flap does NOT provide blood supply nor structural support to the cornea

-Complete corneal coverage by the third eyelid may not be physically possible in breeds/dogs with conformational/physiologic exophthalmos (e.g., Pugs) and an alternative option should be considered and pursued as indicated

-Topical therapy will be significantly impaired by the blockage of the third eyelid tissue over the ocular surface.

-Visualization of the ocular surface for disease monitoring will not be possible with the third eyelid flap in place.

-Third eyelid flap placement may apply **undesirable rubbing forces and pressure on the cornea/ globe.**

-Ensure proper indication, client understanding and, that there are no foreign bodies, aberrant cilia or even excessive irregular follicles (which may cause irritation to the ocular surface and cause, perpetuate or otherwise exacerbate corneal ulceration) under the eyelids or especially under the third eyelid.

Technique:

-General anesthesia (usually); or sedation and/or regional blocks is needed.

-Surgical preparation includes carefully clipping and prepping (with povidone-iodine as above) a small area of skin over the superior orbital rim. The eyelashes are also clipped and the ocular surface cleaned as above.

-Using **2-0 to 4-0 (based on patient size) non-absorbable suture**, (if a stent/stents are to be used, first pass the suture through one at this time) **enter the deep superior lateral**

conjunctival fornix via a bite through the overlying prepared skin. Take care to exit cleanly and avoid damage to the globe

-With awareness and caution regarding suture from the fornix laying across the ocular surface, **elevate the third eyelid and take a bite paralleling its leading margin from lateral to medial and incorporating/around the vertical T cartilage near its junction with the horizontal T cartilage. Ensure that this bite is not full thickness/**does not breach the bulbar aspect of the third eyelid.

-The final bite is back out the deep superior conjunctival fornix medial to the initial entry about equidistant to the length of the third eyelid bite (so that the suture bites form a rectangle) to the skin.

-The suture is tightened, elevating the third eyelid margin deep into the superior lateral conjunctival fornix, pulling the third eyelid over the ocular surface, and tied with or without stent placement.

-Leave suture tags long if attempted untying and replacement without a second procedure is anticipated/desired.

Possible complications and further considerations:

-An e-collar should be used as needed to prevent self-traumatic exacerbation of disease.

-Appropriate medical management of the ulcer (topical antibiotic, oral NSAID/opioid, e-collar, etc.) should be continued until it is healed though again, topical therapy effectiveness will be significantly reduced with the third eyelid flap in place.

-Recheck in 10-14 days (or sooner if the patient seems worse after 24-48h though this may be hard for the client and veterinarian to assess). Sometimes, it is possible to untie the knot securing the third eyelid flap and temporarily reduce it to examine and evaluate the ocular surface and globe conditions, then replace the flap as indicated – this may require sedation. Regardless, repeat or other interventions to promote healing until the ulcer heals are indicated.

-There is risk of suture rub or “cheese-wire” irritation/ulceration during third eyelid flap placement, or if such is positioned wrong (not deep enough in the fornix or full thickness through the third eyelid) or loosens post-operatively.

-The corneal ulcer or other ocular surface condition as well as intraocular disease may worsen under the flap, especially if exacerbated by pressure applied to the globe (e.g., a deep corneal ulcer may perforate).

-The patient will be at least temporarily blinded by the third eyelid flap, and this can be a significant concern/issue in patients with bilateral disease or only one eye.

- The eyelid skin may develop pressure necrosis if the sutures are placed too tightly
- The suture may pull through, releasing the flap but also harboring retained suture that may irritate the ocular surface.

PROLAPSED GNM REPLACEMENT

Indications: Replacement/repositioning of prolapsed gland of the third eyelid ("cherry eye") to reduce risk of development of dry eye and exposure conjunctivitis, and for cosmesis.

Presurgical considerations:

- Replace, **do NOT remove these glands!!** Removal carries a significantly increased risk of development of **dry eye (KCS)**. Even with replacement, animals are at a slightly increased risk of development of dry eye.
- There are several options for replacement with two basic categories: pocket imbrication and tacking (most commonly to the orbital rim)
- The condition is common in young dogs (under 2 years of age) and certain breeds, especially brachycephalics. Beware the "cherry eye" in older patients and especially atypical breeds as these may be associated with other issues including third eyelid neoplasia or chronic inflammation.
- In predisposed breeds, the condition is commonly bilateral – if only one eye is affected at the time of the surgery, the client should be warned that the other eye could be affected and warrant surgery in short order. It is reasonable to wait for this potential for a short period of time so that bilateral surgery may be performed under the same anesthesia if indicated.
- Chronic prolapse has a poorer the prognosis for successful repositioning and avoidance of dry eye.

Technique:

Pocket imbrication: Creates a subconjunctival pocket to house the gland. Does not impact third eyelid mobility/function. **Magnification necessary.**

-**General anesthesia** is needed.

-Surgical preparation includes carefully clipping the eyelashes and povidone-iodine cleaning as above.

-Elevate and evert the third eyelid by grasping it medially and laterally near (not at) its margin on the palpebral side with mosquito hemostats (pinching just a bit of overlying conjunctiva). This will expose the prolapsed gland and its base on the bulbar surface of the third eyelid.

-Using a #15 blade, make an incision in the conjunctiva inferior to and along the base of the gland. Do not go full thickness through the third eyelid. Make a similar incision along the superior aspect of the gland (this will be near the back side of the leading edge of the third eyelid). **These incisions** form a sort-of "moat" **around the base of the gland** but they **SHOULD NOT MEET** at their ends.

-A subconjunctival **pocket is created** by blunt dissection via these incisions in both directions away from the gland (it is often difficult to dissect very far if at all superiorly due to the third eyelid leading edge, but only enough to take suture bites on that side of the incision is necessary).

-The **pocket is then closed, imbricating the gland** into it as follows:

To reduce risk of suture rub, knots are tied on the palpebral side of the third eyelid. Using **6-0 vicryl** take a bite of conjunctiva roughly over one end of the incision and tie a knot. Pass the suture through the third eyelid to the bulbar aspect exiting at the same end of the incision.

Appose the inferior and superior incisions* over the gland using a simple continuous/running pattern – initial sutures may be challenging due to the prolapsed gland being in the way but as bites are taken, the gland should "slurp" into the pocket and be out of the way, allowing completion of the closure.

***With the non-connected inferior and superior incisions, the ends of the wound should be slightly open or puckered (i.e., closure is not complete/sealed)** to allow egress of gland secretions and reduced risk of cyst formation.

With the incision now apposed, pass the needle back into the incision and through the third eyelid to the palpebral aspect overlying the same end of the incision (opposite end as the initial knot). Ensure appropriate tension and closure of the incision without "spanners" or undue puckering and take a bite of conjunctiva and tie the final knot.

Orbital rim tacking: Anchors the gland to the periosteum of the inferior orbital rim. This reduces third eyelid mobility/excursions and thus function. Magnification is not necessary.

-General anesthesia is needed.

-Surgical preparation includes carefully clipping the eyelashes +/- an area of skin over the orbital rim. The remainder of the preparation is as previously described above.

-Incise the skin (or conjunctiva accessed via the fornix) over the inferior nasal orbital rim with a #15 blade

-Using **2-0 non-absorbable suture (nylon, prolene)**, take a **bite of the periosteal rim** – this should be SOLID!

-Tunnel up into the third eyelid and around the edges of the prolapsed gland (in a purse string like pattern), ultimately **returning to the periosteal bite** region (+/- taking a second bite at this point), and **tie**.

-If a skin incision was made over the orbital rim, it should be closed routinely.

Possible complications and further considerations:

-An e-collar should be placed during recovery and healing (~ 10-14 days) to prevent self-trauma and associated complications with possible immediate re-prolapse of the gland or otherwise delayed or complicated healing.

-Prophylactic topical antibiotic TID x 10-14 days, and oral NSAID (unless contraindicated by patient issue) x 3-5 days are indicated

-**Complications** include: **suture rub** with irritation and possible corneal ulceration especially with the pocket imbrication and especially if the knots are not tied on the palpebral aspect of the third eyelid, infection, wound dehiscence, **cyst formation, dry eye**, and **failure with re-prolapse of the gland/recurrence**, as well as again, prolapse of the contralateral gland.

-**Monitor tear production** long term due to risk of dry eye

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