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Fundus Examination: An Approach to Examination and Interpretation

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Approaching the Fundic Examination

The goal of thorough fundus examination is to provide clinical evaluation of the structures of the eye's posterior segment. In dogs and cats, these structures include:

1. Optic nerve head (Cranial nerve II)
2. Retina (and retinal pigmented epithelium)
3. Tapetum
4. Vasculature
 - a. Retinal vasculature
 - b. Choroidal vasculature

As with the general physical examination, fundus evaluation is best achieved by assessing each structure in succession. A thorough examination of the fundus can provide valuable clinical information and is an integral part of the general physical examination. In particular, fundus examination should be considered imperative when investigating:

1. Neurologic disease
2. Vascular disease
3. Blindness/visual impairment
4. Systemic disease

The general approach to fundus examination should follow three phases:

1. Pupillary dilation
2. A "wide angle" scan of the fundus
3. A "zoomed" examination of fundic lesions

1. Pupillary dilation

Pupil dilation is required to evaluate the fundus in its entirety and can be easily achieved with topical pharmacologic agents. The most commonly employed agents are parasympatholytic drugs such as tropicamide or atropine. These

drugs paralyze the smooth muscle of the iris sphincter to allow the pupil to expand. Most ophthalmologists prefer to use **tropicamide**, as this drug is shorter acting than atropine, lasting a maximum of 10-12 hours in dogs and cats. One drop of tropicamide should dilate a normal dog eye within 30 minutes and a normal cat eye within 15 minutes. In addition, the degree and rapidity of dilation can be enhanced by application of a second drop of tropicamide 5 minutes after the first. **Atropine**, while equally effective in producing dilation, has effects that can last for up to 3-5 days in dogs and cats. Sympathomimetic agents such as **phenylephrine** produce pupil dilation by stimulating the adrenergic receptors within the iris dilator muscle. While this can be used effectively in dogs to dilate the pupil, it is ineffective in cats. The primary contraindication for pupil dilation is documented predisposition to glaucoma as it can cause collapse of the iridocorneal angle and obstruct aqueous outflow. It is also of note that eyes with active uveitis dilate less readily than those without.

2. A “wide angle” scan of the fundus

The “wide angle” approach to the fundus is best achieved using **indirect ophthalmoscopy**. Using this technique, a convex lens is positioned between the clinician’s eye and the patient’s eye to create an image. Due to optics of the lens, the image produced is **inverted** and **reversed** (i.e. lesions seen in the dorsomedial fundus are actually ventrolateral). While this technique provides images that are low magnification, a larger field of the fundus can be seen with one view, allowing one to scan the structures for abnormalities. With pupil dilation, this technique is the most appropriate for examination of the peripheral fundus.

The basic equipment necessary for indirect ophthalmoscopy consists of:

1. Bright light source
2. Indirect lens or lenses

While a pen light can be sufficient for fundus evaluation, a Finoff transilluminator or otoscopic light will achieve better illumination for examination. Lenses are available in many different “diopter” strengths. The higher the diopter number, the more the lens bends incident light to produce an image. As this number increases, the magnification of the image and the stereopsis (3-dimensional aspect of the image) both *decrease*. However, the field of view and the ability to examine the fundus through a small pupil are both enhanced. This can be particularly useful in smaller patients or those whose pupils cannot be dilated. In general, most clinicians prefer a 20D lens for examining the dog and cat. The Volk PanRetinal 2.2® is an excellent “hybrid” lens as it provides the magnification of a 20D lens, while also providing the field of view of a 30D lens.

3. A “zoomed” examination of fundic lesions

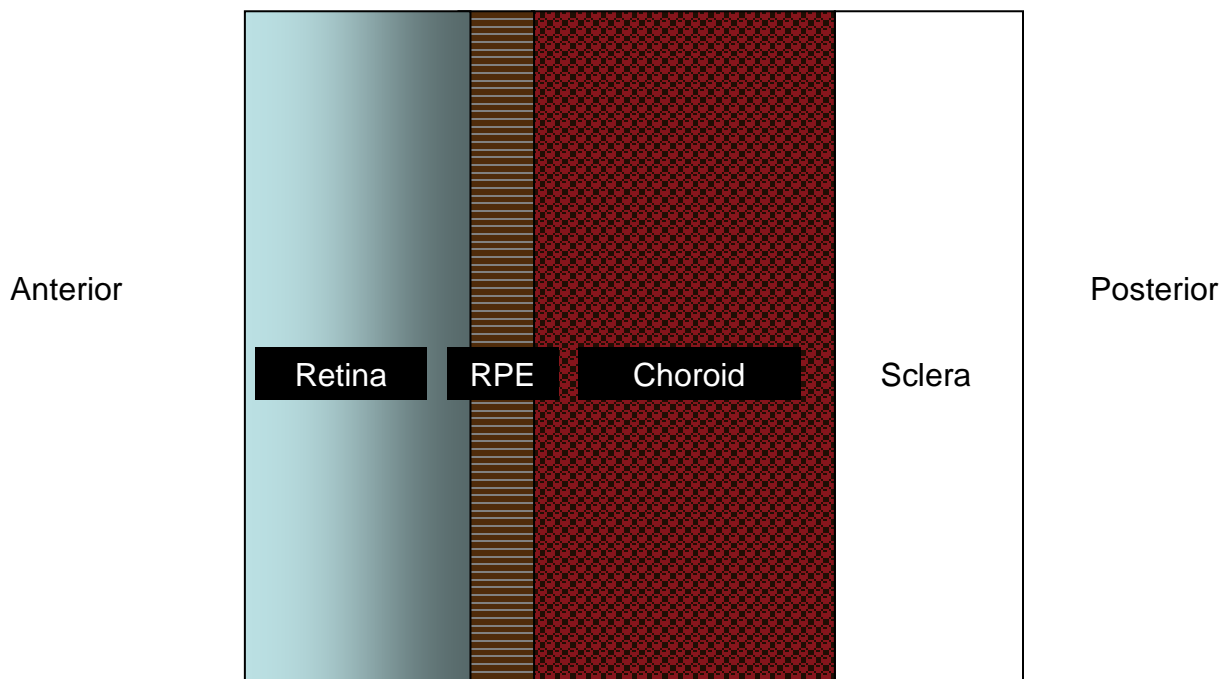
Direct ophthalmoscopy differs from the indirect technique, both in the instrumentation used and the image produced. With direct technique, the image seen is upright. In addition, the magnification is much greater (“**zoomed**”, while the field of view is greatly limited. These features make this technique best-suited to examination of focal areas such as the optic nerve or specific lesions.

Monocular indirect ophthalmoscopy is a technique made possible by newer instrumentation such as the Welch Allyn PanOptic® ophthalmoscope. This produces an upright image of intermediate magnification and field of view to the indirect and direct techniques.

Learning the approach to fundus examination can be different for every clinician, as each will become comfortable with certain equipment and techniques based on their own experience. The techniques of indirect and direct ophthalmoscopy carry their own advantages and disadvantages, but when used in tandem, can provide a comprehensive means of evaluation.

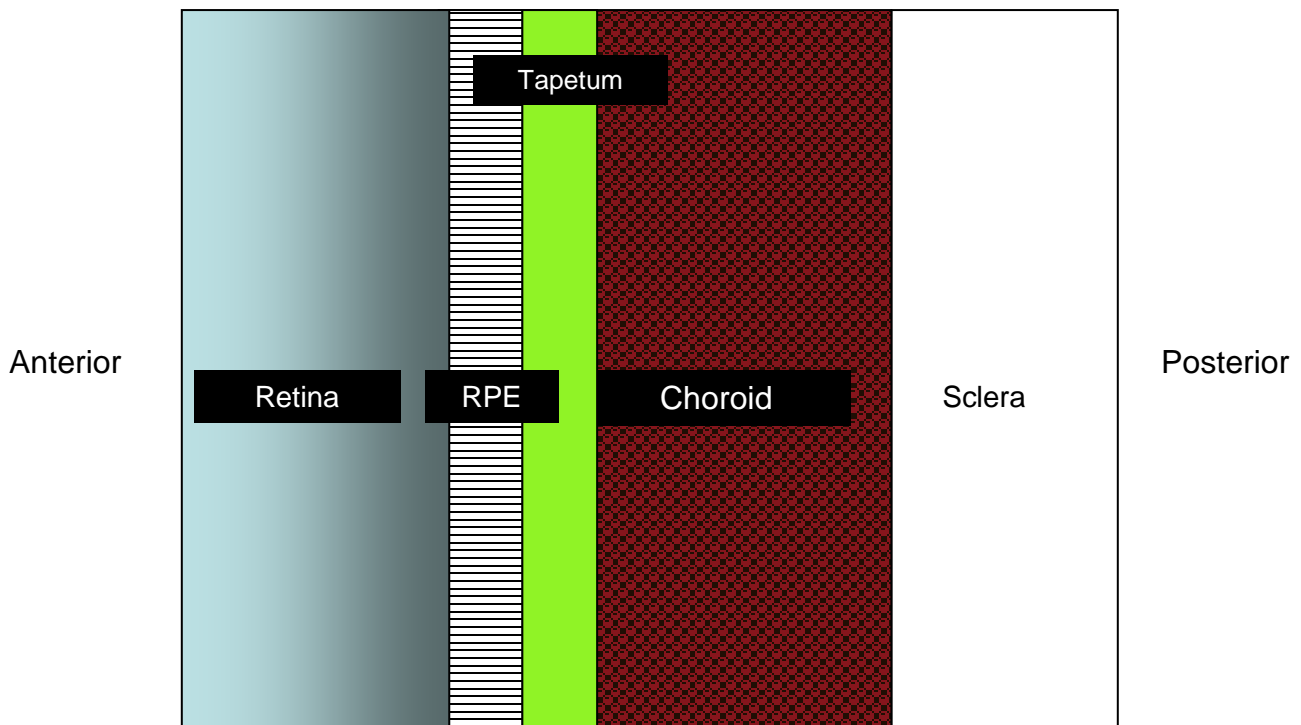
The Fundus – What Am I Seeing?

When examining the fundus, it is important to remember that the image you observe is a composite of a number of layers. Understanding these layers and their anatomy is a key aspect of fundus interpretation. In general, the fundus in dogs and cats can be divided into two regions; the **non-tapetal** fundus and the **tapetal** fundus.



When observing the **non-tapetal fundus**, the optic disk and retinal blood vessels can be seen as the most anterior structures (i.e. closest to the observer). Unless pathology is present, the neurosensory retina is transparent, exposing the brown melanin of the retinal pigmented epithelium. If dense enough, this melanin will obscure the deeper layers, namely the vascular choroid and sclera.

In the **tapetal fundus**, the choroid is modified to contain a highly-reflective anterior cellular layer, the tapetum. This layer is believed to act as a reflecting surface to enhance light stimulation of the retina. As a result, the retinal epithelium in this layer, while continuous with its pigmented counterpart, is void of melanin.



Exposure of the different layers may differ between individual dogs and can be considered a normal finding. For example, some small-breed dogs (Pugs, Chihuahuas) may have tapeta that occupy a smaller area of the fundus, with an expanded non-tapetal area. Merle-coated dogs such as Australian shepherds may have little to no pigment within their retinal epithelium, revealing the underlying choroidal vessels, seen as broad “tiger-stripe” striations. These dogs may also have little to no tapetum. Exposure of the sclera may also be seen in disease states, such as the choroidal hypoplasia characteristic of collie eye anomaly.

Lesions overlying the tapetum may be described as hyperreflective or hyporefective. **Hyperreflective** lesions are so-named due to pathologic thinning of the retina and retinal epithelium and exposure the underlying tapetum,

revealing its iridescent surface. In most cases, hyperreflective lesions are representative of a disease process that is inactive or static, such as a previous inflammatory insult (retinitis/chorioretinitis) or dysplasia of the retina.

Hyporefective represent relative obscuring of the tapetum, usually due to intraretinal or subretinal infiltration of edema, leukocytes, granulomatous inflammation, or hemorrhage. These lesions are representative of an active disease process, very commonly associated with ocular manifestation of systemic disease.

A Focus on Four Distinct Diseases of the Retina

Ivermectin Retinopathy

Ivermectin toxicosis is a well-described syndrome in dogs, most commonly characterized by profound neurologic signs such as ataxia, blindness, obtundation, and death in severe cases. Dogs possessing the MDR-1 gene are particularly at risk as they lack a normal p-glycoprotein-mediated drug removal mechanism at the level of the blood-brain barrier.

Recently, retinal toxicosis has been reported and described in two dogs. Interestingly, neither of these dogs were genetic carriers of the MDR-1 gene. One dog had been receiving oral ivermectin for treatment of demodectic mange. The owners had failed to shake the bottle before each administration, leaving cumulatively higher concentrations of the drug in the bottle after each dose. The other dog was a known “scavenger”, living on a horse farm. Prior to this dog’s presentation, the farm’s horses had been routinely dewormed with ivermectin.

Dogs with ivermectin retinopathy present with acute blindness and mydriasis. Fundus examination reveals multiple linear to curvilinear “worm-like” lesions both within the tapetal and non-tapetal regions. The lesions are representative of subretinal edema and therefore are dark and hyporefective when viewed over the tapetum. In the non-tapetal region, they are seen as gray-white lesions over the melanotic background.

The mechanism by which the lesions develop has not been identified, but it is believed that the excessive GABA-ergic stimulation produces an inflammatory or vascular response. Electroretinogram (ERG) has also confirmed complete extinguishment of retinal function, indicating that the blindness is at least partially explained by direct retinal toxicity of the drug.

In this small case series, both cases recovered vision with supportive care. Return to functional vision was also accompanied by return to normal electroretinographic activity.

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Kenny PJ, Vernau KM, Puschner B, and Maggs DJ. Retinopathy associated with ivermectin toxicosis in two dogs. JAVMA 2008;233:279-284

Feline Central Retinal Degeneration

Taurine is an essential amino acid in cats. Highest tissue levels are generally found in the cardiac muscle and retina, particularly within the retinal photoreceptors (rods and cones).

A syndrome termed feline central retinal degeneration (FCRD) is associated with dietary deficiency of taurine in cats. The pathognomonic fundus appearance is a “cigar-shaped” hyperreflective lesion adjacent to the optic nerve head. This location corresponds to the **area centralis**, the area of highest visual acuity in the feline retina. The corresponding histopathologic lesion is focal retinal degeneration, particularly of the cone cells. A subsequent histologic study has revealed that the photoreceptor degeneration is present even over a more diffuse area than the visible lesion.

While electroretinographic studies reveal impaired retinal function with this lesion, many cats do not demonstrate overt visual impairment. For this reason, this lesion is often an incidental finding. With continued deficiency, however, the disease can progress to complete retinal degeneration and blindness. Recognition of the lesion should prompt a detailed systemic and dietary history as well as cardiac evaluation. Serum taurine levels can be measured and dietary taurine levels of 500 to 750 ppm are considered the minimum to prevent retinal disease.

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Bellhorn et al. Feline central retinal degeneration. Invest Ophthalmol 1974;13:608-16.

Leon et al. Lesion topography and new histological features in feline taurine deficiency retinopathy. Exp Eye Res 1995;61:731-41

Fluoroquinolone-Induced Retinal Degeneration

Enrofloxacin, like other fluoroquinolones, exerts its antimicrobial effect via dose-dependent pharmacokinetics. For this reason, once-daily dosing came into favor in the late 1990's. Subsequently, veterinarians began to recognize occasional cases of acute and often complete retinal degeneration and blindness in cats receiving enrofloxacin. The onset of vision impairment can range from 2 days to 12 weeks after administration of the antibiotic. Fundic changes such as tapetal hyperreflectivity and retinal vessel attenuation have been reported even after one dose. Histopathologic investigations have confirmed severe toxicity to the photoreceptors (rods and cones) of the retina. In most cases, the retinal

degeneration that results is permanent and blindness may therefore be irreversible in severe cases.

Though the toxicity affects approximately 0.0008% of treated cats, several risk factors have been identified. These include:

1. Increasing age
2. Impaired renal and hepatic function
3. Dose (> 5mg/kg/day)
4. Duration of drug administration
5. Intravenous administration

The current recommendation for administration in cats is a dosing regimen of 2.5 mg/kg PO BID.

The toxic potential of other fluoroquinolones has been evaluated in two experimental studies. Cats receiving high oral doses of orbifloxacin subsequently developed areas of tapetal hyperreflectivity, suggesting a dose-dependent toxicity similar to that of enrofloxacin. A similar study was performed with oral marbofloxacin, however no toxicity was noted.

REFERENCES:

Wiebe V and Hamilton P. Fluoroquinolone-induced retinal degeneration in cats. JAVMA 2002;221:1568-71

Gelatt KN et al. Enrofloxacin-associated retinal degeneration in cats. Vet Ophthalmol 2001;4:99-106

Progressive Retinal Atrophy

Progressive retinal atrophy (PRA) is an “umbrella” term for a long list of inherited retinal degenerations affecting both dogs and cats. These retinopathies are often breed-related and differ considerably in their age of onset, progression, and clinical/fundusoscopic appearance. Thus far, all degenerations termed PRA are irreversible and no treatment has been shown to halt or slow the progression of vision loss. Investigators are researching clinical utility of gene therapy and retinal transplantation to treat PRA.

As there is no treatment, early diagnosis and elimination of affected dogs and cats from breeding lines is the key factor in control of the disease. This presents an inherent challenge, however, since many young animals are behaviorally normal until beyond normal breeding age. In recent years, however, candidate gene analysis has permitted the identification of the genetic mutation for more than a dozen forms of PRA. From this knowledge, a company called Optigen® (www.optigen.com) has developed DNA-based assays for these diseases. In general, sampling for these tests is as simple as collection of a buccal swab or a

routine blood sample. There are some disadvantages, however, to these tests. For example, in some breeds, more than one mutation can be responsible for PRA and therefore, a DNA test would only identify a proportion of affected animals. Also, some tests are based upon linkage markers, localizing a mutation to a *region* of a chromosome rather than a definitive location. Chromosomal recombination during the normal process of cellular meiosis can alter these sequences “linked” to the gene, resulting in a false negative.

Ultimately, the success of DNA testing for elimination of these diseases will be highly dependent upon proper identification of affected animals and the cooperation of responsible breeders.

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Bennicelli et al. Reversal of blindness in animal models of leber congenital amaurosis using optimized AAV2-mediated gene transfer. Mol Ther 2008;16:458-65.