Systems Pathology: Eye and Ear

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Contents

About

These notes are a fairly comprehensive collection of information to complement the lectures and labs delivered in VETM2220, Systems Pathology II, on the topic of the pathology of the eye and ear. Although all of the information is useful, certain areas will have been emphasized in lecture, let the areas focused on in lectures and lab guide your studying. There are a few rare conditions that are not discussed in these notes, and you are encouraged to read through the relevant chapters in the textbooks recommended below.

Unfortunately, there are only three lectures assigned to this topic, barely enough time to begin scraping the surface of eye and ear pathology. Reviewing these notes will be critical, and they will hopefully help serve as a reference when you are in practice. Diseases of the eye and ear are **very** commonly encountered, especially in small animal practice. Developing a good understanding of the pathogenesis of the various ocular and aural conditions will serve you well as a practitioner for years to come.

The notes are available online at http://russfraser.ca/eye-ear/, as a PDF on Moodle, and as an Epub (E-book format, suitable for a tablet). Please feel free to provide feedback, whether on content, style, or typos!

Contact me

Please don't hesitate to get in touch if you have any questions.

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Reference material

- Zachary, J. F., & McGavin, M. D. (2016). Pathologic Basis of Veterinary Disease Expert Consult. Elsevier Health Sciences.
- Maxie, G. (2015). Jubb, Kennedy & Palmer's Pathology of Domestic Animals-E-Book (Vol. 1). Elsevier Health Sciences.

Acknowledgements

These lecture notes were prepared in R (R Core Team, 2019) using the bookdown (Xie, 2015), knitr (Xie, 2019), and Rmarkdown (Allaire et al., 2019) packages. Source material was taken from Zachary and McGavin (2016), Dubielzig et al. (2010), Grahn et al. (2019), and Maxie (2015). I gratefully acknoweldge the prior course notes from Dr. Pierre-Yves Daoust. Images are attributed throughout the text; unattributed images are either mine or were found in the public domain.

1 Introduction to pathology of the eye

The eye is a complex, unique structure, and a thorough description of the anatomy and physiology of the eye is far beyond the scope of these notes. An excellent summary is available in Chapter 21, p. 1269-1282 of the reference textbook (Zachary and McGavin), and I strongly encourage you to read it. A PDF copy of the chapter is available in Moodle. It will help provide a solid foundation that will allow you to *understand* the development of ocular disease, rather than simply memorizing the steps and lesions involved.

It is important to understand that the eye is a unique, highly organized structure, and that disruptions to the delicate structures of the globe can have **significant and severe consequences to the health of the eye and to vision**. Furthermore, the globe is a **closed system**, often sparing it from systemic insult, but also depriving it of quick and efficient resolution from damaging events like inflammation or hemorrhage. Recall that, like the brain and the testes, the eye has a form of immune privilege. There are relatively few resident leukocytes, leading to a relative delay in the onset of inflammation. Regeneration and repair is similarly limited in comparison to other tissues. Finally, unlike the liver or other tissues were parenchymal cells can divide and regenerate functional organ mass following injury, the **eye has very little regenerative potential**. Thus, **any damage** is of consequence to the eye.

Most of what we will deal with in this section is the pathogenesis and theory of disease. Where possible, we will look at the gross correlates, but many of the conditions are better appreciated with an ophthalmological exam, requiring specialized tools and techniques. Microscopic images will be used to help reinforce concepts and provide a visual correlate to the theory.

What follows in this chapter is a *minimal* review of the basics of ocular anatomy as it relates to pathology, to help refresh your memory after having read the textbook. I've also put together a general Glossary to help keep track of all the terms that are unique to ocular pathology and ophthalmology, and which seem to make up a language of their own.

1.1 Ocular anatomy

A schematic of the eye is show in Figure 1. The globe is surrounded by muscular tissue, eyelids, and a bony orbit. The globe itself is made up of three conceptual layers: the sclera, which is modified at its anterior end to become the cornea; the choroid, a portion of the vascular supply of the eye; and the retina, the light sensing interior layer. The choroid is continuous with the iris and ciliary body. The lens, a structure designed to refract light, is suspended by zonules originating from the ciliary body. These structures create several compartments within the eye: the anterior chamber, posterior chamber, and vitreous humour.

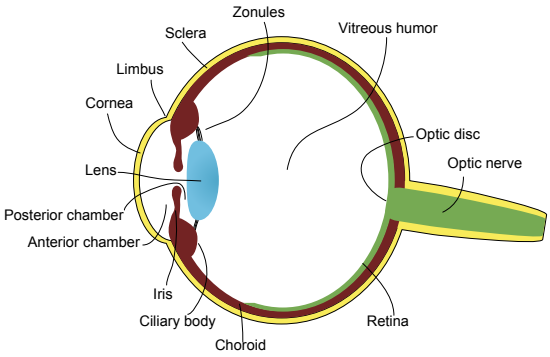

Figure 1: Cartoon of the globe illustrating many of the important anatomical structures. Note that the uvea is composed of the structures coloured red (the iris, ciliary body, and choroid).

Each of these structures is complex and reacts to injury and disease in somewhat different ways.

The eyelids are covered on one side by haired skin, which is histologically similar to skin found in other areas. The other side is covered by conjunctival epithelium, known as the palpebral conjunctiva. Tear film, composed of mucous and fluid, is present between the bulbar and palpebral conjunctiva, and is distributed through the action of blinking. The eyelid margin is where the anterior haired surface and posterior palpebral conjunctiva meet. Cilia, or eyelashes, are present at the eyelid margin, along with a row modified sebaceous glands called **meibomian or tarsal glands**.

The eyelids help protect the eye from physical injury and help remove irritating contaminants from the surface of the eye. The tear film also contains antibacterial peptides. The eyelids respond to injury in much the same way as skin elsewhere in the body responds to injury. Given their role in keeping the eye protected and moist, however, damage resulting in defective function or congenital malformations (for example, Entropion and ectropion) can have significant consequences to the eye.

The conjunctiva is a mucous membrane that extends from the eyelid margin, spreads across the inner surface of the eyelid, and along the scleral surface up until the cornea. It is composed of stratified squamous, non-keratinizing epithelium, with goblet cells scattered throughout the palpebral, but not bulbar, conjunctiva. It is vascularized and innervated.

The sclera forms the bulk of the outer portion of the globe, and is readily identified as the thick, white, fibrous portion of the eye. Continuous with the sclera is the cornea, the clear, slightly bulbous portion of the eye through which light enters. The junction of the cornea and sclera is termed the limbus.

The cornea is a highly specialized piece of tissue and is formed by a unique

arrangement of fibrous connective tissue that allows light to pass through. The cornea is composed of **four layers**: the corneal epithelium, the corneal stroma, Descemet's membrane, and the corneal endothelium. The corneal epithelium, which is stratified squamous, lacks both pigment and keratin, and is replaced frequently – approximately once every 5 - 7 days. The corneal stroma is composed of thin, compact collagen fibrils arranged in parallel and separated by a space that corresponds to the wavelength of light, all of which serve to minimize the scatter of light. Importantly, **the corneal stroma is maintained in a dehydrated state**, through passive and active means. Within the corneal endothelium are energy-dependent sodium-pumps that remove solutes from the corneal stroma, creating an osmotic gradient that allows fluid to exit the stroma. To prevent the entry of fluid, the corneal epi- and endothelium are both maintained by tight intra-cellular junctions. **Fluid within the corneal stroma is a common pathological finding in diseased eyes, and manifests as corneal cloudiness, often with a slight blue tinge**.

The cornea is **avascular**, and therefore must rely on passive diffusion of nutrients and oxygen from conjunctival and scleral blood vessels, as well as from the tear film and aqueous humour. **The presence of blood vessels within the cornea is a sign of pathology, either past or present**.

The uvea is composed of three strucutres: the iris and ciliary body, which form the anterior uvea, and the choroid. **The uvea is the vascular supply to the eye**. The iris is composed of an innervated fibrovascular stroma with varying numbers of melanocytes. Two smooth muscles course through the iris, allowing it to change size and moderate the amount of light passing through the lens and onto the retina. The ciliary body is a small structure that extends from the posterior aspect of the base of the iris to the choroid. An important role of the ciliary body is the production of aqueous humour. It also serves to anchor the lens in place. The choroid supplies nutrients and oxygen to the posterior segment of the eye, most notably to the retina.

The lens refracts light to provide focus, and can change shape depending on the tension applied to the suspending zonules. A more detailed description is found in the section on the Pathology of the lens.

Finally, the retina is the nervous component of the eye, converting light to nervous impulse. The retina is a complex anatomical and physiological structure, and is discussed in more detail in the section on the Pathology of the retina.

1.2 Submitting a globe for histopathology

During the course of your clinical career, you will undoubetdly perform several enucleations, and hopefully you will submit the samples to your local pathologist. Putting the globe directly in formalin will usually provide adequtae results, however, it takes awhile for formalin to perfuse into the eye and fix the retina, leading to the introduction of possible artifact. To avoid this, inject a small

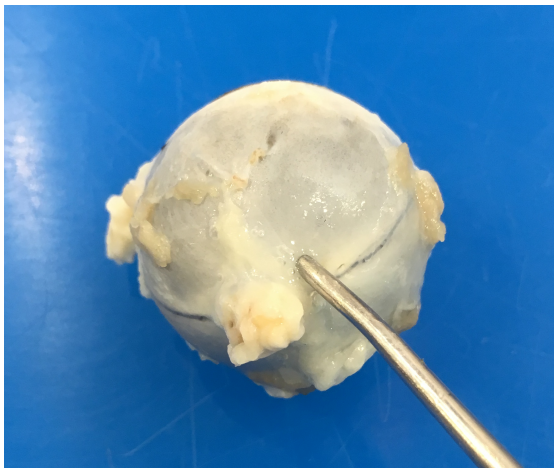

Figure 2: Landmarks for injecting the globe with formalin. The eye is oriented as it would be in a live patient. The probe (representing an ideal location to inject formalin) is at the caudal aspect of the eye, and just slightly dorsal.

amount of formalin into the vitreous of the eye. Use a small gauge needle (25 g or higher), and pierce the globe at an angle. A good place to inject is immediately adjacent to the optic nerve (Figure 2). For small animals, about 0.5 ml of formalin is adequate; for larger animals, up to 1 ml may be required. The globe will fill noticeably taught following the injection.

Always remember to **include a detailed and succinct history**. Many of the eyes that are submitted for pathology are at a similar "end-stage", and determining the underlying etiology is often impossible based on histopathology alone. The more information you provide, the more information the pathologist can then provide back to you. Don't forget to include the duration of the clinical signs, treatments administered, and your differential diagnoses.

2 Pathology of the conjunctiva and eyelids

2.1 Conjunctivitis

A variety of different infectious agents can lead to inflammation of the conjunctiva. Among the most important in a variety of species is *Chlamydophila*. In particular, in the cat, *C. felis* is often associated with a primary conjunctivitis, presenting with mucoid neutrophilic ocular discharge. The condition is dealt with clinically and these globes are rarely progress to the point where they are examined microscopically. Occasionally, conjunctival biopsies may be evaluated.

Figure 3: A dermoid present at the limbus (Image F33854 from Noah's Arkive)

2.2 Dermoid

Dermoids are a form of choristoma: the formation of a normal structure in an abnormal place. In the case of a conjunctival (or corneal) dermoid, there is a nodule of skin present, which may be haired (Figure 3). These lesions are dramatic and odd, but are usually corrected through a keratectomy.

2.3 Meibomian gland adenoma

These are common neoplasms that occur at the eyelid margin, the only place in the body in which Meibomian glands are found. They make up almost 70 % of canine eyelid neoplasms, and are therefore **the most common eyelid neoplasm of the dog**. They are the eyelid equivalent to a cutaneous sebaceous adenoma, and are similarly benign and cured with complete resection. Grossly, they are usually well circumscribed and multilobular. Leakage of gland contents frequently creates a local granulomatous reaction that accompanies the neoplasm, known as a **chalazion**.

2.4 Conjunctival squamous cell carcinoma

Squamous cell carcinomas (SCC) of the conjunctiva or eyelid occur in all species, but are most common and most important in the horse and cow. In fact, SCC and Infectious bovine keratoconjunctivitis are the two most important ocular conditions of cattle. In both horses and cattle, UV light is thought to play a role in the pathogenesis, and those breeds with poorly pigmented skin are at increased risk. These neoplasms are infiltrative and have metastatic potential, though the true metastatic risk is poorly documented, and likely occurs late in disease. There is however a strong possibility that an animal may develop multiple conjunctival SCCs, and whether these separate masses are related is uncertain.

Grossly, conjunctival SCCs are typically raised, tan, and nodular. They are frequently ulcerated, with superifical crusts and hemorrhage. In cattle, they most frequently arise on the bulbar conjunctiva at the limbus, whereas the third eyelid is the most frequently affected in horses. In cats, SCC tends to arise from the skin of the eyelid. For unknown reasons, dogs seem relatively spared from developing SCCs.

2.5 Melanocytic tumours

Melanomas are frequent tumours of the eyelids and conjunctiva, and, in dogs, **prognosis mostly depends on location**. Melanocytic tumours arising at the eyelid margin are benign (like a dermal melanocytoma). Those that arise from the conjunctiva are more invasive and prone to recurrence (somewhat like oral melanomas). Those that arise from the limbus are benign.

2.6 Entropion and ectropion

Entropion refers to the inward folding of the eyelid, and is most common on the upper eyelid. Ectropion refers to an eyelid that turns slightly outward, and is more common in the lower eyelid. These are primarily clinical conditions and the underlying pathology is unremarkable. Both are most commonly seen in dogs, and there are strong breed predilections. Due to mechanical abraision, entropion may result in physical damage to the cornea. The condition is seen routinely and is easily fixed with minor surgery.

3 Pathology of the cornea

3.1 Corneal ulcers

Corneal ulcers - the erosion of the surface epithelium with exposure of the underlying corneal stroma - are **extremely common** and occur for a variety of reasons. A few specific etiologies are dealt with below, however, there are some generalities that can be applied to most corneal ulcers, regardless of cause.

Recall that the corneal stroma is *kept in a dehydrated state*: this is accomplished by having an impermeable epithelial surface, as well as active pumps along the corneal endothelium (explained further Ocular anatomy). Thus, any break to the epithelial barrier will result in **stromal edema** – through the absorption of tear film – that manifests clinically as a blue-ish tinged cloudiness of the cornea. Neutrophils found in the tear film can also enter the stroma through the disrupted barrier.

What happens next is dependent on the degree of corneal injury. If the injury is relatively minor – for example, the erosion of the superficial epithelium and perhaps a small amount of the stroma – then the remaining epithelium can slide over the defect, providing an initial, thin barrier. Mitosis begins within 24 hours so that the epithelium will soon return to its normal thickness. Be aware, however, that for healing to be succesful, **the epithelium must be able to adhere to the underlying stroma**. Some cases of refractory corneal ulcers occur due to the presence of degenerative superficial stroma that fails to provide an adequate foundation onto which the epithelium can anchor. Procedures that remove the uncooperative tissue (e.g. grid keratectomy) allow new granulation to form, thereby providing a scaffold for the epithelium to anchor to.

Deeper wounds – those with more than 1/3 of the stroma affected, give or take – require a bit more investment in healing. Epithelial sliding cannot occur in these cases before the stroma is rebuilt. To rebuild corneal stroma, the keratocytes (fibrocytes of the corneal stroma) undergo fibroblastic differentiation and begin producing ground substance. Fibroblasts and small blood vessels also begin migrating from the limbus, and it is these fibroblasts that are the primary source of collagen. This migration takes time. Approximatley 4 days to get started, then about 1 mm every day thereafter. The new cornea is never quite the same as the original. Over time, the newly deposited collagen will organize to resemble normal stroma, and the tissue will become less cellular, a scar will be detectable. The degree to which a scar affects vision is dependent on the initial insult (Fun fact: I have a scar across my cornea, courtesy of an errant hockey stick. It doesn't obstruct my vision at all). The epithelial component of a larger wound is also different: in large defects, epithelial reserve cells from the limbus are recruited, and these cells have a conjunctival, rather than corneal, phenotype, and may be pigmented, though if the injurius stimulus is removed, these epithelial cells will gradually become more "corneal".

Ulcers that progress may erode through the entire corneal stroma all the way to Descemet's membrane. In these cases, Descemet's membrane may protrude through the corneal defect, creating a small structure known as a Descemetocele. **These cases are clinical emergencies**, as the membrane may rupture at any time, resulting in a full corneal rupture with significant adverse consequences. A ruptured cornea will repair with fibrin, but occasionally the iris may prolapse into the defect, forming an anterior synechia - an irreversible change.

Further complicating matters is whether the injury is sterile or infected. Sterile injuries tend to heal more quickly, while those that are complicated by infectious agents recruit more neutrophils, which induce bystander damage by lysing the corneal stroma (keratomalacia), and may delay healing, or even worse, lead to rapidly progressing corneal damage in the form of a melting ulcer.

3.2 Keratoconjunctivitis sicca

Keratoconjunctivitis sicca (KCS) is a condition in which the cornea desiccates (dries out), usually due to a decreased **quantity** of tear film, and rarely due to an altered quality of tear. The condition is most common in dogs, in which it is progressive and chronic. The etiology is unknown, but the success of immunosuppressive therapy suggests an **autoimmune basis**.

The lesions depend on the degree to which tear film production is affected. Most cases are moderate in onset, and result in chronic injury to the cornea, manifesting as cutaneous metaplasia. As tear film decreases, injury becomes more severe, and corneal ulcers may develop. There is nothing distinctive about these ulcers, with the sole exception that corneal edema may be minimal (as there is no tear film providing water to the cornea).

The condition is readily treated with artificial tears and immunosuppressive therapy.

3.3 Fungal keratitis

Fungal keratitis is a particularly common and important issue in horses. **It is usually iatrogenic**, resulting from the treatment of a routine corneal ulcer with antibiotics, and especially corticosteroids. Colonization of the wound by fungi (usually *Aspergillus*) results in a deep ulcerative keratitis and is accompanied by suppurative keratomalacia that is refractory to treatment with antibiotics. For unknown reasons, the fungi are often found deep in the cornea near Descemet's membrane. This unusual distribution explains why superficial sampling – either corneal scrapes or corneal biopsy – may miss the fungi, and produce false-negative results. Do not be surprised, therefore, when a pathology report from a horse with suspected fungal keratitis informs you that although no organisms were seen, the condition cannot be ruled out!

Figure 4: Herpetic keratitis with dendritic (branching) ulcers. Image from [Sandmeyer et al, 2010](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2885128/)

3.4 Herpesviral keratitis

Feline herpesvirus 1 can cause a keratitis or keratoconjunctivitis. Clinical signs are typically a mucopurulent ocular discharge with conjunctivitis and keratitis (and rhinotracheitis). In younger cats, the disease typically manifests as conjunctivitis without keratitis, whereas in adult cats the opposite is true. In adults, the corneal lesions may present as shallow erosions that appear as very small, multifocal erosions or ulcers that may coalesce and have a branching "dendritic"" appearance (Figure 4). Alternatively, in severe cases usually associated with immunosuppression, a severe keratitis may develop, with notable corneal edema and corneal vascularization.

3.5 Infectious bovine keratoconjunctivitis

Infectious bovine keratoconjunctivitis, also called "pinkeye", is caused by *Moraxella bovis*. **Along with Conjunctival squamous cell carcinoma, it is the most important ocular condition of cattle.**

Cattle are infected by *Moraxella bovis* via fly vectors, and thus the disease is more common during the summer months. Upon infection, the bacteria adhere

and then invade into the corneal epithelium, resulting in a small corneal ulcer accompanied by corneal edema and hyperemia. If left untreated, the ulcer will enlarge, deepen, and become infiltrated by large numbers of neutrophils. Damage from the indiscriminate neutrophils results in keratomalacia. In most cases, healing occurs as the necrotic cornea is shed and granulation tissue fills the wound, eventually scarring over. Despite the often relatively large ulcer found in the acute stages of the condition, the final scar is often small and clinically insignificant.

3.6 Dystrophies and depositions

The accumulation of material within the cornea is relatively frequently seen in clinical practice. It may occur as dystrophies or deposits.

A dystrophy is an inherited, bilateral, defect in structure or function of one of the components of the cornea. It is not triggered by injury or disease, either directly to the eye or elsewhere in the body. The most common, which are seen in dogs, are lipid and crystalline dystrophies. In the case of the former, cholesterol is deposited in the corneal stroma, while in the later mineralization may be present in the superficial corneal stroma.

Corneal deposits typically occur secondarily to metabolic disease or injury. Metabolic deposits include mineral, lipid, or pigment. The most common metabolic deposit, again seen in dogs, takes the form of corneal lipid associated with hyperlipidemia of any cause - though often associated with Cushing's disease, diabetes mellitus, or hypothyroidism.

Corneal deposits secondary to injury are again most common in dogs. Melanin deposits occur in corneas subject to chronic irritation.

4 Pathology of the uvea

Uveitis is commonly encountered, and a good understanding of pathophysiology of the disease will serve you well in practice. Unfortunately, like many other parts of ophthalmology, the terms related to uveitis are confusing, and I suggest you review and then keep the Glossary handy while going through this section.

The uvea represents three structures that compose the vascular supply to the eye: the iris, ciliary body, and choroid (see Figure 1 to refresh your memory). Inflammation of the uveal structures – especially inflammation that is on-going or recurrent – can have a wide range of impacts beyond the uvea itself.

The iris is a relatively porous tissue, and when inflamed, leukocytes, blood and/or fibrin exit vessels and rapidly transit through the iris and into the aqueous. Clinically (or grossly), this manifests as an accumulation of cells and/or protein in the anterior chamber. Hyphema is the presence of hemorrhage within

the anterior chamber, while hypopyon is an accumulation of neutrophils. Aqueous flare is the clinically visualized presence of increased protein in the aqueous humour.

Corneal edema is a reasonably common clinically observed secondary effect of uveitis. It can result from damage to the corneal endothelium, or from a cytokine-mediated increase in vascular permeability in the peripheral limbic vessels.

Fibrin within the anterior chamber may coat the iris, and lead to adherence of the iris to the cornea (anterior synechia) or to the lens (posterior synechia).

A common sequela of inflammation is the development of granulation tissue, and the eye is no exception. In the eye, granulation tissue often forms as a membrane that layers pre-existing ocular structures. Unfortunately for vision, the delicate and carefully organized structures of the eye are frequently altered by these membranes of granulation tissue. The exact consequence of the membrane depends on the location in which it forms: a pre-iridal fibrovascular membrane, for example, forms on the surface of the iris and may a) grow over the iridocorneal angle, leading to glaucoma (see the section on Glaucoma for more details); or it may b) grow over the pupil, leading to complete pupillary block and iris bombe; or it may c) simply cover the iris, and following maturation and contraction, deviate the free edge of the iris forward, leading to ectropion uvea. Alternatively, a membrane developing in the posterior segment over the choroid, known as a cyclitic membrane, may lead to retinal detachment as it matures and contracts (known as tractional retinal detachment).

The lens, too, is susceptible to the secondary effects of uveitis. Cataracts may develop, possibly a result of uveal attachment to its surface (posterior synechia), or an alteration in aqueous flow, or simply by an excess of inflammatory cytokines and by-products appearing in the aqueous. More information can be found in the section on the Pathology of the lens.

There are many causes of uveitis, including a number of infectious organisms that we are not going to cover. Below are some of the more commonly encountered conditions.

4.1 Mycotic endophthalmitis

A variety of different fungal organisms can gain access to the eye. *Blastomyces dermatitis* is the most frequent in dogs, while *Cryptococcus neoformans* is the most common in cats. There is nothing particularly surprising about these agents: they present with a profound, usually pyogranulomatous endophthalmitis that one would expect following a fungal infection. Retinal detachment may result secondary to the accumulation of inflammatory exudates.

4.2 Uveodermatologic syndrome (Vogt-Koyanagi-Harada-like syndrome)

This syndrome is relatively frequently seen in dogs, particularly in arctic-type breeds (Siberian huskies, Alaskan malamutes, Akitas, etc). The root of the condition is an immune-mediated targeting of proteins involved in the production of melanin. The inflammation, **which is granulomatous in nature**, targets the uvea and the skin of the face, though the ocular disease is typically more severe and of more consequence.

Because the inflammation targets the production of melanin, **one of the most notable clinical signs is uveal and dermal depigmentation**. The granulomatous inflammation of the uvea leads to destruction of melanocytes and dispersal of melanin. Inflammation in the choroid tends to be most severe, and can lead to Retinal detachment, PIFM, and glaucoma.

4.3 Canine adenovirus

In North America, canine adenovirus is mostly of historical relevance due to widespread vaccination. In areas with poor vaccination, the ocular manifestation of adenovirus is still significant.

In unvaccinated animals – or, rarely, animals receiving a modified live virus – canine adenovirus infects the uveal and corneal endothelial cells. Damage to uveal endothelium can lead to anterior uveitis, while corneal edema (due to damage to the corneal endothelium) may develop.

4.4 Equine recurrent uveitis

Equine recurrent uveitis (ERU) is **the most common cause of glaucoma, cataracts, and blindness in horses**. Although the condition may start out affecting only one eye, it virtually always ends up being bilateral. As it's name suggests, the disease presents as waxing and waning episodes of uveitis that gradually increase in frequency. The gross/clinical signs of the disease are, like many ocular diseases, a constellation of lesions that require an astute ophthalmological exam. Uveitis, of course, is one of the main features, manifesting as increased proteinaceous content in the anterior chamber ("aqueous flare") and vitreous. Corneal edema is also frequently present. In severe cases, there may be hyphema or hypopyon. In more chronic cases, cataracts, lens luxation, retinal detachment, and glaucoma may all be observed.

Microscopically in the early course of disease, there tends to be neutrophilic inflammation of the iris and ciliary body with fibrin and proteinaceous material found within the anterior chamber. Over a fairly short period of time, the inflammation becomes predominantly lymphoplasmacytic and histiocytic. In

the chronic stages, lymphoplasmacytic inflammation of the entire uvea (panuveitis) dominates, and lymphoid follicles within the iris and ciliary body are characteristic.

The pathogenesis of ERU is still under investigation and is not fully understood. The current favoured theory is that **ERU represents a multifactorial immune-mediated disease**. There is a body of evidence – that is *not* conclusive – that implicates previous exposure or infection to *Leptospira interrogans* serovar *pomona* as an initiating cause. Many cases have been associated with seropositivity for *Leptospira*, and experimental infection can induce the disease; however, **a significant portion of cases are not associated with leptospirosis**, rendering this hypothesis somewhat flawed. Instead, the modern belief is that some initiating cause – at this point, unknown – causes a uveitis that *alters the normal immune privilege status of the eye*. Proteins within the eye that were previously restricted may become accessible to the immune system, and become antigenic stimuli as a result; similarly, antibodies generated through exposure to exogenous sources that may cross-react with ocular antigens may now have access to ocular structures. This breakdown in ocular immune privilege is what may lead to the continuing inflammation within the eye, and regardless of the initial cause, is probably the more important aspect of the disease.

4.5 Feline lymphonodular uveitis

Feline lymphonodular uveitis, also known as feline lymphoplasmacytic uveitis, is the most common cause of uveitis in the cat, and along with Diffuse iris melanoma, is one of the top causes of feline glaucoma. The condition generally starts off unilaterally, however, the contralateral eye is to be considered at risk.

Cats with the condition may present with one or more of the following symptoms: corneal edema with neovascularization; keratitic precipitates (cellular deposits on the corneal endothelium); and/or thickened irides. Eventually, glaucoma may develop, though the mechanism through which this occurs is unknown. Microscopically, the disease is characterized (as expected) by lymphoplasmacytic inflammation of the uvea, particularly within the iris, where lymphoid nodules may develop in severe cases.

The cause of feline lymphondular uveitis is unknown, but the pathogenesis is thought to be similar to ERU.

4.6 Feline infectious peritonitis

As with other locations in the body, feline infectious peritonitis virus can causes a significant vasculitis within the vascular structures of the eye (i.e. the uvea). Pyogranulomatous inflammation, particularly of the anterior uvea, tends to

predominate. Grossly, anterior uveitis, manifesting as aqueous flare, is common. Diagnosis cannot be made on histopathology alone; ancillary diagnostics (e.g. IHC) are required.

4.7 Bovine MCF-associated uveitis

Malignant catarrhal fever virus causes a vasculitis with invasion of the vascular wall by lymphocytes. It is therefore a lymphocytic uveitis. Uveitis and corneal edema are noted grossly, and, when considered with the other gross lesions of MCF, the corneal edema can be particularly useful in helping distinguish between MCF and other mucosal diseases.

4.8 Lens-induced uveitis

(Please refer to the section on the lens for more information on the lens itself).

The lens is an immunologically privileged site, and the proteins that make up the lens fibers are thus not-recognized as self. Exposure of these proteins to the immune system can therefore elicit an immune response, the severity of which depends to some degree on the amount of protein encountered.

4.8.1 Phacolytic uveitis

Phacolytic uveitis refers to a mild to moderate lymphoplasmacytic uveitis resulting from the **leakage of liquefied lens protein through an intact lens capsule**. Liquefaction of lens proteins occurs routinely as cataracts mature; it can be relatively safely assumed that all animals with mature cataract have at least some degree of phacolytic uveitis. This condition cannot be distinguished from other idiopathic anterior uveitis based on histopathology (see Equine recurrent uveitis and Feline lymphonodular uveitis.

4.8.2 Phacoclastic uveitis

In contrast to the relatively mild inflammatory response in a phacolytic uveitis, the inflammation in phacoclastic uveitis is severe, profound, and centered around a **lens material extruded through a ruptured lens capsule**. Rupture of the lens capsule is most often caused by a penetrating foreign object (e.g. a thorn, or, more frequently, the business end of a cat's paw). The type of inflammation is somewhat variable, but in the acute stages is neutrophilic and accompanied by fibrin; in more chronic cases, fibrosis with little inflammation dominates.

Iatrogenic phacoclastic uveitis may occur during cataract surgery, if lens protein is inadvertently left behind.

In rabbits, infection with *Encephalitozoon cuniculi* can lead to a phacoclastic uveitis, presumably through infection derived weakening of the lens capsule. The inflammation is characteristically granulomatous.

4.9 Diffuse iris melanoma

This is an important (and contentious!) condition seen in cats. It is the most common ocular neoplasm of cats. The condition begins as patchy areas of golden brown pigmentation on the anterior surface iris, which progress slowly (over the course of years) to coalesce and gradually expand the iris. The pupil may become irregular. Expansion and invasion into adjacent structures eventually leads to Glaucoma in virtually all cases, but this eventual fate **may take years to occur**. Feline diffuse iris melanomas also have significant metastatic potential. Seeding of the aqueous by neoplastic cells gives them access to outflow and general circulation. The neoplasm may then grow in the lungs, liver, and/or lymph nodes. There is considerable debate regarding the literature and studies on prognosis of cats with diffuse iris melanoma. Some advocate swift enucleation following a diagnosis, arguing that this reduces opportunity for metastasis and thus complications. Others suggest that the metastatic potential is relatively low, and that systemic disease resulting from said metastases is not a guarantee, and thus recommend waiting until complications (i.e. Glaucoma) have occurred prior to enucleation.

4.10 Canine anterior uvea melanocytoma

This is the most frequent ocular tumour of dogs. It presents as an expansile mass originating from the root of the iris that is usually pigmented. Prognosis based on clinical/gross appearance is challenging: a small proportion ($\sim 5\%$) are malignant and have true metastatic potential, but this determination is based on histopathology, and cannot be predicted without a biopsy. However, even those that are histologically benign may represent a significant problem for the globe, as most will grow to occlude the ciliary cleft, leading to Glaucoma.

5 Pathology of the lens

The lens is a disc-like structure suspended by zonules at the posterior aspect of the anterior segment. It is avascular, and relies completely on the diffusion of nutrients from the aqueous humour. It's deceptively simple appearance belies it's important function: the refraction of light onto the retina to provide focus.

The lens is a living tissue, albeit a relatively simple one (See Figure 5). It is enclosed by the lens capsule, which is the basement membrane of the lens epithelial cells that make up the body of the lens. The capsule is *impermeable*

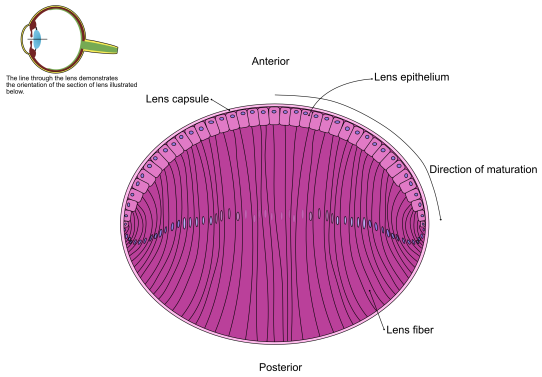

Figure 5: An anterior-posterior illustration of the lens, demonstrating the anterior epithelium, nuclear bow, lens capsule, and lens fibers.

to large proteins, but allows the entry of water and other nutrients, making the lens an immunologically privileged site. The lens epithelium lines the anterior half (and *only* the anterior half) of the lens capsule in a single, cuboidal layer. The lens epithelium is mitotically active, and continually divides to produce additional epithelial cells. These cells migrate centrally and elongate, forming the long fibers that make up the lens. As the epithelial cells differentiate, they lose their nuclei and organelles, forming the clear structure important to its function. Like the cornea, the lens maintains itself in a dehydrated state to help maintain its clarity; this is mediated by an active Na-K pump located on the anterior lens epithelial cells.

The lens survives mainly on glucose delivered by the aqueous humour, which is metabolized via anaerobic glycolysis and the hexokinase pathway to produce energy. This small piece of information is a *critical component to the understanding of the pathophysiology of cataracts.*

5.1 Cataract

A cataract is defined as opacification of the lens. When severe, it is readily diagnosed on histopathology, however, ophthalmological exam is a *far more sensitive and accurate method of diagnosing and describing cataracts.*

The opacification of the lens is the result of alteration of the normally dehydrated lens and its well-organized lens fibers. In response to injury, the lens epithelium may attempt to proliferate, while lens fibers frequently undergo degenerative and hydropic changes. Proliferating epithelial cells may migrate to the normally acellular posterior aspect of the lens, contributing to opacity. The epithelial cells may also become hyperplastic along the anterior edge, and in some cases,

may undergo fibrous metaplasia and produce collagen. Hydropic degeneration of epithelial cells may result in large, rounded cells known as bladder cells. Existing lens fibers may liquefy and fragment, forming characteristic globules of denatured lens proteins known as Morgagnian globules.

With their superior ability to visualize and evaluate cataracts, ophthalmologists are also able to classify cataracts in a variety of different ways, including age of onset (e.g. juvenile vs senile), anatomic location (e.g. subcapsular vs. equatorial), extent (mature vs. hypermature), or pathogenesis. Because this is a course in pathology, and not ophthalmology, we will focus primarily on classifying cataracts according to their pathophysiology, rather than through other metrics.

5.1.1 Inherited

Inherited cataracts are most commonly reported in dogs, and are relatively infrequent in other species. They may be congenital or may appear at any stage in the life of the animal. Diagnosis of an inherited cataract is based on the signalment, paying particular attention to breed predispositions, the age of presentation, and the ophthalmologic type of cataract. Histopathology alone *cannot* distinguish between types of cataracts.

5.1.2 Diabetic cataracts

Diabetic cataracts are one of the most frequently encountered type of cataract seen by practitioners. **They are most common in dogs**.

The pathogenesis of diabetic cataracts relates to the metabolism of glucose. As noted earlier, the lens absorbs glucose from the aqueous humour, and, using the **anaerobic hexokinase pathway**, metabolizes glucose into energy. In diabetic dogs, the concentration of glucose in the blood and aqueous is elevated, and excess glucose enters the lens. The concentration of glucose overwhelms the hexokinase pathway and is shunted into the aldose reductase pathway, which results in the production of **sorbitol**. Sorbitol is too large to exit the lens, and as it accumulates, it causes an increase in the osmotic pressure within the lens, leading to influx of water. The end result is hydropic rupture of lens fibers that manifests clinically as a cataract.

Microscopically, there is nothing distinctive about a diabetic cataract. The diagnosis is based on clinical signs, symptoms, diagnosis of diabetes mellitus, and ophthalmologic type of cataract.

Interestingly, it is not solely an increase in intraocular glucose that leads to cataract. It would appear that there are species differences in the amounts of aldose reductase within the lens, and it is these differences that are thought to

contribute to the frequency of diabetic cataracts in different species. For example, although diabetes mellitus is relatively common in cats, diabetic cataracts are rare, because the concentration of aldose reducates within their lens is low.

5.1.3 Other causes of cataracts

There are several other causes of cataracts. Nutritional cataracts are best described in carnivores that have been fed milk replacer, but the pathogenesis is unclear.

Radiation therapy is a well-known risk factor for the development of cataracts. Cataracts may develop approximately 6-12 months post-therapy, and the risk of development is dependent on the dose received during treatment. The underlying pathogenesis relates to necrosis of the equatorial germinal lens epithelial cells.

Infectious agents may also lead to cataracts. In cattle, infection with bovine viral diarrhea virus (BVDV) *in utero* is associated with cataract development. In fish, infection with the fluke *Diplostomum spathaceum* leads to cataracts.

Finally, luxation of the lens may result in cataract through unknown means, though it is thought that disruption of nutrition is the underlying cause.

5.2 Luxation

Lens luxation (dislocation) may be complete or partial (subluxation). It is a gross or clinical diagnosis: sectioning of the globe for histologic process typically disrupts the normal anatomic position of the lens. A luxated lens may be found partially or completely within the anterior chamber, or it may remain in the posterior chamber. Displacement of the lens into the anterior chamber can disrupt and obstruct the flow of the aqueous, resulting in glaucoma.

Lens luxation may be primary or secondary. Primary lens luxations occur without any known trauma or ocular disease, and may be spontaneous or the result of inherited defects in the zonules.

More common is secondary luxation, or those with a known cause, which may include trauma, weakened zonules due to a greatly expanded glaucomatous globe, or zonules weakened secondarily to uveitis. Note that glaucoma can both cause and be the result of lens luxation, and that it can be difficult to separate cause and effect when presented with a one-time snapshot of the lesions.

5.3 Feline post-traumatic ocular sarcoma

Cats suffering trauma or damage to the lens may present months to years later with a malignant and destructive intraocular neoplasm known as feline post-traumatic ocular sarcoma. Cats typically present with a refractory uveitis,

cataract, and a history of ocular trauma. The neoplasm is thought to arise from malignant transformation of the lens epithelium, possibly mirroring the pathogenesis of post-vaccinal/injection site sarcoma that is occasionally seen in cats.

Grossly, the neoplasm is grey to white and proliferative, often compresses the lens. The mass expands and grows along the circumference of the globe, and is ultimately invasive, frequently infiltrating into the optic nerve or sclera.

6 Pathology of the globe

Although many ocular diseases in reality affect most portions of the globe, in this section we will deal primarily with conditions that have severe consequences to multiple anatomical structures of the eye. The most important condition is glaucoma. The developmental abnormalities discussed below are relatively uncommon, especially when compared to the incidence of glaucoma, which is a **complex, common, and important condition, and one that you should know thoroughly**.

6.1 Glaucoma

Glaucoma is a clinical diagnosis and is by defined by a sustained and damaging increase in intraocular pressure (IOP). Glaucoma has many etiologies, and the effects of increased IOP manifest in just about every structure in the globe. With that in mind, *the impact to the retina and optic nerve are the most important*, as damage to these structures leads to loss of vision and pain.

Glaucoma is most common in dogs, followed by cats and horses. It is the leading cause of enucleation in both dogs and cats.

Intraocular pressure is a balance between the production and drainage of aqueous humour. Aqueous humour is produced by the epithelial lining of the ciliary body and flows into the posterior chamber, where it provides the lens with nutrients and oxygen while removing waste products. From the posterior chamber the aqueous humour flows through the pupil into the anterior chamber, where it provides the same services to the corneal endothelium and stroma. Having served its purpose, the aqueous humour then drains through the trabecular meshwork at the **iridocorneal angle**, located in the anterior chamber at the junction of the cornea and iris. From there, the aqueous humour enters a venous plexus and is returned to systemic circulation.

Although in theory, an increase in intraocular pressure could be due to an increase in production or a decrease in outflow, **glaucoma is *never* due to increased production, and is always the result of decreased outflow**.

The pathological changes to the eye caused by glaucoma can be related to four basic pathophysiologic processes:

1. Direct or indirect physical effects on cells caused by increased IOP.
2. Compression of vasculature from increased IOP leading to hypoxia.
3. Stagnation of the flow aqueous humour.
4. Autotoxicity.

Let's consider each of the structures of the globe and how they may be affected by each process, and what the consequences would be. Remember, though, that it is the **damage to the retina and optic nerve that leads to blindness in these patients**.

Globe:

- Increased IOP may lead to an enlarged globe that protrudes slightly from the orbit (buphthalmos). This change is dependent to a degree on the age and species of the animal; younger animals with more elastic collagen are more likely to experience a stretch in the sclera.

Cornea:

- A buphthalmic globe is susceptible to corneal desiccation and lack of proper protection from the eyelids. This can result in exposure keratitis leading to ulceration or epidermalization.
- The corneal endothelium may be damaged by a) direct pressure; b) lack of proper aqueous flow (remember, the endothelium obtains nutrients, etc, from aqueous); and c) a stretched globe that results in a stretched and permeable endothelial barrier. These changes result in corneal edema.

Uvea:

- Pressure-induced hypoxia to the uvea can lead to atrophy of the uveal tissues, a change more commonly seen in chronic cases.
- The damaged retina may release cytokines leading to a pre-iridial fibrovascular membrane.
- Pressure-induced hypoxia to the vascular endothelium can lead to the leakage of proteins into the aqueous.

Lens:

- The decreased flow of aqueous humour can lead to cataract formation.
- Buphthalmos may cause stretching and tearing of the zonular ligaments and luxation of the lens.

Retina:

- Damage to the retina is most profound on its inner most aspect, affecting the ganglion cells and the nerve fibers that carry sensory information from the retina to the optic nerve. In severe cases, atrophy can affect the entire retina (most often seen in dogs, see the section on retina for more information).
- Although an exact understanding of the pathophysiology of glaucomatous retinal atrophy is incomplete, certain elements are known: a) increased pressure on axons of ganglion cells interferes with axonal transport and contributes to ganglion cell degeneration; and b) severely increased IOP interferes with retinal blood supply, leading to ischemic injury.

Optic nerve:

- Cupping or bowing of the optic disc is characteristic and caused by increased IOP and/or decreased numbers of axons following ganglion cell death.
  - Cupping of the optic disc is a *pathognomonic* lesion: in other words, it is a lesion found uniquely in glaucomatous globes.

Unfortunately, the lesions of glaucoma rarely give us insight into the underlying cause of increased IOP. The etiologies of glaucoma are many and varied, and broadly can be divided into two categories: primary and secondary glaucoma.

6.1.1 Primary glaucoma

Primary glaucomas arise **without significant acquired alteration or disease to other structures of the globe**. Primary glaucomas can be subdivided further into those which show maldevelopment of the trabecular meshwork at the iridocorneal angle, a phenomenon known as **goniodysgenesis**, and those which do not, typically referred to as 'open-angle glaucoma'.

Most dogs with primary glaucoma have goniodysgenesis. Goniodysgenesis is present at birth and is thought to be inherited, yet glaucoma typically only manifests in older dogs (5-12 years old). This finding, combined with the fact that not all dogs with goniodysgenesis will develop glaucoma, suggests that it is not the absence of the trabecular meshwork itself that is the cause of glaucoma, but some other (less well appreciated) alteration – either physical, or, more likely, functional – that leads to increased IOP. Thus, **goniodysgenesis should be regarded as a risk factor, but not a cause, for glaucoma**. A dog that develops primary glaucoma and is observed to have goniodysgenesis is at high risk for developing glaucoma in the other eye.

Primary open-angle glaucoma is uncommon, and is caused by dysfunctional drainage at the iridocorneal angle, rather than abnormal iridocorneal anatomy. It occurs in dogs, horses, and cats.

6.1.2 Secondary glaucoma

Secondary glaucoma, as it's name would suggest, is diagnosed when **acquired** changes to structures of the globe interfere with the drainage of the aqueous humour. If you know and understand the path of aqueous outflow, then it is possible, to some degree, to intuit some of the changes that might impede the flow of the aqueous humor. Some examples include, but are not limited to:

- Infiltration of the drainage angle by inflammatory cells or metastatic neoplastic disease
- The development of a fibrous membrane that spans the iridocorneal angle
- Adhesion between the pupil and the iris (posterior synechia)

6.1.2.1 Pre-iridial fibrovascular membranes (PIFM)

Fibrovascular membranes develop when the concentration of angiogenic factors in the vitreous and aqueous of the eye exceed normal levels. A pre-iridal fibrovascular membrane (PIFM, pronounced "piff-em") is one such membrane that develops on the anterior surface of the iris. Excess angiogenic factors like VEGF are produced in a variety of conditions, including corneal neovascularization (e.g. from an ulcer), inflammation (e.g. chronic uveitis), neoplasia, and retinal hypoxia following retinal detachment.

If a PIFM extends down the iris and across the pectinate ligament and blocks the trabecular meshwork, thus obstructing the passage of aqueous humor, secondary glaucoma is the result. Alternatively, PIFMs can grow towards the lens, and can lead to an adhesion of the iris of the lens (posterior synechia). If the adhesions spans the full 360 degrees of the lens, it can obstruct the flow of aqueous from the posterior chamber, resulting in pupillary block and forward bowing of the iris, known as iris bombe ("bomb-ay"), and glaucoma.

PIFMs are the most common cause of secondary glaucoma in the dog.

6.1.2.2 Cellular infiltration

As is the case with the drain in a sink, small holes can be easily plugged by debris, preventing adequate drainage. In the case of the eye, the trabecular meshwork is particularly susceptible to becoming clogged by cells, typically from neoplasia. Just like the sink, a clogged trabecular meshwork does not drain properly, leading to accumulation of aqueous humour and increased IOP.

In dogs, obstruction of the trabecular meshwork is most commonly obstructed by neoplastic infiltrates, usually Canine anterior uvea melanocytoma.

In cats, Diffuse iris melanoma can directly obstruct the trabecular meshwork and lead to glaucoma, and, along with Feline lymphonodular uveitis, is the main cause of secondary glaucoma in this species.

6.2 Developmental abnormalities

True developmental abnormalities of the globe are rare. They include anophthalmia, or complete absence of the eye (extremely rare and usually bilateral); microphthalmia (a small, disorganized globe present within a normal eye socket); and cyclopia (a single eye that failed to divide) or synophthalmia (a single structure that contains duplicates of multiple portions of the eye).

A coloboma is a hole in one of the structures of the eye. They can occur in the iris, retina, choroid, or optic disc.

7 Pathology of the retina

The retina is a beautifully complex piece of tissue that functions to convert light to the neuronal impulses interpreted by the brain, manifesting as vision. The retina is microscopically composed of 10 layers, each with an important function. The photoreceptors, composed of rods and cones, are the outermost layer, and are the neurons that convert light to electrical impulse. Impulses are then transmitted through various modulatory layers, including the outer and inner nuclear layers, to reach the ganglion cell layer. The axons of the ganglion cell layer travel along the inner most aspect of the retina and exit the eye through the lamina cribrosa, forming the optic nerve.

Understanding the vasculature of the retina is of some importance, and will help the pathogenesis of some of the lesions described below become more intuitive. The retina is supplied by two sources of blood: the choriocapillaris within the choroid, from which the outer most aspect of the retina obtains its requirements by diffusion; and retinal blood vessels found within the inner most aspect of the retina. Because the inner retina has its own blood supply, it is less susceptible to ischemic injury as compared to the outer retina.

Damage to the retina leads to loss or impairment of vision, and is therefore quite important.

7.1 Retinal detachment

Retinal detachment is a common sequela of a number of different conditions, and the immediate consequence is loss of vision. Because the outer most part of the retina obtains its oxygen and nutrients from the choroid, it quickly becomes hypoxic and atrophic when separated and releases angiogenic factors, which can lead to a PIFM.

7.2 Progressive retinal atrophy

Progressive retinal atrophy (PRA) is a term applied to a collection of diseases with a common outcome: photoreceptor degeneration or disorder. These disorders are congenital and/or inherited, are progressive, lack an inflammatory or toxic cause, and may result in blindness. Histopathology is not particularly helpful for determining the underlying etiology in these cases: they all have the same appearance.

7.3 Collie eye anomaly

Collie eye anomaly is an **inherited, congenital, and bilateral condition seen in collies and other breeds**. The condition is a failure of embryonic development of the choroid, tapetum lucidum, and sclera. Choroidal hypoplasia is common, as are colobomas near the optic disc.

7.4 Sudden acquired retinal degeneration

This is a rapidly progressing degeneration of photoreceptors that leads to blindness. It is a bilaterally symmetric disease and typically affects adult and/or older dogs of any breed. Loss of photoreceptors leads to blindness, and eventually the condition proceeds to complete retinal atrophy. In its chronic stages, it is indistinguishable histologically from PRA – thus, clinical progression is likely to be of great help to the pathologist.

7.5 Hypertension

Hypertension induced retinopathy is common in dogs and cats. The small vessels of the choroid are particularly affected, which therefore leads to atrophy of the outer retina, and potentially blindness. Leaky hypertensive vessels may lead to retinal detachment through ischemic necrosis of the retinal pigmented epithelium, which normally provides a barrier against fluid loss from the choroid.

8 Glossary

Anophthalmia The complete absence of a globe.

Anterior synechia Adherence of the iris to the corneal.

Anterior uveitis Inflammation of the iris and ciliary body.

Buphthalmos Enlargement of the globe, often presenting as eyes mildly protruding from the orbit.

Cataract The opacification of the lens.

Choroiditis Inflammation of the choroid.

Coloboma A hole in one of the structures of the eye, typically the iris, but may be present in the retina, choroid, or optic disc.

Conjunctiva The mucous membrane extending from the palpebral margin of the eyelid to the edge of the cornea.

Descemetocele Protrusion of Descemet's membrane through a defect in the corneal stroma, typically the result of a melting ulcer.

Ectropion uvea Abnormal deviation of the iris anteriorly (towards the cornea), often caused by contraction of a pre-iridial fibrovascular membrane.

Endophthalmitis Inflammation of the iris, ciliary body, choroid, anterior and posterior chambers, and/or vitreous.

Entropion uvea Abnormal deviation of the iris posteriorly (towards the lens), often caused by contraction of a posterior iridial fibrovascular membrane.

Globe The eyeball without its appendages.

Hyphema Blood within the anterior chamber.

Hypopyon Pus within the anterior chamber.

Iris bombe Anterior bowing of the iris secondary to increased pressure within the posterior chamber caused by a complete posterior synechia.

Keratitis Inflammation of the cornea.

Keratomalacia Liquefactive necrosis of the corneal stroma.

Limbus The junction of the cornea and the sclera.

Melting ulcer A rapidly progressing ulcer, in which the ulcer deepens, often leading to Descmetocoele.

Microphthalmia A small globe within a normal orbit.

Panophthalmitis Inflammation of the sclera in addition to the same structures as endophthalmitis.

Phthisis bulbi An end-stage globe that is shrunken and disorganized.

Posterior synechia Adherence of the iris to the lens capsule.

Synechia Adherence of the inflamed iris to either the lens or cornea (see anterior and posterior synechia).

Uvea The vascular portion of the eye, composed of the iris, ciliary body, and choroid.

Uveitis Inflammation of the iris, ciliary body, and choroid.

9 Ear

9.1 External ear

9.1.1 Otitis externa

Otitis externa will be one of the most common conditions you encounter in small animal clinical practice, and is most frequently see in dogs. It will no doubt have been covered extensively in classes on dermatology, and will likely have been considered in the sections on dermatopathology as well. It is a complex problem, and one that can be frustrating for both owners and veterinarians alike.

The external ear is essentially a modified extension of the skin, and conditions that affect the skin can equally affect the ear. **Atopy or food allergy are the most common primary causes of otitis externa**. There are many other factors, however, that predispose dogs to otitis externa:

- pendulous ears (e.g. cocker spaniel)
- hairy ear canals (e.g. poodles)
- excess cerumen production (e.g. German shepherds)
- stenotic ear canals (e.g. Shar peis, or as a result of chronic otitis externa)
- ear mites
- aural tumours
- foreign bodies

Grossly, ears with otitis externa are inflammed (as demonstrated by warm, red auricles), and the ear canal often contains abundant discharge, with or without hemorrhage. The ears are frequently quite painful. The environment of the external canal becomes warm and moist, favouring the growth of bacteria normally found on the skin. The inflammation, which in acute cases is predominantly neutrophilic, promotes epidermal and glandular hyperplasia. In chronic cases, macrophages, lymphocytes, and plasma cells tend to dominate, and the hyerplastic changes become more dramatic. In the most severe cases, fibrous connective tissue replaces adnexa, markedly distorting the internal environment of the ear canal. The additional tissue, along with marked epidermal hyperplasia and hyperkeratosis, results in a stenotic ear canal, which in turn limits treatment and resolution of the condition.

Otitis media and Aural hematoma are relatively common complications of otitis externa.

9.1.2 Aural hematoma

The constant head shaking of dogs with Otitis externa can cause small fractures to the auricular cartilage. These fractures may produce sharp edges that lacer-

ate capillaries, leading to hemorrhage that accumulates, presenting as a grossly swollen, warm ear. Left to heal on its own, the ear will fibrose and contract, resulting in a cosmetically damage, but otherwise functional, ear. Dogs presenting with aural hematomas should be checked for Otitis externa.

9.1.3 Parasitic diseases

There are a number of ectoparasites that affect the ears. Of the most important is *Otodectes cynotis*, especially in cats, in which they often cause a secondary otitis externa. Infection with *Otodectes* results in a thick, waxy, brown discharge that obstructs the ear canal. Auricles are often alopecic.

9.1.4 Neoplasia

Unlike the inflammatory conditions of the ear, neoplasms are typically unilateral. Several of the common dermal neoplasms, including histiocytomas, sebaceous gland tumours, mast cell tumours, and plasma cell tumours, can occur in the ear.

9.1.4.1 Squamous cell carcinoma

Squamous cell carcinoma of the ear is an invasive and malignant neoplasm most commonly seen in white cats, and is believed to be the result of UV radiation. They are typically raised, nodular, and ulcerated. Metasasis through vascular or lymphatic invasion is relatively common.

9.1.4.2 Ceruminous gland adenocarcinoma

Cerumins gland adenocarcinomas comprise approximately 2 % of all feline neoplasms, making them an important condition. They are the exception to the rule of unilateral neoplasia: approximately 25 % of cases have a bilateral presenation.

9.2 Middle ear

9.2.1 Otitis media

Otitis media affects all species, but is least common in the cat. It is usually bacterial. Access to the middle ear can be either through rupture of the tympanic membrane or through ascension up the auditory tube.

In **dogs**, otitis media is most frequently due to perforation of the tympanic membrane secondary to otitis externa. Note that the tympanic membrane can

heal very quickly, so the presence of an intact tympanum does not rule out otitis media.

In **cats**, otitis media is usually thought to be the result of migration of bacteria up the auditory tube. It is **not usually associated with otitis externa**.

In **dairy calves**, *Mycoplasma bovis* is frequently found alongside concurrent pneumonia.

In **pigs**, impaired function of the auditory tube can lead to ascension of *Mycoplasma hyorhinis*, *Pasteurella multocida*, or *Truperella pyogenes*.

Otitis media may be unilateral or bilateral. Inflammation is typical, as is exudate within the tympanic bulla, either purulent or caseous. Severe inflammation may lead to lysis of the bony ossicles.

9.2.2 Inflammatory polyps

These are extremely common in cats, and are typically found in *young* animals. They are thought to originate from the middle ear, and can exit either through the external ear ('aural' polyps) or pharynx ('nasopharyngeal' polyps). The clinical signs, and associated pathology, depends to some degree on where they grow.

Polyps are typically composed of fibrous connective tissue with abundant small blood vessels, and are *lined by a ciliated epithelium*. The cell of origin and their pathogenesis remain uncertain, however. It is thought they may be granulation tissue arising from a chronic infection either to the auditory tube or middle ear. Complete removal of polyps is curative; however, if some of the polyp is left behind, it may regrow.

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